PHARMAC
Pharmaceutical Management Agency

MEMORANDUM FOR BOARD MEETING 8 JUNE 2016

To: PHARMAC Directors

From: Chief Executive

Date: June 2016

Proposal to list ledipasvir with sofosbuvir (Harvoni), paritaprevir with ritonavir and ombitasvir with dasabuvir (Viekira Pak), and paritaprevir with ritonavir and ombitasvir with dasabuvir with ribavirin (Viekira Pak-RBV) for the treatment of chronic hepatitis C

Recommendations

It is recommended that having regard to the decision criteria set out in Section 2 2 of PHARMAC's Operating Policies and Procedures you:

resolve to approve the resolutions outlined in Appendix One of this Board paper;

resolve to approve the 22 April 2016 agreement with Gilead;

resolve to approve the 20th April 2016 agreement with AbbVie Ltd subject to an amendment to apply a prescriber restriction to the listing from 1 July 2016 to 1 October 2016; and

resolve that the consultation on this proposal was appropriate, and no further consultation is required.

Harvoni Proposal

SUMMARY OF PHARMACEUTICAL			
Brand Name	Harvoni	**Chemical Name**	Ledipasvir with sofosbuvir
Indications	Chronic hepatitis C with/without ribavirin	**Presentation**	Tablet with 90 mg of ledipasvir and 400 mg of sofosbuvir, 28 tablet pack
Therapeutic Group	Infections agents for systemic use, Antivirals, Hepatitis C agents	**Dosage**	One tablet once daily, taken orally with or without food
Supplier	Gilead Sciences	**Application Date**	February 2015
MOH Restrictions	Prescription medicine	**Proposal type**	New Listing
Current Subsidy	N/A		
Proposed Subsidy	$24,363 46 per 28 tablets	**Manufacturer's Surcharge**	Nil
Proposed Restriction	Special Authority		
OP	No	**Section F**	No

Market data	**Year ending**	**30 Jun 2017**	**30 Jun 2018**	**30 Jun 2019**
Number of patients		150	250	224
Number of Maori or PI people		31	52	47
Combined Pharmaceuticals	Subsidy (gross)	Withheld	Withheld	Withheld
	Net cost to Schedule	Withheld	Withheld	Withheld
	Net present value	Withheld		
	Net distribution costs	$0	$0	$0
	Net cost to DHBs	Withheld	Withheld	Withheld
	Net present value	Withheld		
Other DHB costs	Net cost to DHBs	($100,000)	($450,000)	($430,000)
Total	Total cost to DHBs	Withheld	Withheld	Withheld
	Net present value	Withheld		

1 Notes:
2. Subsidy (gross) = forecast of spending on Harvoni at the proposed subsidy.
3. Net cost to Schedule = forecast of change in total spending on pharmaceuticals listed on the Schedule compared with status quo.
4. Net cost to DHBs = Net cost to the Schedule plus any additional costs/savings the pharmaceutical is expected to generate in other health budgets – 3 additional GP visits per patient on treatment for monitoring.
5. All costs are expressed ex manufacturer, excluding GST.
6. NPV is calculated over 5 years using an annual discount rate of 8%.
7 The proposal is expected to minimally affect DHBs income from patient co-payments and not affect distribution costs met by the DHBs
8. Calculations in A913360

Viekira Pak Proposal

SUMMARY OF PHARMACEUTICAL			
Brand Name	Viekira Pak	**Chemical Name**	Paritaprevir/ritonavir, ombitasvir, dasabuvir +/ ribavirin
Indications	Genotype 1 chronic hepatitis C infection	**Presentation**	Film coated immediate release tablets. Each daily dose pack contains: 2 x 75 mg paritaprevir/ 50 mg ritonavir/ 12.5 mg ombitasvir tablets and 2 x 250 mg dasabuvir tablets +/- 1 ribavirin (dose adjusted to body weight)
Therapeutic Group	Infections – Agents for Systemic Use; Antivirals; Hepatitis C Treatment	**Dosage**	2 tablets paritaprevir/ritonavir, ombitasvir once daily (am) with food plus dasabuvir 1 tablet twice daily with food
Supplier	AbbVie	**Application Date**	May 2015
MOH Restrictions	Prescription medicine	**Proposal type**	New Listing
Current Subsidy	N/A		
Proposed Subsidy	Withheld under section 9(2) Withheld under section Withheld under Withheld under Withheld	**Manufacturer's Surcharge**	Nil
Proposed Restriction			
OP	No	**Section F**	No

Market data	Year ending	30 Jun 2017	30 Jun 2018	30 Jun 2019
Number of patients		3,000	4,000	4,000
Number of Maori or PI people		627	836	836
Combined Pharmaceuticals	Subsidy (gross)	Withheld under	Withheld under	Withheld under
	Net cost to Schedule	Withheld	Withheld	Withheld
	Net present value	Withheld		
	Net distribution costs	$0	$0	$0
	Net cost to DHBs	Withheld	Withheld	Withheld
	Net present value	Withheld		
Other DHB costs	Net cost to DHBs	$660,000	($1,010,000)	($3,800,000)
Total	Total cost to DHBs	Withheld	Withheld	Withheld
	Net present value	Withheld		

1. Notes:
2 Subsidy (gross) = forecast of spending on Viekira Pak/ Viekira Pak-RBV at the proposed subsidy
3. Net cost to Schedule = forecast of change in total spending on pharmaceuticals listed on the Schedule compared with status quo.
4. Net cost to DHBs = Net cost to the Schedule plus any additional costs/savings the pharmaceutical is expected to generate in other health budgets – 3 additional GP visits per patient on treatment for monitoring
5 All costs are expressed ex manufacturer, excluding GST
6. NPV is calculated over 5 years using an annual discount rate of 8%.
7. The proposal is expected to minimally affect DHBs income from patient co-payments and not affect distribution costs met by the DHBs.
8 Calculations in A913360

Combined Proposals

SUMMARY OF PROPOSAL				
Market data	**Year ending**	**30 Jun 2017**	**30 Jun 2018**	**30 Jun 2019**
	Number of patients	3,295	4,491	4,441
	Number of Maori or PI people	689	939	928
Combined Pharmaceuticals	Subsidy (gross)	Withheld under	Withheld under	Withheld under
	Net cost to Schedule	Withheld	Withheld	Withheld
	Net present value	Withheld under		
	Net distribution costs	Withheld	Withheld	Withheld
	Net cost to DHBs	Withheld	Withheld	Withheld
	Net present value	Withheld under		
Other DHB costs	Net cost to DHBs	$560,000	($1,460,000)	($4,230,000)
Total	Total cost to DHBs	Withheld	Withheld	Withheld
	Net present value	Withheld		

Executive Summary

- The proposal involves the funding of two new hepatitis C treatments:
    - Ledipasvir with sofosbuvir (brand name Harvoni), supplied by Gilead Sciences (NZ) Ltd, subject to restrictions administered via a panel
    - Paritaprevir and ritonavir and ombitasvir with dasabuvir (Viekira Pak), and paritaprevir and ritonavir and ombitasvir with dasabuvir with ribavirin (brand name Viekira Pak RBV), supplied by AbbVie Ltd subject to prescriber restrictions for 3 months and then open listed.
- We are presenting the two provisional agreements for hepatitis C treatments as one funding proposal because we consider that the products treat the same disease in similar ways. While it would be possible to amend the proposal to enable the listing of only one of the hepatitis C treatments, we consider that listing both treatments at the same time would offer the best possible health outcomes from within the available funding.
- Current treatments for chronic hepatitis C include boceprevir, pegylated interferon and ribavirin. These treatments are associated with poor success rates when compared to the proposed new treatments In addition, as well as being contraindicated in a substantial number of patients, side effects are experienced by up to 80% of patients. In some cases, this results in treatment having to stop.
- The cost of distributing the proposed new treatments through a standard pharmacy chain would result in a cost of Withhel (5yr NPV) for the DHBs, which is one reason why the proposal is to implement direct distribution
- The proposal is expected to have a combined cost effectiveness (for both Harvoni & Viekira Pak) of approximately With QALYs/$1m (Withheld per QALY)
- The proposal, if approved, would be a cost to the CPB of approximately Withheld under section over 5 years (NPV, 8%); there would be no pharmaceutical costs to DHB hospitals as a result of this proposal. Conversely, in the long run, reduced attendances in hospitals for management of clinical consequences of infection would be a significant saving.

Harvoni

- Harvoni may be used in hepatitis C patients of all genotypes. The clinical advice we have received indicates that more than 90% of people who take these treatments for their chronic hepatitis C will be free of the virus 12 weeks after their treatment has stopped.
- We anticipate that Harvoni would with proposed criteria potentially provide a cure for hepatitis C for up to 150 people per annum who are most severely clinically affected by their disease
- The cost effectiveness of this listing is expected to be Wit QALYs/$1m.
- The proposal would be a cost to the CPB of approximately Withheld under section over 5 years (NPV, 8%), and Withheld under section to DHBs overall.

Viekira Pak/ Viekira Pak-RBV

- Viekira Pak and Viekira Pak RBV are only indicated for patients with chronic hepatitis C genotype 1 (57% of the patient cohort in New Zealand) The clinical advice we have received indicates that more than 90% of people who take these treatments for their chronic hepatitis C will be free of the virus 12 weeks after their treatment has stopped.
- A number of concerns, regarding Viekira Pak/Viekira Pak RBV were raised during consultation about primary care needing extra time to adjust to a large scale programme prescribe this treatment To address these concerns we are proposing that, from 1 July 2016 to 1 October 2016 a prescriber restriction would be in place requiring the prescriber to either be an infectious diseases specialist (ID), a gastroenterologist or a hepatologist After 1 October 2016, it is proposed that this requirement be lifted and Viekira Pak/ Viekira Pak-RBV, such that would be listed without any restrictions.
- We anticipate that Viekira Pak/ Viekira Pak-RBV would allow access and potential cure for hepatitis C for people with chronic hepatitis C genotype 1 who are not contraindicated to treatment Staff note there are approximately 11,000 people diagnosed in New Zealand who are in this situation. This is approximately 57% of the population of people in New Zealand who have been diagnosed with chronic hepatitis C In addition there are estimated to be 17,100 people with Hepatitis C genotype 1 currently undiagnosed.
- This proposal is expected to be cost saving in terms of cost effectiveness, due to the substantial offsets from reduced treatment for the clinical consequences of hepatitis C for patients in future.
- The proposal, if approved, would be a cost to the CPB of approximately Withheld under section 9(2)(b) over 5 years (NPV 8%) to the CPB and Withheld under section 9(2)(b) to DHBs overall

Why Proposal Not Decided Under Delegated Authority

The proposal outlined in this Board paper has not been dealt with by the Chief Executive under delegated authority because:

- The estimated Financial Impact (NPV) of this proposal is more than $10,000,000 of the Pharmaceutical Budget. The Financial Impact (NPV) is calculated on the basis of the net present value of the proposed subsidy (ex manufacturer exclusive of GST) over 5 years at a discount rate of 8% to be paid by the funder for the product(s) and the forecast demand, taking into account any effect of the change /decision on that demand, versus the status quo;
- At its April 2016 meeting, the PHARMAC Board directed staff to consult on both Abbvie and Gilead proposals for hepatitis C treatments and indicated it wished to review this funding proposal at a future meeting.

Hepatitis C Treatments

Ledipasvir/sofosbuvir (Harvoni) proposal

Harvoni would be listed in Section B, and in Part II of the Section H of the Pharmaceutical Schedule, at a price of $24,363 46 per 28 capsules from 1 July 2015

A confidential rebate would apply to Harvoni which would reduce the net price to Withheld per pack of 28 tablets, and Harvoni would have subsidy and delisting protection until 1 July 2019

Harvoni would be listed subject to access criteria, detailed in the resolutions in Appendix 1. We note that the provisional agreement requires that the access criteria that would apply to Harvoni would be determined by PHARMAC in its absolute discretion. Eligibility would be assessed via application to a Hepatitis C Treatment Panel (HepCTP), to be established by PHARMAC

A distribution arrangement would be in place and managed by PHARMAC that would mean that Harvoni is distributed outside of the standard pharmacy chain Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j) Withheld under section 9(2)(b)(ii) and 9(2)(j) Withheld under section 9(2)(b)(ii) and 9(2)(j) Withheld under section 9(2)(b)(ii) and 9(2)(j) Withheld under section 9(2)(b)(ii) and 9(2)(j)

Harvoni is an oral capsule that usually requires administration in combination with another tablet, ribavirin Ribavirin is already funded for patients who meet certain Special Authority requirements, and it is proposed that ribavirin be direct distributed to patients who need it along with Harvoni.

Paritaprevir and ritonavir and ombitasvir with dasabuvir (Viekira Pak) proposal

Viekira Pak (paritaprevir (75 mg)/ritonavir (50 mg) /ombitasvir (12.5 mg) (56 tablets) with dasabuvir (250 mg) (56 tablets)) and Viekira Pak RBV (paritaprevir (75 mg)/ritonavir (50 mg) /ombitasvir (12.5 mg) (56 tablets) with dasabuvir (250 mg) (56 tablets) with ribavirin (200 mg) (168 tablets) would be listed in Section B, and in Part II of Section H of Pharmaceutical Schedule, at a price of $16,500 per pack from 1 July 2017

Viekira Pak and Viekira Pak RBV would have subsidy and delisting protection until 1 July 2019.

A confidential pricing arrangement would apply to Viekira Pak/Viekira Pak RBV. Withh Withheld under section 9(2)(ba)(i), and 9(2)(i) Withheld under section 9(2)(ba)(i), and 9(2)(i)

A distribution arrangement would be in place and managed by AbbVie that would mean that Viekira Pak and Viekira Pak RBV would be distributed outside of the standard pharmacy chain. Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j) Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j) Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)

No clinical access criteria would apply to Viekira Pak/Viekira Pak RBV however it is proposed that, from 1 July 2016 to 1 October 2016, a prescriber restriction would be in place requiring the prescriber to either be an infectious diseases specialist, a gastroenterologist or a

hepatologist. After 1 October 2016, we propose that this requirement is lifted and thereafter no restrictions would apply to the funding of Viekira Pak/ Viekira Pak RBV

.We note that the provisional agreement, and subsequent consultation, is for unrestricted listing; however, after carefully considering the feedback from consultation we recommend that a prescriber restriction be put in place for the first three months to ensure that the sector has adequate time for preparation and education around prescribing hepatitis C treatments.

PHARMAC staff can make the provisional agreements available to any Board member who wishes to review them in detail.

Applications, distribution and administration

It is proposed that these treatments be managed via direct distribution as the cost of managing Harvoni and Viekira Pak/Viekira Pak RBV through a standard pharmacy chain would result in a cost of Withheld (5yr NPV) for the DHBs. Additionally, the very high pack price is likely to create cashflow issues for pharmacy, and the Australian experience has demonstrated the impact of this

Ledipasvir/sofosbuvir (Harvoni) proposal

Clinical criteria would have to be met in order to receive subsidised Harvoni. It is proposed that a new panel, the Hepatitis C Treatments Panel (HepCTP) would be established The panel's role is to assess whether a patient meets the access criteria and is eligible for funding. PHARMAC staff recommend that a panel is established, rather than Harvoni being administered via a Special Authority as the potential fiscal risk associated with patients accessing treatment who do not meet criteria is substantial. Although staff have done their utmost to negotiate a lower price, the high price of Harvoni means that we will have to target treatment Oversight by a panel will allow us to target treatment and assess each individual application. Administration via Special Authority introduces some risk of additional patients accessing treatment who are not part of the target group Should this happen, even a small variation in the number of patients could undermine our ability to fund other treatments. We acknowledge the clinician burden associated with such an approach, but consider this is necessary

Noting this risk, PHARMAC staff propose that access to subsidised Harvoni should be for those patients who have a MELD score of 15 or greater A MELD score is a liver assessment tool that is used to categorise the degree of liver impairment that is present. The use of this assessment tool again would assist in targeting treatment to those patients at highest clinical need

The administration of the HepCTP would require a co coordinator and staff resource PHARMAC staff consider this approach is appropriate to ensure appropriate eligibility It is considered likely that the HepCTP would remain in place until the fiscal risk associated with treatment is negated through future commercial activity. Staff consider this likely to happen in 2018/2019 when increased competition in this market, along with the removal of subsidy and delisting protection for Harvoni, is expected. PHARMAC staff note that a number of senior clinicians who are key specialists in Hepatitis C treatment have agreed to participate in the HepCTP.

It is proposed that applications could be made by any relevant practitioner, to ensure that patients living in remote areas, are not disadvantaged due to lack of access to a specialist. However, PHARMAC staff note that, as the funding criteria identifies those patients with end

stage liver disease, it is likely that applications will only be received from specialists, or from other practitioners under the guidance of a specialist No issues were raised in consultation to suggest that allowing applications from relevant practitioners for Harvoni would be clinically inappropriate. However a requirement for prescriber education in relation to the access criteria was raised in consultation and has been addressed as part of the implementation plan.
It is proposed Harvoni be listed as XPharm and that a direct distribution mechanism be used to dispense and distribute it PHARMAC staff are negotiating with our current vaccine distributor to amend our service agreement to include the dispensing and distribution of both Harvoni and ribavirin. The distributor will sub contract with a single pharmacy for all dispensing and has confirmed that the cost for storage, insurance, repacking and dispensing of this additional product would be Withheld under section per annum.

Harvoni is an oral capsule that usually requires administration in combination with another tablet, ribavirin. Ribavirin is currently subsidised for patients who meet the Special Authority requirements It is supplied under an agreement with Roche Pharmaceuticals in the form of a combination pack with pegylated interferon. It is proposed that ribavirin should also be provided to patients who qualify for funding with Harvoni. The reason for this is that the cost of ribavirin is negligible for the treatment duration when compared to the cost of Harvoni and, , without the co administration of ribavirin, the required treatment duration for Harvoni increases from 12 to 24 weeks. This would result in a total cost of Harvoni treatment of Withheld (with ribavirin) and Withheld (without ribavirin). We note that a proportion of patients would be eligible for access to funded ribavirin via the Special Authority.

If the proposal that ribavirin also be distributed with Harvoni where prescribed is approved, staff plan for PHARMAC to purchase approximately 1 years' stock of the combination pack directly from Roche Pharmaceuticals and store this at the distributors. The distributor has a licence to repackage and will remove the unrequired pegylated interferon and dispose of this safely. It would then be stored at the distributors until required. When required, the ribavirin would be sent to the pharmacy along with the Harvoni for dispensing. This approach is recommended by staff as it allows both medicines to be dispensed together which means the patient would not have to go to both a pharmacy to collect a prescription for ribavirin (which could be confusingly dispensed along with pegylated interferon) and receive Harvoni via a direct distribution mechanism. Ribavirin as a single pharmaceutical is not currently available to us, but we are in discussions with a supplier in an attempt to achieve this.

Paritaprevir and ritonavir and ombitasvir with dasabuvir (Viekira Pak) proposal

It is proposed that Viekira Pak/ Viekira Pak-RBV be listed from 1 July 2016 with a prescriber restriction limiting access to ID specialists, gastroenterologists and hepatologists. It is proposed that from 1 October 2016, this requirement be lifted and all relevant prescribers would be eligible to prescribe Viekira Pak/ Viekira Pak-RBV. This is a change from consultation where we proposed that no funding nor prescriber restrictions be in place from a listing date of 1 July 2016

Concerns were raised in consultation by a number of different parties including MoH, specialists and GPs in relation to the support required to prescribe these treatments and GP readiness for this. It is pertinent to note that the proposal to allow GPs to prescribe was met with a lot of support, with many observing that it supports wider access to these treatments which will further reduce disease burden and will help to ensure patients are managed in the right service. However, it was pointed out that this is a new class of treatments for GPs to prescribe and that issues such as the various and potentially serious drug drug interactions associated with Viekira Pak/ Viekira Pak-RBV mean that training and resources to support GPs would be required.

PHARMAC staff have developed a comprehensive implementation plan to support the proposed listing which includes both education and decision support tools Considering the desires expressed by specialists to access treatment now and by GPs to access this treatment in the long term, PHARMAC staff propose a period of 3 months where funding is restricted to specialists only This would allow time for GPs to become familiar with these treatments while also allowing specialists to prescribe these treatments. In addition, we consider the vast majority of patients who would be eligible for funded treatment with Viekira Pak/ Viekira Pak RBV would be in a clinical state where a 3 month delay in accessing funded treatment (compared with the proposal as consulted on) would not have a significant impact on their health. For those in whom there may be a deterioration in health between July and October, funded treatment could be accessed by a specialist

Viekira Pak consists of a daily regimen of 4 tablets. Again, ribavirin may be required; however in this instance it would be provided by the supplier

It is proposed Viekira Pak/ Viekira Pak RBV be listed as XPharm and that a direct distribution mechanism be used to dispense and distribute it. The provisional agreement with AbbVie Ltd provides that the dispensing and distribution of Viekira Pak/ Viekira Pak RBV would be the responsibility of the supplier Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)
Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)

In order to ensure patient confidentiality, it is proposed that PHARMAC manage the receipt of prescriptions for Viekira Pak/ Viekira Pak-RBV and forward these directly to the distributor and dispensing pharmacist. This may have workload implications for PHARMAC staff; Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)
Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)

Estimate of the Effects of the Proposals

Harvoni Proposal

Clinical
Impact on disease burden to the patient and society

This proposal, if approved, would mean patients with hepatitis C of any genotype, with end stage liver disease, have their quality of life significantly improved, have a reduced need for liver transplant, and have a reduced risk of developing complications such as liver cancer and liver failure.

Impact on services

Information PHARMAC received as a result of the RFI it issued in August 2015 and consultation responses indicate that DHB clinicians consider that this proposal would have a positive effect on DHB hospital and GP services The curative nature of the treatments means that a patient's risk of developing complications such as liver cancer, portal hypertension and ascites would be reduced. We anticipate that this would reduce the workload of associated with managing such events. However we acknowledge that they may still require significant health system intervention

Patients who would be eligible for treatment with Harvoni would have already developed end stage liver disease with a MELD score of >15, so PHARMAC staff consider that laboratory and scanning assessments would have already be performed for such patients. The funding of Harvoni is therefore unlikely to impact these services

Although application to the HepCTP would be accessible by any relevant practitioner, PHARMAC staff consider that, due to the nature of the clinical information required to meet the proposed funding criteria, it is likely that applications will only be made by specialist centres, or by GPs with oversight from these centres who would already be managing these patients. We also note the limited number of patients that are expected to meet the proposed funding criteria.

Fiscal

Cost of treatment

The net cost per 12 week weeks of treatment with Harvoni would be Withheld. The net cost of ribavirin treatment for 12 weeks is Withhel The total net cost of treatment would therefore be Withheld compared to a list price of total treatment of $76,960.38.

Staff note that, in some instances, ribavirin treatment is contraindicated, in those patients 24 weeks of treatment with Harvoni may be required. Expert advice on the frequency of ribavirin contraindications indicates that ribavirin may not be able to be used in 3.6% of cases In these cases the total net cost of treatment may be up to Withheld; and these costs have been included this in the budget impact analysis.

Cost offsets to the CPB

Cost offsets included in the analysis include the cost of the current treatments, boceprevir, pegylated interferon and ribavirin.

Impact to CPB and DHBs

The funding of Harvoni is expected to have a budget impact to the CPB of Withheld under and Withheld under to DHBs overall (NPV 5 yrs, 8% discount rate) We estimate that approximately 250 patients per annum would be eligible for treatment in out years, with 140 patients in year 1. Feedback we have received from consultation indicates that, due to a MELD score of 15 or greater being required, that patient numbers may be as low as 100 patients per annum

The introduction of Harvoni would be associated with some savings to the DHBs as a result of reduced risk of patients presenting with complications of end stage liver disease, progression to liver cancer and liver transplant; however, PHARMAC staff note that these patients already have severe liver disease and therefore there would still be costs associated with ongoing monitoring. In addition the effect of treatment means that they would be less likely to die, and therefore health sector support costs would be incurred as a result of people living for a longer duration

Cost of distribution from operations budget

Withheld under section 9(2)(b)(ii) and 9(2)(j)
Withheld under section 9(2)(b)(ii) and 9(2)(j)
Withheld under section 9(2)(b)(ii) and 9(2)(j)
Withheld under section 9(2)(b)(ii) and 9(2)(j)

Cost-effectiveness

The cost effectiveness of funding Harvoni as proposed is estimated at Wit QALYs per $1 million spent, with a likely range of Withheld QALYs/$1m. The majority of patients who would be eligible for treatment are those with decompensated cirrhosis While achieving eradication of the virus would not revert the damage done to the patient's liver, it would improve their quality of life and would reduce the probability of further progression to liver cancer and death Overall, we expect treatment would give on average Wit extra QALYs at an additional cost of Withheld: about Withheld for the treatment and Withheld for additional support costs.

Viekira Pak/ Viekira Pak RBV Proposal

Clinical

Impact on disease burden to the patient and to society

This proposal would mean that approx. 90% of patients who are genotype 1 (~57% of the hepatitis C population) would potentially be able to be cured from the disease It is considered that patients who are cured before they develop cirrhosis would be able to be discharged from frequent ongoing monitoring. They would have significantly reduced risk of developing cirrhosis, liver cancer, liver failure, requiring liver transplant and eventually dying compared to someone who has not been cured.

Viekira Pak/ Viekira Pak RBV may be used under specialist care for those patients who have developed cirrhosis (it is contraindicated in patients with decompensated cirrhosis). Again, these patients would have a reduced risk of developing liver cancer, liver failure, requiring liver transplant and eventually dying compared to those with cirrhosis who have not been cured. These patients would require ongoing 6 monthly monitoring which involves ultrasound scanning and blood tests to monitor for development of liver cancer.

Impact on services

There are both long term and short term impacts as a result of this proposal. In the short term, there may be an impact on testing and prescribing Identification and management of chronic hepatitis C requires laboratory confirmation of disease, assessment of stage of disease and genotyping. As a result, initially, there could be increased testing requirements for patients

However, with regards to long term impacts, given there is a high cure rate this would be offset by a significant reduction of any ongoing health resource required for management of the disease (e.g clinic visits, monitoring for cirrhosis, blood tests, transplants, management of symptoms etc). Information from the New Zealand Liver Transplant Unit indicates that up to 50 liver transplants are performed each year, with the most common indication being hepatitis C related cirrhosis It is considered that the availability of Viekira Pak/ Viekira Pak RBV to patients before cirrhosis develops would reduce the number of hepatitis C infected patients requiring transplants.

In relation to service impact, we note that all DHB regions have committed to implementing integrated hepatitis C services in their regions. This is as a result of Ministry of Health (MoH) work related to issuing guidance to support the development of regional services to deliver identification and treatments for people at risk or with hepatitis C. Midland and Central regions are implementing from 1 July 2016 and Northern and Southern regions are

implementing from 1 October 2016. This guidance issues minimum requirements in relation to assessment and treatment services The required clinical pathway identified in MoH guidance direct that a patient suspected of having hepatitis C receive diagnosis; should chronic hepatitis C be identified, genotyping and liver assessment are required as part of the pathway These factors influence a patient's eligibility and likely success with current treatment, and also the monitoring and advice that the patient requires. We note that all DHB regions are working with the MoH already to implement these requirements and the mandated pathway is likely to be issued shortly As such, PHARMAC staff consider the likely increased demand on laboratory and liver assessment services would happen whether this proposal is approved or not. This proposal; however, may bring forward these costs that may otherwise have been incurred later

Information PHARMAC received as a result of the RFI it issued in August 2015 and consultation responses indicate that DHB clinicians consider that this would have a positive impact on secondary care services Information received from clinical experts in hepatitis C indicated that a large proportion of people with hepatitis C could be treated in the community should a novel direct acting anti viral for hepatitis C be funded. As Viekira Pak/ Viekira Pak RBV would be able to be prescribed in primary care from 1 October 2016, we consider there would be a reduction on secondary care resources to manage these patients. Due to the low success rates of current treatments, resource is often taken up by managing the symptoms associated with progression of the disease Due to the chronic progressive nature of disease, with patients living for several decades with the disease, impact on clinical resource associated with managing the disease for secondary care can be significant.

The potential impact on GP practices was highlighted in consultation responses. As discussed above, we consider that the requirement to provide services to identify and treat patients with hepatitis C would happen over the next few years whether this proposal to fund new pharmaceutical treatments is approved or not, noting the upcoming MoH requirements in relation to assessment and treatment services. Furthermore information obtained from tertiary care facilities indicate that they are planning for increased service provision for a 6 12 month period in expectation to support GPs as a result of this work. The availability of a potentially curative treatment before patients develop fibrosis would allow patients to flow through this system and be treated, rather than remain in the system

Provision of funding for GPs provision of these services was also raised in consultation responses PHARMAC staff acknowledge that when a patient is receiving treatment, more clinic appointments may be required in order to monitor the patient. The funding of these services are outside of PHARMACs remit, however it has been taken into account in the cost utility analysis and in the budget impact for DHBs

Fiscal

Cost of treatment

The commercial arrangement that has been negotiated with AbbVie means that the price per cure would be Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j):

Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)

Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)
Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)
Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)
Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)
Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)

This arrangement would be in place until 30 June 2019, when subsidy and delisting protection would end Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)
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- There are an estimated 11,400 people in New Zealand who are diagnosed with chronic hepatitis C who are genotype 1 In addition, there are estimated to be a further 17,100 people who have chronic hepatitis C who are yet to be diagnosed.
- We are aware that the MoH are due to start activities in relation to hepatitis C services which include targeting detection of hepatitis C. The key performance indicators which must be reported 6 monthly will likely include the number of people diagnosed with hepatitis C and the number of people receiving PHARMAC funded antiviral treatment (we note that these are yet to be finalised, however MoH is waiting for a decision by the PHRAMAC Board in relation to hepatitis C treatments before finalisation).
- Patients (from 1 October 2016) would be able to access funded treatments from their GPs and therefore we do not anticipate that limited resource in secondary care would create a barrier for the numbers of patients able to access treatment.

PHARMAC staff estimate that the likely patient number will be approximately 2000 patients in year 1, with increases in years 2 and 3 to approximately 4000 patients. Withheld under section 9(2)
Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)

Following 30 June 2019, Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j):

Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)

PHARMAC notes that by 2019, a number of other hepatitis C treatments which treat all genotypes are anticipated to be registered and protection would have expired for both Harvoni and Viekira Pak/Viekira Pak RBV PHARMAC staff plan to run a competitive process in early 2019 to maximise this opportunity and hope that expanded access to all patients would be achievable at that time, if not before.

Cost offsets

Cost offsets included in the analysis include the cost of the current treatments, boceprevir, pegylated interferon and ribavirin.

Impact to CPB and DHBs

The funding of Viekira Pak/ Viekira Pak RBV is expected to have a budget impact to the CPB of Withheld under section 9(2)(b)(ii), and Withheld under section 9(2)(b)(ii) to DHBs overall (NPV 5 yrs, 8% discount rate). We estimate that over 1500 people per annum will access treatment.

The introduction of Viekira Pak/ Viekira Pak-RBV is likely to be cost-saving to DHBs in the long term We note that it may be hypothesised that increased staff may be required to manage an expected increase in workload. However, any increase in workload as a direct result of this proposal would be likely to be temporary as services and GPs become adept at triaging and managing these patients In addition, these patients are unlikely to be in an urgent clinical condition requiring immediate treatment. PTAC, at its August 2015 meeting considered that, should current treatment options remain the only funded therapy for hepatitis C, the numbers of patients who progress to end stage liver disease would continue to rise as would associated costs. However, the availability of Viekira Pak/ Viekira Pak-RBV to those who are yet to develop disease is likely to substantially reduce the cost that the DHB would otherwise be funding for support services for these people if they weren`t treated as their liver disease developed.

Cost of distribution from operations budget.

Withheld under section 9(2)(b)(ii) and 9(2)(j)

Withheld under section 9(2)(b)(ii) and 9(2)(j)

Withheld under section 9(2)(b)(ii) and 9(2)(j)

Withheld under section 9(2)(b)(ii) and 9(2)(j)

Cost-effectiveness

The cost-effectiveness of funding Viekira Pak is cost-saving On average a patient in this group requires $27,000 of support over their lifetime (discounted at 3.5% pa). Given Viekira Pak's cure rate and the reduction in costs from a successful cure, each attempted treatment saves on average Withheld under section 9(2)(b)(ii) The average cost of Viekira Pak treatment varies depending on uptake but will in practice be significantly less than Withheld under section 9(2)(b)(ii). Hence, funding Viekira Pak would be cost-saving to DHBs This saving is in addition to an average Wit under section 9(2)(b)(ii) QALYs gained per person given the treatment, coming from improved quality of life and prevention of progression into worse states and to death.

PHARMAC Staff View

PHARMAC staff support the proposals for both Harvoni and Viekira Pak/Viekira Pak RBV PHARMAC staff note that there are two separate proposals that the Board could choose to approve one and not the other. However PHARMAC staff consider that both proposals should be approved The rationale for this is as follows:

Clinically these treatments offer high cure rates in excess of 90%, and treatment which is far superior to those currently available both in terms of success, but importantly in terms of side effect profile and contraindications Availability of Harvoni to those with severe disease would reduce the chances of patients developing liver cancer and liver failure and need for liver transplantation Availability of Viekira Pak/ Viekira Pak RBV would allow a substantial number of patients with chronic hepatitis C to eradicate their disease prior to developing cirrhosis. This would allow avoidance of any further increased risk of consequences such as liver cancer, liver failure etc In addition, once cured, patients would no longer be able to transmit disease to others.

With a potential to be able to cure up to approximately 28,000 patients, the Viekira Pak/ Viekira Pak RBV proposal offers significant advantages to start reducing the burden of chronic hepatitis C in New Zealand. This is not the case for the Harvoni proposal, which would have minimal impact in terms of reduced societal disease burden. However Harvoni may be used in patients with severe liver disease (decompensated cirrhosis) and in patients of all genotypes whereas Viekira Pak/ Viekira Pak RBV is contraindicated in patients who are at risk of decompensated cirrhosis and is also only indicated in genotype 1 patients.

The Harvoni proposal would mean that any end stage liver disease patient, no matter what genotype have a treatment option It also provides a treatment option for where none currently exist for example, in patients who have failed treatment with boceprevir.

PTAC has identified a population which it recommended funding Harvoni with a high priority; this population include those identified in the proposed restriction criteria. PHARMAC staff recommend that the full population identified by PTAC is not funded at this time, based on potential fiscal risk. PTAC recommended the funding of Viekira Pak/ Viekira Pak-RBV with a low priority based purely on fiscal risk. PHARMAC staff consider it has mitigated this fiscal risk with a maximum spend of up to Withhel per annum and Withheld under section 9(2)(b)(ii), 9(2) Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j).

A direct distribution mechanism allows these expensive treatments to be distributed without attracting substantial cost (namely mark ups on the list price and dispensing fees) to the DHB However, we acknowledge concerns that avoiding a community pharmacy dispensing would mean that a safety check in terms of drug-drug interactions would be lost. This is particularly relevant for the Viekira Pak/ Viekira Pak RBV proposal (as Panel oversight would be provided for those applying for Harvoni and prescribing is most likely to occur through specialist hepatitis C clinics). We also note those treated with Harvoni are likely to be under the oversight of a specialist prescriber.

PHARMAC staff intend to mitigate the concern in relation to the loss of safety check in terms of drug-drug interactions by ensuring the provision of decision support tools for use at the time of prescribing. This would help to ensure this check is performed adequately at the point of prescribing. For example, we expect that the request form to gain access to Viekira Pak/ Viekira Pak-RBV will have requirements listed which would include that prescribers have read prescribing guidance, have checked their patient's current medications, had a discussion with the patient about potential interactions and what to avoid during treatment etc. In addition we hope to have this made available via the prescriber software. This will also be supported by an education package, details of which are provided in the implementation plan (Appendix 2). AbbVie has also provided a comprehensive summary of the support services which it anticipates providing This involves a community pharmacist checking potential drug-drug interactions with the patient. A summary of AbbVie's intentions in this area have been provided as (Appendix 3).

As noted above, PHARMAC staff support funded access to these treatments outside secondary care This is because it would allow patients who may have restricted access to a specialist, due to their rural location, to still access treatment

In relation to Viekira Pak/Viekira Pak RBV, a specialist restriction would increase pressure on secondary care, whereas the proposal (from 1 October 2016) allows appropriate patient management i.e. those who require specialist oversight can be referred to secondary care, whereas those who are in secondary care but could be managed in the community can be discharged to their GP.

We note the concerns raised in relation to GP readiness to prescribe Viekira Pak/Viekira Pak RBV, and have adjusted our recommendation accordingly, allowing a 3 month hiatus between the listing for specialists and removing the prescriber restriction. This is discussed above

PHARMAC staff note that the current proposals do not address the health needs of patients with hepatitis C and genotypes 2-6 who do not have end stage liver disease. We also note there would be a small group of genotype 1 patients in whom Viekira Pak/Viekira Pak-RBV is not an appropriate treatment PHARMAC would continue to remain open to any potential negotiations with suppliers for the funding of treatments for these groups

PHARMAC staff note the fiscal implication of funding these treatments, however, we also note the outstanding cost effectiveness of these treatments. Viekira Pak/ Viekira Pak-RBV is considered to be cost saving, whereas the cost effectiveness of Harvoni is in the likely range of Withheld QALYs/$1m

In addition, PHARMAC staff anticipate opportunities for savings in this market from 2019 along with expanded access for all genotypes and are comfortable with the proposal to provide subsidy and delisting protection up to 30 June 2019.

Background

PHARMAC staff issued a Request for Information (RFI) on treatments for hepatitis C in August 2015 The purpose of this RFI was to seek information from suppliers of novel direct acting antiviral agents for the treatment of hepatitis C. It also sought information from clinicians, hepatitis C healthcare professionals, others who provide support for people with hepatitis C, and those people who are affected by hepatitis C on the services that are provided for people with hepatitis C and the resourcing required for these services. Feedback to the RFI helped to inform our analysis and development of the proposals in this paper.

The disease - chronic hepatitis C

Chronic hepatitis C is a disease that is caused by infection with the hepatitis C virus (HCV). The virus causes inflammation in the liver. Over time, this inflammation can result in scaring of the liver, known as fibrosis As fibrosis develops, liver cirrhosis may develop which means the liver stops working properly. The damage inflicted on the liver as a result of the virus can lead to serious health outcomes such as liver failure, liver cancer and potentially death.

Stage of liver disease	Impact
Stage 1	Some inflammation but minimal effect on function
Stage 2	Some limited accumulation of scar tissue (fibrosis). Liver function is minimally impacted
Stage 3	Extensive fibrosis and scarring but with relatively normal functioning.
Stage 4	Substantial cirrhosis damaging liver and impairing the vital functions is performs.

There are also complications that can be encountered as a result of the liver disease:

Decompensated cirrhosis – this situation occurs when a patient's disease progresses from cirrhosis and any of the following symptoms occur:

- Bleeding varices (internal bleeding);
- Ascites (fluid in the belly);
- Encephalopathy (confusion); and
- Jaundice (yellowing of eyes and skin).

This means that a patient's liver is extensively scarred and unable to perform its vital functions properly. This indicates severe disease; patients with decompensated cirrhosis generally require admission to hospital with poor prognosis and liver transplant may be required

Cryoglobulinaemia this situation occurs when large amounts of proteins known as cryoglobulins become insoluble at reduced temperatures These proteins come out of solution and can block vessels which in turn can cause complications such as gangrene in fingers and toes

In New Zealand, there are approximately 20,000 people who have been diagnosed with chronic hepatitis C There are thought to be a further 30,000 people who have chronic hepatitis C who aren't yet diagnosed with the disease.

Current data also suggests that Māori are over represented in the population of people living with chronic hepatitis C.

Approximately 900 people each year are newly infected with chronic hepatitis C.

There are six major genotypes of HCV, which are indicated numerically from one to seven Generally, patients are only infected with one genotype Please see table X for NZ genotype prevalence information.

Genotype	NZ prevalence
1	57%
2	7%
3	35%
4	0 5%
5	0%
6	1%

HCV is spread primarily by blood to blood contact associated with intravenous drug use, poorly sterilized medical equipment, and transfusions. Tattooing is associated with two to threefold increased risk of hepatitis C. Personal-care items such as razors, toothbrushes, and manicuring or pedicuring equipment can be contaminated with blood and sharing such items can potentially lead to exposure to HCV. Vertical transmission of hepatitis C from an infected mother to her child occurs in less than 10% of pregnancies and there are no measures that alter this risk

Without treatment, between 5-15% of those with HCV will become cirrhotic after 20 years of infection and 3% will develop liver cancer. 40% of those with cirrhosis will be referred for liver transplantation However these numbers are disputed as the long course of the disease, usually stretching over several decades, makes it difficult to accurately ascertain probabilities of progressing to each stage

Level of disease can be assessed using a number of different methods. The common assessments include transient elastography, Child Pugh and MELD score. A summary of these methods has been included as Appendix 7 In summary, it was decided that MELD score was the most appropriate score to use for criteria as it allows more precise targeting, the alternative scores are broader and would capture large numbers of patients in each group which would be unaffordable

Goal of treatment

The goal of treatment in patients with chronic HCV infection is to eradicate HCV RNA, which is predicted by the attainment of a sustained virologic response (SVR) An SVR (undetectable viral load 12 weeks after cessation of therapy; written as SVR12) is associated with a 99 percent chance of being HCV RNA negative during long term follow-up Attaining an SVR has been associated with decreases in all cause mortality, liver-related death, the need for liver transplantation, hepatocellular carcinoma rates, and liver-related complications. Both fibrosis (stage) and inflammatory activity (grade) usually regress If an SVR is achieved patients are no longer able to transmit HCV to other parties.

Current treatment options

PTAC considers that there are currently no treatment options for:

- Patients with advancing fibrosis who have not achieved SVR with currently funded treatments;
- Patients with cirrhosis at risk of liver decompensation;
- Patients whose co-morbidities that preclude interferon-based treatment - including patients with mental health problems or poor social supports; and
- Patients with renal disease

Boceprevir in combination with pegylated interferon and ribavirin (BOC/PEG-IFN+RBV)

In September 2013 following a competitive process PHARMAC funded boceprevir for hepatitis C genotype 1 patients with IL28 genotype CT or TT, for those who are treatment-naive or who were previously treated with pegylated interferon and were responder relapses or partial responders. Boceprevir is used in combination with pegylated interferon and ribavirin. SVR rates depend upon prior treatment but range from 59-66% in treatment experienced patients and 67 68% for treatment naïve patient

There are a number of common side effects with boceprevir. The most common side effects of boceprevir include fatigue, anaemia, nausea, headache, and dysgeusia. Other side effects include dry mouth, vomiting, diarrhoea and neutropenia In most cases, provided the side effects are not severe, the approach is to try to provide supportive care while maintaining the patient on the boceprevir if possible. Real world data on boceprevir was reviewed by PTAC at its February 2016 meeting The Committee noted that serious adverse events were reported in 12% of patients, 66% of patients experienced anaemia, 90% of patients had adverse events that led to a prescription, treatment, or dosage change and 39% of patients discontinued treatment early, most commonly because of adverse events (18%) or lack of efficacy (16%). It noted that hepatic decompensation events occurred in 3% of patients and five deaths occurred and 52% of all patients achieved a sustained virologic response. The Committee noted the declining usage of subsidised boceprevir and considered that this study was consistent with the clinical experience in New Zealand and that this contributed to the declining use of boceprevir in New Zealand

BOC/PEG-INF+RBV is contraindicated in a number of situations most notably those patients with hepatic decompensation (i.e. those patients with severe liver disease), patients that are receiving medicines that are dependent on the enzyme CYP3A4/5 for clearance and pregnant women and their male partners.

Pegylated interferon with ribavirin (PEG-IFN+RBV)

For patients who do not meet the funding criteria for boceprevir, the current funded treatment is pegylated interferon and ribavirin for 24 to 48 weeks depending on HCV genotype This treatment achieves a sustained virological response (SVR) in approximately 45% of patients infected with HCV genotype 1 and 65% of those infected with genotypes 2 or 3

Pegylated interferon with ribavirin is associated with significant adverse effects, from flu like symptoms, fever, rash, anorexia, thyroid dysfunction, to dose related life threatening cytopaenias and mood disorders. Side effects result in a dose reduction in 60–80% of patients and treatment withdrawal in 5–10%.

PEG IFN+RBV is contraindicated in a number of situations most notably those patients with hepatic decompensation (i e those patients with severe liver disease), in patients with haemoglobinopathies (e g thalassaemia, sickle-cell anaemia and pregnant women and their male partners. .

New Treatments
Harvoni

Ledipasvir is a replication complex inhibitor that targets domain 1 of the hepatitis C virus (HCV) NS5A protein, a protein which is essential for both RNA replication and the assembly of HCV virions

Sofosbuvir, is a pan genotypic inhibitor of HCV NS5B RNA polymerase, preventing viral replication.

In combination, Harvoni is registered in New Zealand for the treatment of chronic hepatitis C Harvoni may be administered in combination with ribavirin depending on whether cirrhosis is present, prior treatment and genotype of disease

Ribavirin interferes with RNA metabolism required for viral replication. Ribavirin dosage is weight based, up to 1200 mg may be required (6 tablets) per day. Ribavirin is currently subsidised via Special Authority for those patients with chronic hepatitis C for those with chronic hepatitis C, genotype 1, 4, 5 or 6 infection; or co-infection with HIV; or patient has genotype 2 or 3 and has received a liver transplant.

In patients who can use ribavirin, Harvoni is administered as a tablet taken once daily for 84 days in combination with ribavirin. In patients who are contraindicated to ribavirin, Harvoni is administered once a day for 168 days.

Adverse events associated with LD/SOF are limited. At its May 2015 meeting, PTAC considered that generally Harvoni is well tolerated. It considered that the discontinuation rates in trials were around 0-2% which it considered to be low. It considered that that newer treatments had markedly improved efficacy and tolerability and reduced treatment duration over currently funded chronic hepatitis C treatments. There are a relatively few drug-drug interactions associated with the use of Harvoni. A full table of drug drug interactions has been included as Appendix 4

Compared to currently funded treatments there are relatively few ongoing monitoring requirements

PHARMAC staff noted that, as a result of the distribution mechanisms, and the requirement for review by the HepCTP, there may be a delay in a patient accessing treatment. However, PHARMAC staff note that the agreement with Gilead requires that dispensing be done on an ad-hoc basis should the need arise as a result of an urgent case.

PHARMAC staff propose that an agreed delivery address should be identified by the patient during discussion with their prescriber Staff are aware of the varied population that this medication may be required by and that flexibility may be required to allow maximum benefit for the patient and their clinician. For example, it may be that a preference for delivery to a hepatitis clinic would be identified by some, whereas others may express a preference for delivery to be to their GPs. We acknowledge that there may be some risk in the identification of a suitable delivery address, however staff consider that the benefit in this instance outweighs this risk and that the risk is mitigated by the requirement to have a discussion with the prescriber on this issue and insurance coverage for courier deliveries.

Viekira Pak and Viekira Pak RBV

Paritaprevir/ritonavir, ombitasvir, dasabuvir +/ ribavirin is indicated for the treatment of genotype 1 chronic hepatitis C infection, including patients with compensated cirrhosis

Paritaprevir/ritonavir, ombitasvir, dasabuvir contains three direct-acting antiviral (DAA) agents:

DAA Agent	Action
Paritaprevir	Hepatitis C virus (HCV) NS3/4A protease inhibitor – this protease is required for proteolytic cleavage of HCV proteins
Ombitasvir	HCV NS5A inhibitor this protein is required for viral replication.
Dasabuvir	HCV RNA dependent RNA polymerase inhibitor (NS5B inhibitor) this enzyme catalyses the replication of the viral RNA.

Along with these DAA agents, the pharmaceutical also contains ritonavir, a protease inhibitor which acts by inhibiting the host enzymes which metabolise protease inhibitors. Therefore it increases plasma concentrations of the DAAs allowing reduced dosages of DAAs to be administered In certain situations ribavirin may also be provided within the pharmaceutical Ribavirin interferers with the RNA metabolism required for viral replication; however the mechanism of this action is unknown.

The Viekira Pak regimen requires that the patient take 4 tablets daily, 2 x 75 mg paritaprevir/ 50 mg ritonavir/ 12.5 mg ombitasvir tablets (both taken in the morning with food) and 2 x 250 mg dasabuvir tablets (one taken in the morning with food, one taken in the evening with food. The supplier has developed packaging to support this dosage regimen Each daily wallet is packaged into a weekly carton, then further into a monthly carton.

The VIEKIRA PAK packaging Daily Dose Pack (Wallet)

Treatment duration depends on the clinical situation but ranges from 12 to 24 weeks. PHARMAC staff note that this variation in treatment duration would not affect the cost of this treatment

The most common adverse effects associated with treatment are fatigue, nausea, pruritus, insomnia, asthenia and anaemia
There are a number of drug-drug interactions which may occur as a result of using Viekira Pak/Viekira Pak RBV. These may require that dosage of a treatment is adjusted, or that treatment is not commenced Drugs which should not be co administered with Viekira Pak/ Viekira Pak-RBV include some antiarrhythmic, some anticonvulsants, clarithromycin and the asthma drug salmeterol. A full table of drug drug interactions has been included as Appendix 4

Distribution

As this is a new medication that would be dispensed XPharm, concerns were raised in consultation with regard to a lack of pharmacy oversight. In particular, ability for a pharmacist who is dispensing to a patient without having familiarity with the patient, the ability to review the patients dispensing record or be able to discuss the situation, to dispense safely PHARMAC staff acknowledge this concern and have developed a number of strategies in order to mitigate this risk. As has AbbVie Ltd. AbbVie are contractually obliged as a result of the provisional agreement to provide counselling

We note that this risk in relation to a pharmacist being unfamiliar with a patient exists currently in relation to a patient attending a pharmacy that they do not usually attend

Awareness, screening and disease management in New Zealand MoH work

In 2010, the Ministry of Health contracted the Hepatitis Foundation of New Zealand to undertake the Improvements in Hepatitis C Services planning project This pilot scheme was run for two years. Following review, the information obtained from the pilot was used to inform a revised approach on the delivery of hepatitis C services across New Zealand Resources are being directed towards detection, management and treatment of hepatitis C populations. The focus is on a co-ordinated primary and secondary health care model. The DHBs have been separated into four regions to complete this work

All four regions have committed to implementing integrated hepatitis C services in their region by the end of the 2015/2016 year. Our latest information indicates that this will occur:

- Midland – 1 July 2016
- Central - 1 July 2016
- Northern – 1 October 2016
- Southern 1 October 2016

Guidance has been provided in the form of high level clinical pathways, minimum requirements, quality assurance frameworks, minimum standards and data that is required from all DHBs. These are based on best clinical practice and PHARMAC funded antiviral therapy MoH is planning on issuing further, updated, guidance once a decision has been made by the PHARMAC Board in relation to Harvoni and Viekira Pak/Viekira Pak RBV.

The minimum requirements are as follows:

Minimum requirements
Hepatitis C services across New Zealand will provide quality identification, through testing and diagnosis; assessment; triage; and management, including monitoring, support and education to people with hepatitis C.
Hepatitis C pathways will be based on best clinical practice and available antiviral therapy. A common clinical pathway will be followed across New Zealand to ensure equity of care for all New Zealanders living with hepatitis C.
Current people with Hepatitis C participating in the HFNZ Pilot programmes will transition smoothly into the new integrated model with no gap in service
Regionally led hepatitis C services will deliver integrated services across primary and secondary care. The national clinical pathway will be tailored to meet the needs of regional populations
Hepatitis C identification will be primarily directed towards targeted testing for people who are at increased risk including: those who have ever injected drugs; ever received a tattoo or body piercing using unsterile equipment; had a blood transfusion before 1992; ever lived or received medical treatment in a high risk country; ever been in prison or have been born to a mother living with hepatitis C. It will also seek to identify those who have been previously diagnosed and lost to follow up
Primary and secondary care services will be extended to provide improved assessment and follow up services for people with hepatitis C, including community based fibroscanning.
Providers of hepatitis C services will be required to work with local organisations in their region that provide services to the population that are at high risk for hepatitis C virus infection. This includes needle exchange services, community alcohol and drug services, prisons and community based services hepatitis C clinics.

Clinical pathway key components include:

- raising community and GP awareness and education of the hepatitis C virus and the risk factors for infection;
- providing targeted testing of individuals at risk for hepatitis C virus exposure;
- raising patient and GP awareness of long-term consequences of the hepatitis C virus and the benefits of treatment, including lifestyle management and antiviral therapy;
- providing community based access to hepatitis C virus testing and care that will include Fibroscan services to all regions as a means for assessment of disease severity and as a triage tool for referral to secondary care and prioritisation for antiviral therapy;
- establishing systems to report on the delivery of Fibroscans in primary and secondary care settings ;
- providing community based ongoing education and support (including referral to needle exchange services, community alcohol and drug services, GP primary and community care services or social service agencies);

- providing long term monitoring (life long in people with cirrhosis and until cured in people without cirrhosis);
- providing good information sharing with relevant health professionals; and
- working collaboratively with primary and secondary care to improve access to treatment.

A full copy of this guidance is included as Appendix 5.

PTAC View

PTAC considered applications for both Harvoni and Viekira Pak/ Viekira Pak-RBV at its May 2015 and August 2015 meeting respectively Relevant minutes are attached as Appendix 6. A brief summary of the most relevant points to this proposal are provided below:

Harvoni

At its May 2015 meeting, PTAC reviewed the evidence presented for ledipasvir/sofosbuvir. The Committee considered that the evidence for Harvoni is strong and of very high quality for hepatitis C virus genotype 1. However, the Committee considered that there is a lack of mature data on the use of the ledipasvir component of this pharmaceutical in hepatitis C virus genotypes 2 and 3, although preliminary data shows good efficacy. The Committee noted that ledipasvir/sofosbuvir demonstrates a >90% sustained virologic response 12 weeks after cessation of treatment (SVR12) across genotypes, across different disease states, independent of prior treatment and that these SVR12 rates were markedly superior to rates achieved with the currently funded therapies. We note that SVR12 is clinically considered to represent a cure Members also discussed the issues relating to delaying curative treatment at different stages of disease progression They considered that, even if an SVR12 is achieved, those patients that had already progressed to cirrhosis would be at increased risk of potential life threatening complications including hepatocellular carcinoma and oesophageal varices The Committee considered that these patients would likely require indefinite follow up involving surveillance for these complications. The Committee considered that should an SVR12 be achieved prior to progression to cirrhosis, it is likely that a patient will be able to be discharged from ongoing follow up. Some members considered that while those who are in more advanced stages of disease are at greater risk, earlier treatment could provide the greatest gains. Other members noted that, due to the slow progression of disease, early treatment may mean treating a patient who would not have experienced a significant health loss.

The Committee recommended that Harvoni should be funded with a high priority for the following subpopulations:

- HCV patients with decompensated cirrhosis (all genotypes)
- HCV patients pre/post liver transplant (all genotypes)
- HCV patients with essential mixed cryoglobulinaemia (with associated purpuric skin rash, cryoglobulinaemic glomerulonephritis and systemic vasculitis).

The Committee **recommended** that ledipasvir with sofosbuvir should be funded for all other subpopulations of patients with chronic hepatitis C with a low priority based solely on fiscal risk.

Viekira Pak/ Viekira Pak-RBV

At its August 2015 meeting, PTAC discussed an application for Viekira Pak/ Viekira Pak RBV (referred to as PROD by the Committee). The Committee noted that PROD is indicated for the treatment of genotype 1 chronic hepatitis C infection, including those patients who have compensated cirrhosis. The Committee noted that there is a contraindication in patients with Child Pugh class C hepatic impairment, which includes decompensated cirrhosis.

The Committee considered that the evidence presented was strong and of very high quality for genotype 1. The Committee noted that the six pivotal studies had large patient numbers and consistently demonstrated SVR rates in excess of 90% in treatment naive, treatment experienced, non cirrhotic and cirrhotic patients. The Committee considered that the SVR rates were comparable to ledipasvir with sofosbuvir for genotype 1 patients.

The Committee considered that the treatment duration of PROD and reduced toxicity when compared to the currently available treatments may allow primary care facilities to undertake treatment.

The Committee considered that if PROD were funded, there would still be a need for another agent to treat other genotypes and decompensated cirrhotic patients as PROD is only effective in genotype 1 patients, does not have a role in patients with decompensated cirrhosis, and that use in a post transplant settings are complex due to ritonavir drug interactions with immunosuppressive therapy, it therefore does not address the needs of many of the high need groups as it defined at its May 2015 meeting.

At its May 2015 meeting, PTAC discussed the issues relating to delaying curative treatment at different stages of hepatitis C disease progression. They considered that, even if an SVR12 is achieved, those patients that had already progressed to cirrhosis would be at increased risk of potential life threatening complications including hepatocellular carcinoma and oesophageal varices. The Committee considered that these patients would likely require indefinite follow up involving surveillance for these complications The Committee considered that should an SVR12 be achieved prior to progression to cirrhosis, it is likely that a patient will be able to be discharged from ongoing follow up

The Committee noted that treating all currently diagnosed New Zealanders with genotype 1 virus would not be financially possible, and considered that restrictions on PROD should be based solely on fiscal impact. The Committee recommended that PROD should be funded for the treatment of chronic hepatitis C genotype 1 infection in adults with a low priority based solely on fiscal risk PHARMAC staff consider we have overcome this fiscal risk and therefore mitigated PTACs concern.

The Dynamics of the Market for Hepatitis C Treatments

Cost of Current Treatments

The current cost of treatment with the funded agents is as follows:

Pharmaceutical	List price	Treatment length	Net cost per boceprevir course	Net cost per PEG-IFN+RBV course
Boceprevir	$5,015 per 8 weeks	Est 30 weeks average	Withheld	
Pegylated interferon	$1,290 per 4 weeks	48 weeks	Withheld	Withheld
Ribavirin	$350 per 4 weeks	48 weeks	Withhel	Withhel
Total drug cost			Withheld	Withheld

Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)
Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)
Withheld under section 9(2)(b)(ii), 9(2)

Use of Current Treatments

The last 5 financial years of usage data relating to the currently funded agents is as follows:

FYE	Boceprevir (listed 1 August 2013)	Pegylated interferon with ribavirin
2010	N/A	711
2011	N/A	529
2012	N/A	488
2013	N/A	380
2014	124	323
2015	65	234

This has been measured using approved initial Special Authority applications for these medications for the treatment of hepatitis C.

Although boceprevir has only been listed since 1 September 2013, PHARMAC staff note that uptake since listing is substantially lower than was forecast. Notably, the number of patients accessing PegIFN treatment has also decreased substantially in this time period PHARMAC staff understand that there is an approach by some patients to wait and see if the PegIFN free treatments become available before they choose to commence treatment. This is supported by PTAC who noted in May that the number of New Zealand patients accessing currently funded treatments is declining with less than half the number of patients treated in

2014 via the Pharmaceutical Schedule compared with the more than 700 patients treated in 2010 The Committee considered that contributing factors to this reduction may be due to the suggestion that boceprevir may be more toxic than indicated in clinical trials, that some patients are currently able to access clinical trials for novel chronic hepatitis C treatment and that the majority of patients who could wait were postponing treatment in the hope that access to novel agents will be available in a short timeframe.

No data are available to compare uptake rates for current treatments by Maori and Pacific people when compared with other ethnic groups.

Based on this information, we consider that the numbers of patients accessing the currently funded treatments will continue to decline. However, we consider the introduction of Harvoni and Viekira Pak/ Viekira Pak RBV would significantly expedite this reduction. Although we consider some very small usage may remain due to non genotype 1 patients accessing these treatments. We anticipate that the majority of genotype 1 patients who are not cirrhotic would switch to treatment with Viekira Pak/Viekira Pak RBV

The offsets of patients switching treatment have been included in budget impact described above Should this proposal be approved we would estimate there would be approx 150 patients receiving treatment with Harvoni in the first, year and plateauing to around 250 per annum by year 3. We estimate that in excess of 1500 patients will receive treatment with Viekira Pak/Viekira Pak RBV

Net annual expenditure for the 2014/15 financial year, on hepatitis c treatments was approximately Withheld under section 9(2)(ba)(ii) Should the two new treatments be funded we anticipate that this would grow to approx. Withheld under section 9(2)(ba)(ii) per annum

International Prices for the Pharmaceuticals

Harvoni

A comparison of international prices for Harvoni is outlined below:

Country	Source	Strength	Pack Size	Local Price	Exchange Rate (31-05-2016)	Price ($NZ)
Proposal		LDV 90mg/SOF 400mg	28	-	-	Withhel
United Kingdom	BNF			£12,993.33	0.4584	$25,196.44
Australia	PBS			$22,213 54	0 9299	$23,731 75
United States*	HCV Medications			$31,500	0.7003	$44,982.33
Canada	Alberta Health			$22,333.33	0.8931	$25,007.93

Note: Prices are expressed ex manufacturer, excluding GST.

* Wholesale acquisition cost

Gilead, the supplier of Harvoni, generally bases its pricing on the gross national income of the country it is supplying to In the US, Gilead Sciences Ltd has an active Harvoni patient assistance program for eligible patients with hepatitis C who do not have insurance and do not have coverage through Medicaid or Medicare.

In Canada, British Columbia and Ontario jointly led negotiations with the drugs' manufacturer through the pan-Canadian Pharmaceutical Alliance (pCPA). The alliance's process allows participating provinces and territories to leverage their collective buying power and negotiate better prices for new drugs Each participating jurisdiction can choose whether to accept the deal and cover the drugs on their public drug plans. Prices and terms for this negotiation are confidential.

Viekira Pak/ Viekira Pak-RBV

A comparison of international prices for Viekira Pak/ Viekira Pak-RBV is outlined below:

Country	Source	Strength	Pack Size	Local Price	Exchange Rate ([Source/date])	Price ($NZ)
Proposal*		paritaprevir (75 mg)/ ritonavir (50 mg) /ombitasvir (12 5 mg) with dasabuvir (250 mg)		-	-	Withheld
United Kingdom – PROD	BNF		28 days	£10,733.33	0.4584	$20,813.88
Australia PROD	PBS			$13,900.06	0.9299	$14,791.08
Australia PROD RBV	PBS			$14,000.00	0.9299	$14,898.56
United States PROD	Wall Street Journal			$27,767	0.7003	$39,651.57
Canada PROD	HepC BC			$18,620	0 8931	$20,849 90

Note: Prices are expressed ex manufacturer, excluding GST.

Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)

Withheld under section

In the US, AbbVie Ltd has a patient assistance programme to aid patients who are uninsured We are also aware that AbbVie has negotiated confidential discounts with organisations such as Express Scripts and Veteran's Affairs in the US.

Comments from Interested Parties

Section 49(a) of the New Zealand Public Health and Disability Act 2000 (the Act) requires PHARMAC to consult, when it considers appropriate to do so, on matters that relate to the

management of pharmaceutical expenditure with any sections of the public, groups or individuals that, in the view of PHARMAC, may be affected by decisions on those matters

Accordingly, a consultation letter was circulated on 4 May 2016 to all suppliers and other parties that, in the view of PHARMAC, may be affected by the recommendations contained in this paper The development of this consultation database began in relation to the hepatitis C treatments RFI and involved seeking feedback from a number of advocacy groups, suppliers and clinicians to identify key stakeholder in this area. PHARMAC staff received 54 submissions, 29 from clinical groups or clinicians, 10 from patients, 6 from advocacy groups, 4 from government groups, 3 from suppliers and 2 from pharmacy groups.

The consultation letter, the distribution list, and all responses received by 26 May 2016 are attached as Appendix 8 Summaries of what PHARMAC staff believe are the significant matters raised in these responses are provided below. For the full response, please refer to Appendix 9.

Stakeholder group	Theme	PHARMAC Staff comment
ADHB Antimicrobial Stewardship Committee; Haemophilia Foundation; CCDHB Addiction Services; Drugs Health and Development Project; A Joughin (unknown); P O'Connor MCDHB; J Bourke Nurse Specialist; Prof C Stedman; Regional Project Managers working on Hep C services; ASID; Dr K Read, ID Specialist Waitemata DHB; CDHB; AbbVie; D Ray-Chaudhuri NZLTU Auckland DHB; F Weilert, Gastroenterologist and Hepatologist; RNZCGP; Hepatitis Foundation; NZSG; Paediatric Gastro team ADHB; G Noller, Researcher Substance Use and Policy Analysis; Patient Wit; WDHB CADs Regional Consumer Advisory; Patient Wit; Patient Wi; Patient Wit; C Henderson; Needle Exchange Services Trust; NMDHB Strategy and Planning; NZ Sexual Health Society; NZNO; E Gray; Clinical Pharmacology and ID, CDHB; J Perry, Gastro WDHB; MSD; Gastro at SDHB; Pharmaceutical Society NZ	Support for the proposal to fund new treatments for hepatitis C noting the potential for curative treatment in a substantial number of the population with hepatitis C. This was considered to help address disease burden, ongoing impact to the health system and impact on people with hepatitis C	Noted
J Bourke – Nurse Specialist; R Medlicott, Medical Director RNZCGP; Prof E Gane, NZLTU Auckland DHB; Prof C Stedman; D Ray-Chaudhuri NZLTU Auckland DHB; CDHB; AbbVie; F Weilert, Gastroenterologist and Hepatologist; MoH Hep C Implementation Advisory Group; RNZCGP; Hepatitis Foundation; Patient Wit; Clinical Pharmacology and ID, CDHB	Supported community access for treatments should these be prescribed appropriately	Noted.

Dept of Gastroenterology, Christchurch Hospital; Hepatitis C Resource Centre Otago Southland; F Weilert, Gastroenterologist and Hepatologist; Patient Wit	Suggest that PHARMAC consider some form of alternative regimens for genotypes 2, 3 and 4. Sofosbuvir in combination with daclatasvir (a BMS product) was mentioned by several respondents	Withheld under section 9(2)(b)(ii) and 9(2) Withheld under section 9(2)(b)(ii) and Withheld under section 9(2)(b) PHARMAC staff note that, by not supplying sofosbuvir which has to be used in combination with other supplier's medications, Gilead is preventing other suppliers from entering this part of the market. Other hepatitis C treatments for people who are not covered by this proposal are still an option for investment. PHARMAC staff will pursue these should the opportunity arise.
E Gray, ID Physician WDHB; Hepatitis Foundation; J Wong HVDHB; ACC; Regional Project Managers working on Hep C services; Dr K Read, ID Specialist Waitemata DHB; Patient Wit; Prof E Gane, NZLTU Auckland DHB; Hepatology SDHB; CDHB; Clinical Pharmacology and ID Depts Christchurch; M Chamberlain (unknown); C Henderson, PWID advocate; D Ray-Chaudhuri, NZLTU Auckland DHB; Gilead; NMDHB; Northern Regional Alliance; Patient Wit; RNZCGP; Prof C Stedman; Hepatitis C Resource Centre Otago; J Bourke Nurse Specialist; F Weilert, Gastroenterologist and Hepatologist; MoH Hep C Implementation Advisory Group; NZSG; Patient Wi; Needle Exchange Services Trust; NZ Sexual Health Society	Suggest that PHARMAC needs to investigate additional treatment options for Hep C patients with genotypes 2-6 They consider the current proposal creates inequity as non-genotype 1 patients will not have improved access to treatment as a result of this proposal	PHARMAC staff note that other new hepatitis C treatments are still an option for investment and we would pursue these should the opportunity arise We note that Harvoni is available for patients of all genotypes, who meet the proposed restrictions.
J Bourke, Hep C Nurse; K Braddock, Chair of the GP Council of NZMA; ADHB Antimicrobial Stewardship Committee; J Perry, Gastro WDHB; Clinical Pharmacology and ID depts Christchurch; MSD; Prof C Stedman GE and Clinical Pharmacologist Christchurch Hospital; HepC Resource Centre Otago; NZMA; NZSG; Dr K Read, ID Specialist Waitemata DHB; ASID; Prof E Gane, NZLTU Auckland DHB; D Ray-Chaudhuri NZLTU Auckland DHB; CDHB; F Weilert, Gastroenterologist and Hepatologist; Clinical Pharmacology and ID, CDHB; J Perry, Gastro WDHB	The majority of respondents acknowledged Viekira Pak offers very effective therapy, but expressed concerns in relation to safety in patients with decompensated liver disease, non-genotype 1 patients, drug-drug interactions and teratogenicity of ribavirin Respondents had the following suggestion: a restriction so only vocationally registered GPs and other specialists could prescribe proposed new treatments, GP accreditation, and CME for prescribing and monitoring of patients on the treatments	Following consideration of this feedback we are proposing that funded access to Viekira Pak for primary care prescribers should be delayed to 1 October 2016, to allow sufficient time for GPs to become familiar with these treatments From 1 July 2016, a prescriber restriction would be applied to Viekira Pak/Viekira Pak RBV allowing only infectious diseases specialists, gastroenterologists and hepatologists to access funded treatment for the first 3 months of listing. We consider this 3 month hiatus, along with the education and support that would be provided, would allow primary care prescribers time to familiarise themselves with the treatments.

Hepatitis Foundation; R Medlicott, Medical Director RNZCGP; Regional Project Managers; Chair of the GP Council of NZMA; J Waddell, Clinical Director Comprehensive Care Ltd; ASID; Dr K Read, ID Specialist Waitemata DHB; ADHB AMS and ID groups; Christchurch Hep C Resource Centre; Prof E Gane, NZLTU Auckland DHB; CDHB; Depts Clinical Pharmacology and ID, CDHB; AbbVie; Prof C Stedman, GE and Clinical Pharmacologist Christchurch Hospital; D Ray-Chaudhuri NZLTU Auckland DHB; F Wilert, GE and Hepatologist Waikato Hospital; MoH Hep C Implementation Advisory Group; Northern Regional Alliance; RNZCGP; Hepatitis Foundation; NZSG; ADHB Antimicrobial Stewardship Committee; F Weilert, Gastroenterologist and Hepatologist	In order to prescribe the new treatments, clinicians should receive specialised education/training/support. This is particularly important for GPs prescribing Viekira Pak. GPs would not have had previous experience with these classes of treatment and there won't be oversight by a clinical panel in this situation .	In addition to the delay in funded access for GPs described in the above comment, a comprehensive implementation plan has been developed which involves GP education (Appendix 2) Educational material for primary care would be produced and disseminated through multiple channels: BPACnz, Goodfellow, RNZCGP, Ministry of Health and the PHARMAC website In addition there would be online training offered for GPs (CME accredited and endorsed by RNZCGP). We are also aware that the supplier (Abbvie) and the Ministry of Health are developing education for prescribers. AbbVie would provide a number of resources, detailed in its consultation response, which include an ePrescribing alert, websites for clinicians and patients, educational resources, a counselling service for patients and email and telephone support to clinicians. AbbVie also intends to attend a number of clinical education meetings to discuss its products.
Regional Project Managers working on Hep C services; Prof E Gane, NZLTU Auckland DHB; Prof C Stedman; D Ray-Chaudhuri NZLTU Auckland DHB; AbbVie; Northern Regional Alliance; RNZCGP; CDHB; C Henderson, PWID advocate; Hep C Resource Centre Otago; MoH Hep C Implementation Advisory Group; Needle Exchange Services Trust; NMDHB; NZ Sexual Health Society; NZNO; Hepatitis Foundation; NZSG	Funding should be provided for the additional GP consultations required for patients to receive the new proposed treatments. New funding for resources will be required in the community for implementation activities, patient counselling and in DHBs for additional diagnoses burden (laboratory tests etc)	The funding of services is outside of PHARMACs control, however PHARMAC staff will raise the concerns with relevant Health sector agents who are involved in service funding We note these costs have been included in our cost effectiveness and budget impact calculations where they are costs to the DHB. PHARMAC staff note that cost of service impacts may be short term, as, given there is a high cure rate, this would be offset by a significant reduction of ongoing management of the disease (e.g. clinic visits, monitoring for cirrhosis, blood tests, transplants etc) in the long term
Hepatitis Foundation; K Braddock, Chair of the GP Council of NZMA; G Noller, Researcher Substance Use and Policy Analysis; ADHB Antimicrobial Stewardship Committee; Pharmacy Guild; AbbVie; F Weilert, Gastroenterologist and Hepatologist; NMDHB; Northern Regional Alliance; NZMA; RNZCGP; Hepatitis Foundation; Pharmaceutical Society NZ	Expressed concerns regarding the direct distribution model of Viekira Pak due to the requirement for a secondary check for drug-drug interactions, need of ongoing patient monitoring and keeping patients' GPs informed.	Noted. The responsibility for distribution would lies with the supplier in this instance PHARMAC staff are aware that the supplier intends on purchasing services from community and hospital pharmacies to counsel patients and provide clinical oversight including engagement with the prescribing clinician A detailed summary on what services are anticipated by AbbVie in relation to counselling are included as Appendix 3

Hepatitis Foundation; Regional Project Managers; RNZCGP	Expressed concerns regarding the possibility of inequitable national roll out and clinical management in relation to people with hepatitis C	PHARMAC notes that these concerns relate to the Ministry of Health work on the implementation of regional approaches to hepatitis C detection, management and treatment PHARMAC staff note that 2 of the regions (Midland and Central) are expected to have plans implemented by 1 July 2016, with the following 2 regions (Northern and Southern) following on 1 October 2016. We note that this implementation is outside of PHARMAC control, however we are working closely with the MoH and have an implementation plan that supports this work to provide a 'whole of government' approach In addition, staff note that conversations with the clinicians involved in the Northern and Southern regions indicate that they consider their services would be in a position to manage these patients from 1 July 2016.
J Bourke – Nurse Specialist; Hep C Community Clinic Christchurch; ACC; Dr K Read, ID Specialist Waitemata DHB; ADHB AMS and ID groups; Drugs Health and Development Project; WDHB CADs Regional Consumer Advisory; Christchurch Hep C Resource Centre; Prof E Gane, NZLTU Auckland DHB; Hepatology SDHB; J Perry, Gastro WDHB; CDHB; Gastro at SDHB; Depts Clinical Pharmacology and ID, CDHB; M Chamberlain (unknown); Patient Wit; C Henderson, PWID advocate; Prof C Stedman, GE and Clinical Pharmacologist Christchurch Hospital; D Ray-Chaudhuri NZLTU Auckland DHB; F Weilert, Gastroenterologist and Hepatologist; Gilead; HFNZ; Hep C Resource Centre Otago; MoH Hep C Implementation Advisory Group; NZ Sexual Health Society; NZNO; patent relative; Patient Wit; NZSG; patient advocate; ADHB Antimicrobial Stewardship Committee; Hepatitis Foundation; Patient Wit; Advocate for Patient Wit; Family of Patient Wit	Request that access criteria for Harvoni is widened. This included a lower MELD score, the inclusion of patients where Viekira Pak is not a treatment option (e g in patients who have previously failed boceprevir treatment) or where treatment with Viekira Pak fails.	PHARMAC staff note that other new hepatitis C treatments are still an option for investment and we would pursue these should the opportunity arise.
Prof C Stedman; F Weilert, Gastroenterologist and Hepatologist	Amendments should be considered for the cryoglobulinaemia criteria. The proposed criteria would very seldom occur in conjunction with each other in a clinical situation.	Noted PHARMAC staff have proposed amendments to the criteria.
Prof C Stedman; D Ray-Chaudhuri NZLTU Auckland DHB; F Weilert, Gastroenterologist and Hepatologist; MoH Hep C Implementation Advisory Group; Hepatitis Foundation	Indicated that assessment of liver fibrosis should be performed before treatment commences.	Noted.

ASID; Dr K Read, ID Specialist Waitemata DHB	Ribavirin should be provided in a form where it is not co-packaged with pegylated interferon.	Ribavirin (in relation to the supply of Harvoni) would be dispensed directly from the distributing pharmacy without pegylated interferon.
Prof E Gane, NZLTU Auckland DHB; Prof C Stedman; D Ray Chaudhuri NZLTU Auckland DHB; F Weilert, Gastroenterologist and Hepatologist; NZ Sexual Health Society; Withheld under (unknown);	Access to Harvoni should be widened to patients with HIV and/or hepatitis B coinfection.	PHARMAC staff note the clinical advice we have received indicates that being co infected with HCV and HIV is not, in itself, a reason to prioritise funding with a new hepatitis C treatment Patients who are co-infected with hepatitis C may access Harvoni and Viekira Pak/Viekira Pak-RBV under the same requirements as those patients who are not co-infected. PHARMAC is willing to seek further clinical advice on these groups of patients should further information be submitted that supports earlier access to these treatments
NZSG	Children with chronic hepatitis C should only receive treatment under the care of a specialist.	Education around this issue would be included in the information provided to clinicians.
Patient Wit	Unsupportive of Gilead aspect noting medical, ethical and fiscal reasons. The respondent considers the supplier's behaviour has been profiteering and that in letting patients become cirrhotic before treatment, they create incurring ongoing costs to the health system.	Noted.
MSD	Concern that the commercial terms of listing would provide a barrier to entry to other products prior to July 2019	Noted This aspect was considered prior to entering into the provisional agreements with Gilead and AbbVie PHARMAC staff note that all potential suppliers of hepatitis c treatments were given equal opportunity to submit pricing for the supply of their products and were advised that PHARMAC may choose to contract with just one supplier following assessment of proposals.

Legal Advice

Where necessary, management will obtain legal advice on issues such as whether any proposal is consistent with PHARMAC's legislative and public law obligations, including those which may have specific relevance to the particular proposal eg human rights implications of a proposal. If the Board considers that further legal advice is required on any issue, this should be communicated to management in advance of the Board meeting. Management will then obtain the required advice

Legal Advisors' View

[redacted] Withheld under section 9(2)(j)

[redacted] Withheld under section 9(2)(j)

Implementation

PHARMAC staff have developed a comprehensive implementation plan which outlines all proposed implementation activities to support the listing of Harvoni and Viekira Pak/Viekira Pak RBV This is attached as Appendix 2.

Decision Criteria

Set out below is PHARMAC staff's assessment of the application of the decision criteria in section 2 2 of the Operating Policies and Procedures This assessment is intended for discussion purposes, is not necessarily exhaustive and is not a substitute for the analysis contained in the paper The Board is not bound to accept PHARMAC staff's assessment of the application under the decision criteria and may attribute different weightings to each of the criteria from those attributed by PHARMAC staff.

1 *The health needs of all eligible people within New Zealand;*

Hepatitis C is estimated to affect 50,000 New Zealanders. The Harvoni proposal is expected to provide a treatment option for approximately 250 patients per annum with end stage liver disease The Viekira Pak proposal would provide a treatment option for up to 28,500 patients. Treatment is considered to be curative in more than 90% of people. This would help reduce the risk of these people developing serious liver disease and the complications of this disease

In addition, a patient who is cured would no longer be able to transmit the infection.

2 *The particular health needs of Māori and Pacific peoples;*

Māori are considered to be over represented in the population with hepatitis C. There is no data in relation to Pacific people.

3 *The availability and suitability of existing medicines, therapeutic medical devices and related products and related things;*

There are currently 2 treatment options, pegylated interferon/ribavirin and boceprevir. Harvoni and Viekira Pak would offer clinical advantages over currently funded options, in that current options have lower treatment success rates, are contraindicated in a large number of people and have significant adverse effects.

4 *The clinical benefits and risks of pharmaceuticals;*

These new treatments are considered to be curative in more than 90% of people who take them. They are considered to be less toxic than current treatments; however there are significant interactions associated with the use of Viekira Pak PHARMAC staff have proposed a number of mitigations in the implementation plan to address these.

5. *The cost-effectiveness of meeting health needs by funding pharmaceuticals rather than using other publicly funded health and disability support services;*

The proposal to list Viekira Pak is cost saving to DHBs as well as giving a large health gain per person The proposal to list Harvoni gives about Wit QALYs per $1 million spent (likely range Withhel QALYs/$1m).

6. *The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule;*

The Harvoni proposal would have a 5-year NPV budget impact of approximately Withhel Withhel to the CPB and Withheld under to DHBs overall. The Viekira Pak proposal would have a 5-year NPV budget impact of approximately Withheld under to the CPB and Withhel Withhel to DHBs overall.

7. *The direct cost to health service users;*

It is proposed that a co-payment waiver would be sought for these treatments noting that they will be dispensed via direct distribution. It is also noted that patients may require additional GP visits while on treatment

8. *The Government's priorities for health funding, as set out in any objectives notified by the Crown to PHARMAC, or in PHARMAC's Funding Agreement, or elsewhere; and*

PHARMAC staff note the MoH key performance indicators in relation to the development of regional services to deliver identification and treatment for people at risk of or with hepatitis C These include a measure of people receiving PHARMAC funded antiviral treatment. We consider the availability of a further two treatments for hepatitis C would support this initiative.

One of the government's priority areas is care closer to home. The Viekira Pak proposal involves funding a new oral treatment for hepatitis C that can be started and managed in the community, which allows patients the option of receiving treatment closer to home.

9 *Such other criteria as PHARMAC thinks fit*

No other criteria are relevant to assessing this proposal

Appendices

Appendix 1 Resolutions

Appendix 2 - Implementation plan

Appendix 3 AbbVie's plans in relation to distribution support

Appendix 4 Drug drug interaction chart

Appendix 5 – Ministry of Health Guidance to support the development of regional services to deliver identification and treatment for people at risk or with hepatitis C

Appendix 6 PTAC minutes

Appendix 7 Methods used to assess liver disease

Appendix 8 Consultation Letter

Appendix 9 – Consultation Responses

MINUTES OF THE PHARMACEUTICAL MANAGEMENT AGENCY (PHARMAC)

BOARD TELECONFERENCE MEETING, 8 JUNE 2016

The meeting was held by teleconference, starting at 6:00pm with the following attendees:

Present

Stuart McLauchlan	Chairman
David Kerr	Acting Deputy Chairman, Board Member
Jens Mueller	Board Member
Jan White	Board Member
Nicole Anderson	Board Member
Mark Weatherall	Observer, PTAC Chair
Shane Bradbrook	Observer, CAC Chair
David Lui	Observer, CAC Deputy Chair
Nigel Murray	Observer, DHB

In attendance

Steffan Crausaz	Chief Executive
Sarah Fitt	Director of Operations
John Wyeth	Medical Director
Lizzy Cohen	Board Secretary

Lisa Williams, Danae Staples-Moon, Geraldine MacGibbon, Adrienne Martin, Katie Appleby and Anthony Bull (PHARMAC staff) attended.

1. Budget Impact Supplement to 2016/2017 Investment Proposals

1.1. Budget 2016 supplementary Board paper

noted this paper

2. hepatitis C treatments

2.1 Proposal to list hepatitis C treatments

resolved to approve the resolutions outlined in Appendix One of this Board paper;

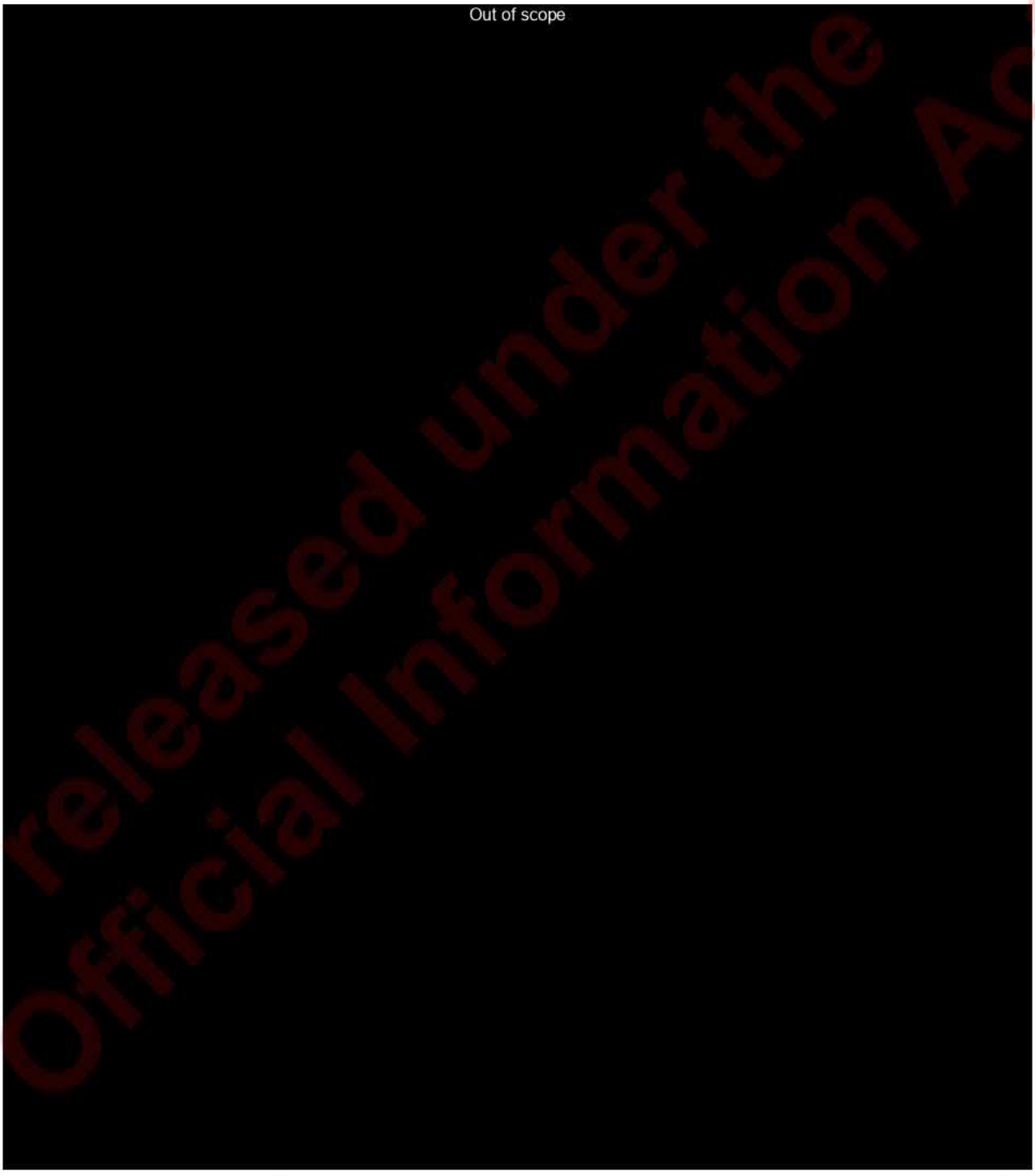
resolved to approve the 22 April 2016 agreement with Gilead;

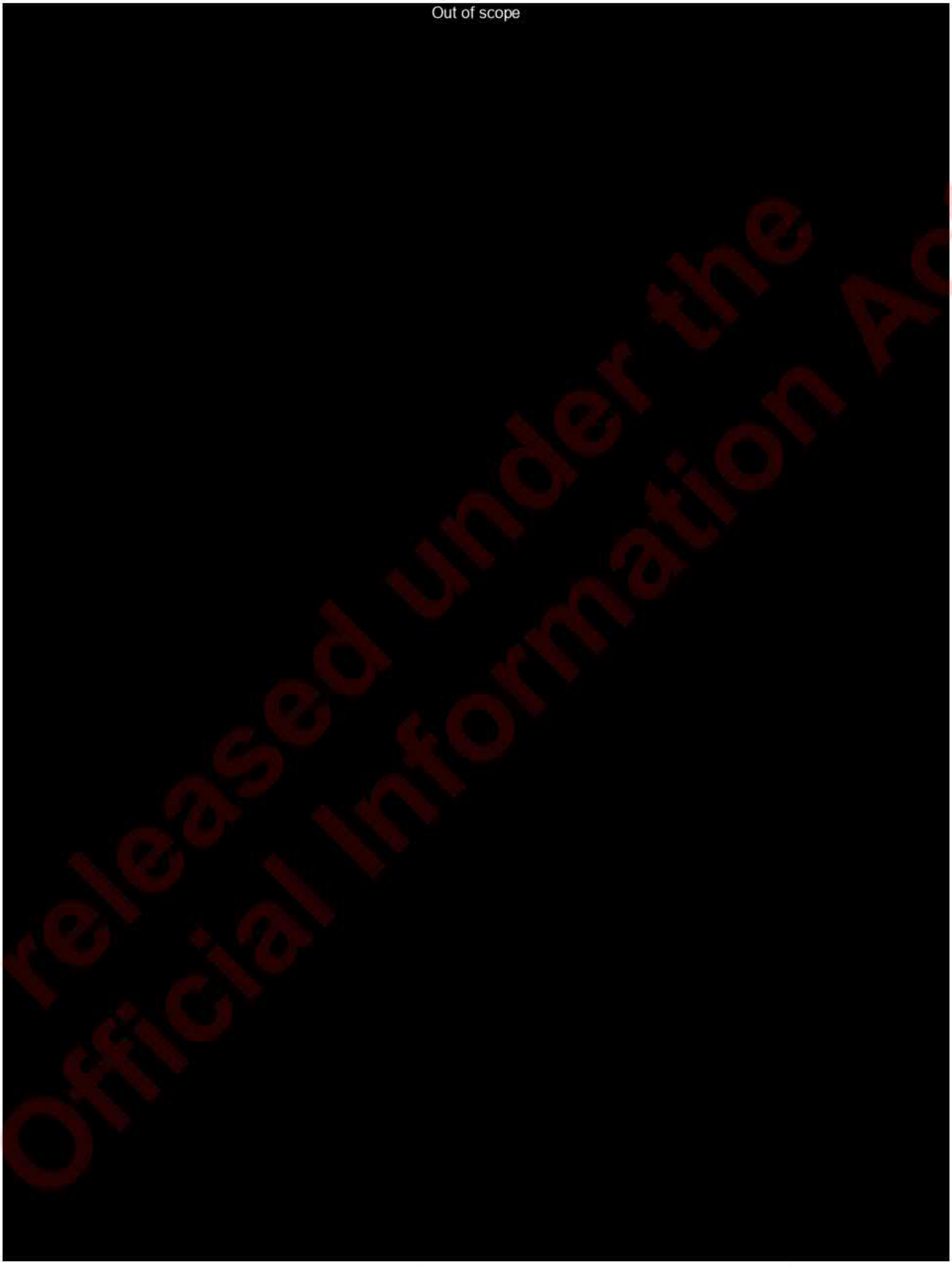
resolved to approve the 20th April 2016 agreement with AbbVie Ltd subject to an amendment to apply a prescriber restriction to the listing from 1 July 2016 to 1 October 2016; and

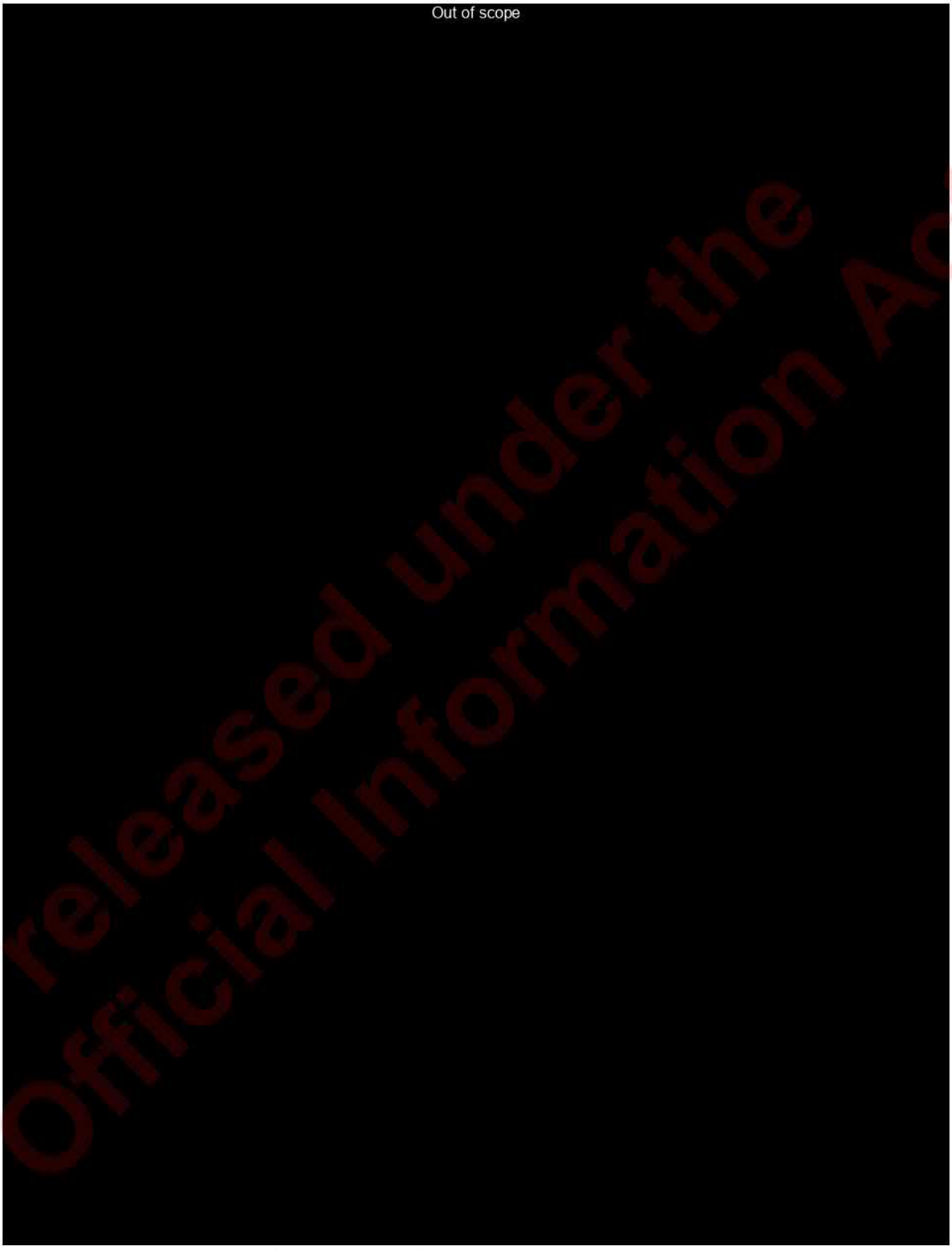
resolved that the consultation on this proposal was appropriate, and no further consultation is required.

Jens Muller and Jan White **(carried)**

3. nivolumab (Opdivo) for advanced melanoma







Date of Next Meeting

The date for the next Board meeting is set for Friday 1 July 2016 (June Board meeting) in Wellington, commencing with the Directors only from 9.30am, and attendees and relevant staff from 10.00am.

The meeting closed at 6.50pm

Chairman

9 June 2016

Date

PHARMAC
Pharmaceutical Management Agency

MEMORANDUM FOR CONSIDERATION BY DIRECTOR OF OPERATIONS UNDER DELEGATED AUTHORITY

To: Director of Operations

From: Manager Pharmaceutical Funding

Date: May 2017

Proposal to widen funding criteria for Ledipasvir with Sofosbuvir (Harvoni)

Recommendations

It is recommended that having regard to the decision making framework set out in PHARMAC's Operating Policies and Procedures you exercise your delegated authority and:

resolve to expand funded access to ledipasvir with sofosbuvir (Harvoni) tab 90 mg with sofosbuvir 400 mg from 9 June 2017 by changing the current access criterion for patients with decompensated cirrhosis to reduce the MELD score from 15 or greater to 12 or greater;

resolve to amend the restriction for ledipasvir with sofosbuvir (Harvoni) tab 90 mg with sofosbuvir 400 mg in Section B of Pharmaceutical Schedule from 1 July 2017 to as follows (additions in bold, deletions in strikethrough):

Access criteria:
Chronic hepatitis C – Advanced disease– where ribavirin is not contraindicated. Applications from any relevant practitioner. Approvals valid for 12 weeks for applications meeting the following criteria:
All of the following:
1. Patient has chronic hepatitis C (any genotype); and
2 Ribavirin treatment is not contraindicated; and
3. Any of the following:
- 3 1 Patient has decompensated cirrhosis with a MELD score of ~~15~~ **12** or greater; or
- 3.2 Patient has been accepted onto a list for a liver transplant or has received a liver transplant; or
- 3.3 Patient has essential mixed cryoglobulinaemia with associated purpuric skin rash and; Either
  - 3.3.1 Cryoglobulinaemic glomerulonephritis; or
  - 3 3 2 Systemic vasculitis

Chronic hepatitis C – Advanced disease where ribavirin is contraindicated Applications from any relevant practitioner. Approvals valid for 24 weeks for applications meeting the following criteria:
All of the following:
1. Patient has chronic hepatitis C (any genotype); and
2. Ribavirin treatment is contraindicated; and
3. Any of the following:
- 3.1 Patient has decompensated cirrhosis with a MELD score of ~~15~~ **12** or greater; or
- 3 2 Patient has been accepted onto a list for a liver transplant or has received a liver transplant; or
- 3 3 Patient has essential mixed cryoglobulinaemia with associated purpuric skin rash and; Either
  - 3 3 1 Cryoglobulinaemic glomerulonephritis; or
  - 3.3.2 Systemic vasculitis.

note no restriction change is required for Part II of Section H of the Pharmaceutical Schedule as hospital access requires patients to have a valid Special Authority approval according to the criteria set out in Section B of the Schedule;

note that widening of access to ledipasvir with sofosbuvir (Harvoni) tablets as detailed above would appear in the printed and online Pharmaceutical Schedule from 1 July 2018;

note that funded access from 9 June 2017 would be possible to implement without a change to the printed or online Pharmaceutical Schedule because the funding and distribution of ledipasvir with sofosbuvir (Harvoni) is managed by PHARMAC and the application form is not a standard Special Authority;

note that updated application forms would be distributed to relevant clinicians along with notification of the decision;

resolve that consultation on this proposal was appropriate, and no further consultation is required.

SUMMARY OF PROPOSAL				
Market data	**Year ending**	**30 Jun 2017**	**30 Jun 2018**	**30 Jun 2019**
	Number of total patients	102	86	67
	Number of additional patients from this proposal	22	37	37
Combined Pharmaceuticals	Subsidy (gross)	Withheld	Withheld	Withheld
	Net cost to Schedule	Withheld	Withheld	Withheld
	Net present value	Withheld		
	Net distribution costs	$0	$0	$0
	Net cost to DHBs	Withheld	Withheld	Withheld
	Net present value	Withheld		
Hospital Pharmaceuticals	Expenditure (gross)	$0	$0	$0
	Net cost to DHBs	$0	$0	$0
	Net present value	$0		
Other DHB costs	Net cost to DHBs	($37,000)	($100,000)	($120,000)
Total	Total cost to DHBs	Withheld	Withheld	Withheld
	Net present value	Withheld		

Notes:

1. Subsidy (gross) = forecast of spending on ledipasvir+sofosbuvir (Harvoni) at the proposed subsidy.
2. Net cost to Schedule = forecast of change in total spending on pharmaceuticals listed on the Schedule compared with status quo.
3 Other DHB costs = management and monitoring of patients with decompensated cirrhosis
4. Costs before 1 July 2017 due to patients being treated before 1 July 2017.
5. Net cost to DHBs = changes in DHB costs associated with successful treatment of patients.
6. Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j) Distribution reflects the entire prescription distributed at one time
7 All costs are expressed ex manufacturer, excluding GST
8. NPV is calculated over 5 years using an annual discount rate of 8%.
9. Calculations in A1034765.

Why proposal should be considered by the Director of Operations under Delegated Authority

The proposal involves a Schedule change that has an estimated Financial Impact (NPV) of less than $10,000,000 and:

- will not result in the Pharmaceutical Budget or its future funding path being exceeded;
- is not inconsistent with previous Board decisions; and
- is not considered contentious by PHARMAC staff

Background and Analysis

Background

- Ledipasvir and sofosbuvir (Harvoni) is a combination treatment of two antiviral agents that is active against all genotypes (1-6) of the hepatitis C virus.
- In May 2015, PTAC reviewed the application for Harvoni and recommended it should be funded for all patients with decompensated cirrhosis with a high priority.
- Since July 2016, two new treatments have been funded for hepatitis C: Harvoni (ledipasvir with sofosbuvir) and Viekira Pak (paritaprevir with ritonavir and ombitasvir with dasabuvir) and Viekira Pak-RBV (paritaprevir with ritonavir and ombitasvir with dasabuvir and ribavirin)
- Ledipasvir with sofosbuvir (Harvoni) is currently funded for patients with chronic hepatitis C with advanced disease who meet the access criteria (as detailed above without the marked up changes) on application to the Hepatitis C Treatment Panel. Current access criteria require patients to have decompensated cirrhosis with a MELD score of 15 or greater This criteria was put in place to target funding to the paients with the highest health need and limit the financial impact of funding Harvoni. PHARMAC previously indicated that once further information was obtained in relation to uptake and use of Harvoni, the requirement to have a MELD score of 15 or greater may be reviewed.
- Viekira Pak is active against genotype 1 of the hepatitis C virus and is listed on the Pharmaceutical Schedule without any funding criteria restrictions
- Applications for Harvoni are considered by the Hepatitis C Treatment Panel, which include hepatitis C treatment specialists, and are approved subject to confirmation of eligibility criteria. Following a decision, the PHARMAC Hepatitis C Panel Co ordinator organises for the medicine to be dispensed from a central pharmacy and delivered to a specified address.
- In June 2016, when PHARMAC announced the decision to fund Harvoni and Viekira Pak for hepatitis C from 1 July 2016, we noted that we had received feedback from our consultation requesting that access to ledipasvir with sofosbuvir (Harvoni) be widened via reduction of the end stage liver disease (MELD) score
- PHARMAC staff estimate that a change of the MELD score from 15 to 12 (as is proposed) would benefit around 30 45 people per year, with costs as set out above, and a cost-effectiveness of around Wit QALYs per $million invested (TAR available at

Objective ID A1039635)

- Although this proposal has not been formally prioritised, a proposal for funding all patients with decompensated cirrhosis and all non genotype 1 hepatitis C has been prioritised at number Wit out of Wit proposals on the Options for investment list. PHARMAC staff believe that the proposal to reduce the MELD score to 12 compares favourably to other proposals that are being recommended for funding from 1 July 2017.

Proposal

- The proposal is to widen the funding criteria for Harvoni for the treatment of hepatitis C to include patients with a lower end stage liver disease (MELD) score of 12 or greater.

Agreement (if applicable)

- There is an existing agreement with Gilead for the supply of Harvoni signed 22 April 2016. The proposal to widen access has been discussed with Gilead during the consultation. A confidential rebate applies and there would be no change to terms of this agreement (Objective ID A927889)

Health Need

- The hepatitis C virus (HCV) is a small, enveloped, single-stranded, positive-sense RNA virus. HCV patients are typically infected with 1 of 6 viral genotypes. In New Zealand, this is dominated by genotypes one (56%) and three (35%) Genotype two (8%), four (0.5%) and six (1%) make up a small percentage overall (Gane, et al. NZMJ 2014;127(1407):61-74).

- Hepatitis C virus can cause both acute and chronic hepatitis. The acute process is self limited, rarely causes hepatic failure, and usually leads to chronic infection. Approximately 25% of HCV infected patients spontaneously clear the virus without treatment. Chronic HCV infection often follows a progressive course over many years and can ultimately result in cirrhosis, hepatocellular carcinoma, and the need for liver transplantation. Hepatitis C is now the most common reason for liver transplant in New Zealand (in 2013, 54% of all adult transplants were attributable to HCV). It is estimated that 50,000 people in NZ are infected with HCV; of those infected, 50 60% are undiagnosed.

- People infected with Hepatitis C who have decompensated cirrhosis and a MELD score of 15 or more are considered eligible for a liver transplant Without the transplant, their chance of surviving more than 12 months is around 85%. People with a MELD score of 11 have a one year survival rate of around 94%

- 10% of people receiving a liver transplant die with 12 months, even if their Hepatitis C infection has been cured Mortality rates in later years are about 2%

- For people infected with Hepatitis C with decompensated cirrhosis and an existing MELD score under 15, the median increase in MELD score is approximately 3 2 points per year (O'Leary, et al Gastroenterology 2011; 140(7): 1871 1874) Hence under current funded treatment, all people with a MELD score of 12 and greater are likely to become eligible for a transplant if they live for more than one year, when continuing liver damage will likely raise their MELD score above 15.

- The New Zealand population with chronic Hepatitis C has an average age of 45 (standard deviation +/ 15 years); 42% are women.

- A pilot program in two regions found a higher prevalence in Maori (19% vs census 14%). A 2002 paper suggested no difference by ethnicity, but it had little data. Hepatitis C is more prevalent in injecting drug users and in prisoners, more of whom may be Maori.

- Viekira Pak and Viekira Pak RBV are registered for hepatitis C patients with genotype 1, and has high efficacy across a broad range of patients, including those with cirrhosis of the liver, but they are contraindicated for patients with decompensated cirrhosis

- Harvoni is currently listed on the Pharmaceutical Schedule for the treatment of hepatitis C patients of all genotypes with severe liver disease (MELD score of 15 or greater) and is combined with ribavirin in patients with decompensated cirrhosis Treatment in combination with ribavirin is 12 weeks. Where ribavirin is contraindicated, a treatment course of Harvoni is 24 weeks.

- There is a current unmet health need for HCV infected patients with decompensated liver disease who have a MELD score of less than 15 PHARMAC received numerous responses to consultation on the proposal in this paper requesting either that the MELD score criteria be reduced further or removed entirely and funded access of Harvoni be available for all HCV infected patients with decompensated cirrhosis PHARMAC staff are continuing to assess this option.

Health Benefit

- In May 2015, PTAC reviewed the application for Harvoni and recommended it should be funded for all patients with decompensated cirrhosis with a high priority
- Lowering the minimum MELD score criterion for Harvoni funding from 15 to 12 would approximately double the number of patients for the first 1 to 2 years, but thereafter the expected number should fall back to 30-50 patients per annum that will be eligible to access funded treatment earlier in their disease course. We are proposing to widen funded access before 1 July 2017 following approval of this proposal to utilise available funding from the 2016/2017 financial year; it is estimated that an additional 22 patients could access Harvoni in this financial year.

- Reducing the MELD score requirement to 12 and above would improve the likelihood of preventing patients with advanced liver disease from dying or deteriorating to the point where they are placed on a waiting list for a liver transplant Over 5 years, it is estimated that there is an approximate 25% reduction in deaths due to treating patients at MELD score 12 rather than MELD score 15. Clinical feedback received in consultation noted that reducing the MELD score requirement to 10 or removing it entirely would better target those patients that have the most to gain from not having a liver transplant

- The chance of a Sustained Virological Response (SVR) varies by genotype. Reported trials suggest that for people with advanced disease, the proposed treatments achieve an SVR in 86 to 88% of people infected with genotype 1, and 65% in genotype 3. There is a paucity of data available on the efficacy of the regimen for genotype 2 patients, however, SVR generally falls in between that of rates achieved for genotype 1 and 3 and is assumed to be approximately 80%

- The efficacy of Harvoni for patients infected with HCV genotype 3 with

decompensated cirrhosis is reduced compared to other genotypes with an SVR12 of 65%. Historically genotype 3 has been difficult to treat, but all currently funded treatments require the use of peginterferon, which is contraindicated in patients with decompensated cirrhosis Harvoni represents an improvement on treatment options available for this sub-population of patients.

- Earlier treatment is likely to result in reduction in the number of patients that require liver transplants, freeing up space in the liver transplant unit for other patients.

- Overall, we estimate that compared to the status quo, the incremental health gain per person treated under the proposal would be 1.66 Quality-adjusted life years per person (NPV at 2.5%).

We have not identified any information as to the extent to which the proposal could provide significant health benefits to others.

Suitability

- Harvoni is administered as a single daily tablet with a relatively short duration of treatment for most patients of 12 weeks Harvoni has a low side effect profile, and can be taken with or without food.

Costs and Savings

- A course of treatment with Harvoni is around Withheld, including all associated costs of tests. Distribution of Harvoni is paid by Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j) Withheld under section 9(2)(b)
- A single liver transplant costs DHBs $141,900. Other annual costs including hospital administration, and management and monitoring of patients with decompensated cirrhosis are in the range of $8,000 to $16,000 per year, some but not all of which would be reduced in the case of a successful SVR. Also, because mortality is reduced by the proposals, in later years more people will be under treatment, increasing some costs
- PHARMAC staff estimate that the proposal would cost the Combined Pharmaceutical Budget (CPB) around Withheld under (5 year NPV, 8%) The cost offsets expected to DHBs are estimated to be a savings of Withheld (5 year NPV, 8%).
- We are proposing to widen funded access from 9 June 2017 to utilise available funding from the 2016/2017 financial year. It is estimated that an additional 22 patients could access Harvoni in this financial year (2016/17) at a total cost to the CPB of Withheld, which reflects distribution of the full prescription, however, the number of patients is difficult to accurately estimate.
- The key risk in the budget impact analysis is that patient numbers could be above that forecast (forecasts are based on actual treatment uptake to date), however PHARMAC staff note that actual patient numbers to date have been below that originally forecast in 2016 in the original listing

Cost-effectiveness

- PHARMAC staff estimate that the benefits and costs discussed above mean that the likely incremental value of the proposal is between Wit and Wit QALYs per $million invested
- PHARMAC staff note that removing the MELD criterion altogether is estimated to have an incremental value of between Withheld QALYs per $million invested and this may be the subject of a future proposal once patient numbers and the fiscal impact

has been assessed, and the availability of funding is confirmed

Comments from Interested Parties

Section 49(a) of the New Zealand Public Health and Disability Act 2000 (the Act) requires PHARMAC to consult, when it considers appropriate to do so

Accordingly, a consultation letter was circulated on 21 April 2017. The consultation letter and all responses received by 26 May 2017 are attached as Appendix 1.

Eighteen responses were received in relation to the widening of access to Harvoni; responders included clinicians and other groups/individuals.

Summaries of what PHARMAC staff believe are the significant matters raised in these responses are provided in the table below

Stakeholder group	Theme	PHARMAC Staff Comment
NZ Society of Gastroenterology Gastroenterology Department Christchurch Hospital	Supportive of the proposal Reduction of the MELD score to 12 and above will improve the likelihood of preventing these patients from requiring transplantation or death.	Noted.
	The efficacy of Harvoni (with/without ribavirin) is lower in patients infected with HCV genotype 3 (SVR12 of 65%). Noted that EPCLUSA is a pangenotypic regiment with improved efficacy for HCV genotype 3 infection.	While the efficacy of Harvoni is reduced in Genotype 3 HCV patients, Harvoni represents an improvement on treatment options available for this high need sub-population of patients
	Widening of access to Harvoni will not be enough to impact HCV prevalence, incidence or meet WHO targets.	PHARMAC notes that 50-60% of HCV infected individuals in NZ are currently undiagnosed. The identification and treatment of these individuals will be critical for reducing the incidence of and reinfection rates of HCV PHARMAC understands the MoH and other relevant stakeholder groups are working hard to improve the diagnosis and treatment of undiagnosed and high risk individuals
	Funding of Viekira Pak for genotype 1 patients has already resulted in a 20 fold increase in treatment uptake.	Noted.
	Large unmet health need for patients with HCV genotypes 2 6; the funding of pangenotypic direct-acting antiviral regiment (DAA) to treat these patients is needed.	Even further widening of funded access remains an option for PHARMAC We are aware that a number of suppliers are developing DAA hepatitis C treatments to treat all genotypes. We continue to explore the options for widening funded access to DAAs within the available budget

Royal New Zealand College of General Practitioners	Supports widening of access Large unmet health need for patients with HCV genotypes 2 6 Notes significant resource and effort to improve diagnosis but significant barriers to treatment still exist. GP consultations for Viekira Pak are more complicated, take longer and have administrative burden to source the medicine Note increased pressure from patients to provide access to unfunded generic treatments. The funding of pangenotypic direct-acting antiviral regiment (DAA) to treat these patients is needed.	See above Noted. See above.
Frank Weilert Waikato DHB	Requests that the MELD score requirement be 10 or above for patients with decompensated cirrhosis Considers this would target those patients with the most to gain from not having a liver transplant	Noted. PHARMAC will continue to assess potential options for expansion of funded access to DAA hepatitis C treatments
Gastroenterology team at Southern DHB (Margaret Fraser, Michael Shultz, Margaret Pickles, Merrilee Williams, Elizabeth Glen)	Support widening of access Request funding for patients that are decompensating and contraindicated for Viekira Pak with a lower MELD score. Consider this will reduce cost to health system. Greatly appreciate funding of Viekira Pak plus ribavirin, but note that many patients are unable to be treated due to comorbidities and poly-pharmacy. Note that GPs are resistant to prescribe, treat and monitor due to drug interactions and time required. Request funding of Zepatier for genotype 1 patients due to simplicity of treatment regime and less drug interactions Request funding of generic sofosbuvir to be used with Viekira Pak and Zepatier for the treatment of genotype 1 and genotype 3 HCV infected patients	 Noted PHARMAC will continue to assess potential options for expansion of funded access to DAA hepatitis C treatments. Noted PHARMAC is working closely with the MoH and clinicians to understand any barriers and improve diagnosis and prescribing of hepatitis C treatments in primary care. Noted. See above
Simon Clayton (Hepatitis C NZ – patient support group)	Supports widening of access Notes that the current drug company pricing prevents treatment of the Hepatitis C epidemic in NZ. Suggests that PHARMAC fund cheaper generic drugs for large-scale treatment of Hepatitis C	Noted

The Drugs, Health and Development Trust	Support widening of access and raised concern that patients accessing generic Harvoni from overseas may not receive professional advice and follow up care Note that extra information and prevention campaigns in prisons may help prevent reinfections	Noted PHARMAC understands the MoH, clinicians and other stakeholder groups are working hard to improve the diagnosis and treatment of high risk individuals with hepatitis C, including individuals in prisons.
Northern Region Hepatitis C Steering Group	Fully endorse the lowering of the MELD score threshold to 12 Request that PHARMAC address funding for all Hepatitis C patients independent of genotype or degree of liver function.	Noted. PHARMAC will continue to assess potential options for expansion of funded access to DAA hepatitis C treatments.
Matua Raki National Addiction Workforce Development The Addiction Practitioner's Association Aotearoa NZ (dapaanz)	Support the widening of funding, but note that it is insufficient to reduce the harm associated with chronic HCV. Support the widening of funded access to anyone with non genotype 1 HCV, which will reduce the need for patients to access cheaper overseas alternatives which may be potentially harmful	Noted. PHARMAC will continue to assess potential options for expansion of funded access to DAA hepatitis C treatments.
Ministry of Health HCV Implementation Committee	Reduction of the MELD score to 12 and above will improve the likelihood of preventing these patients from requiring transplantation or death The efficacy of Harvoni (with/without ribavirin) is lower in patients infected with HCV genotype 3 (SVR12 of 65%). Noted that EPCLUSA is a pangenotypic regiment with improved efficacy for HCV genotype 3 infection. Funding of Viekira Pak for genotype 1 patients has already resulted in a 20 fold increase in treatment uptake. Large unmet health need for patients with HCV genotypes 2 6; the funding of pangenotypic direct-acting antiviral regiment (DAA) to treat these patients is needed.	Noted. While the efficacy of Harvoni is reduced in Genotype 3 HCV patients, Harvoni represents an improvement on treatment options available for this high need sub-population of patients Noted. PHARMAC will continue to assess potential options for expansion of funded access to DAA hepatitis C treatments.
Dr. Allan Moffit, ProCare	Supportive of the proposal. Notes that access to Harvoni from primary care rather than secondary care specialist services would provide a logical extension for Hepatitis C management	All prescribers, including general practitioners, can apply to the Hepatitis C Treatment Panel for funded Harvoni for eligible people The application form can be found on PHARMAC's website here.

Auckland DHB Antimicrobial Stewardship Committee	Supportive of the proposal Request funding for patients coinfected with HIV or hepatitis B and contraindicated for Viekira Pak earlier in their disease course as well as patients unable to be treated with Viekira Pak due to drug interactions	Noted PHARMAC has received clinical advice regarding the funding of Harvoni for patients co infected with HIV and Hepatitis C and will continue to assess potential options for expansion of funded access to DAA hepatitis C treatments.
The Hepatitis Foundation of New Zealand	Consider the proposal to widen access to patients with a MELD score of 12 or greater is a minor extension to the current funding and in the Bay of Plenty DHB will only allow treatment of one additional patient. Note inequities in availability of funded treatments dependent on genotype Request PHARMAC to expedite assessment of glecaprevir and pibrentasvir, which is suitable treatment for all HCV genotypes	Noted PHARMAC will continue to assess potential options for expansion of funded access to DAA hepatitis C treatments
Medicines Utilisation Committee, Canterbury DHB	Supportive of the proposal	Noted.
Gilead Sciences	Requests that funding be widened to include all HCV infected individuals with decompensated liver disease who are Child Pugh B or C Request Harvoni funding be widened to include treatment of patients with non genotype 1 HCV, contraindicated for Viekira Pak or failed Viekira Pak treatment.	PHARMAC will continue to assess potential options for expansion of funded access to DAA hepatitis C treatments.
Pharmacy Guild of New Zealand	Supportive of the proposal. Requests that PHARMAC change the distribution arrangement for Harvoni to involve community pharmacy.	Noted PHARMAC staff note the distribution of Harvoni was thoroughly considered at the time of the initial listing in 2016 and PHARMAC staff consider this system remains appropriate for now We note the distribution mechanisms for Harvoni and Viekira Pak are different for several reasons, including differences in access criteria, cost and patient numbers
Ministry of Health	Note that there no technical or resource impacts are anticipated because of the proposal	Noted

Legal advisors' view

Legal advice has not been sought on this proposal because PHARMAC staff do not consider it to be contentious or to raise any issues of legal concern

Implementation

Section 49(b) requires PHARMAC to take measures to inform the public, groups and individuals of PHARMAC's decisions concerning the pharmaceutical schedule Accordingly, if the Director of Operations adopts the recommendations contained in this paper PHARMAC

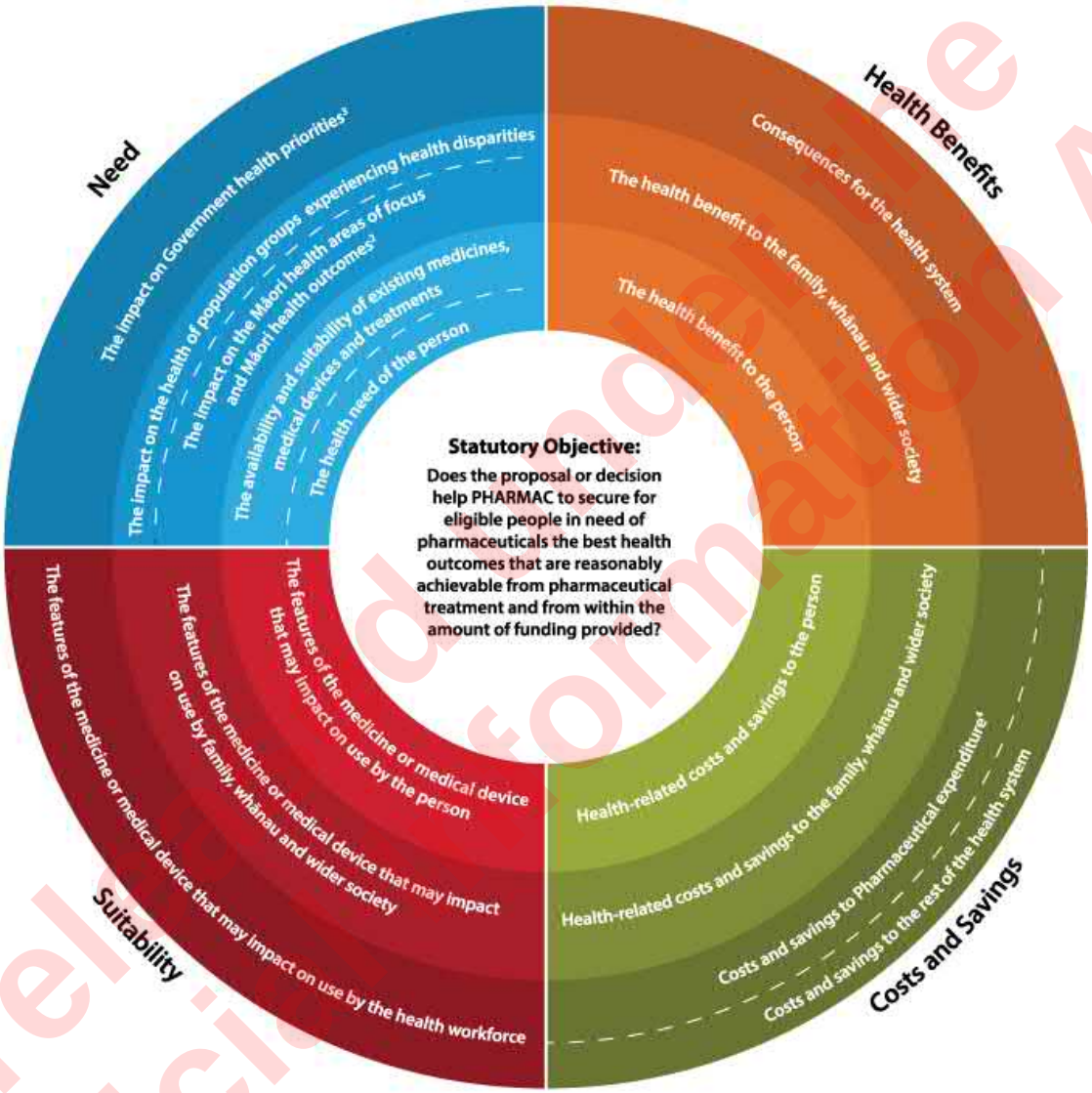
staff will notify all suppliers, and implement the listing of these products via the usual Schedule processes

To implement this change, PHARMAC staff would do the following:

- Notify all suppliers and respondents to consultation, and implement the changed listing via the usual Schedule processes
- Write to all relevant prescribers (particularly in secondary care and those that have previously applied to the Panel for funded access to Harvoni patients with a MELD of 15 or higher) to notify them of the decision to widen access and:
    - confirm the new access criteria;
    - detail how to apply & enclose updated application forms;
    - encourage prompt submission of applications to ensure we can process applications and dispense treatment promptly in order to make use of available funding from the 2016/2017 financial year
- Update website
    - Panels information and application forms
    - Access criteria information
- Set up an urgent Panel meeting to ensure any applications received from 9 June onwards can be promptly considered.

Factors for Consideration

This paper sets out PHARMAC staff's assessment of the proposal using the Factors for Consideration in the Operating Policies and Procedures. Some Factors may be more or less relevant (or may not be relevant at all) depending on the type and nature of the decision being made and, therefore, judgement is always required The decision maker is not bound to accept PHARMAC staff's assessment of the proposal under the Factors for Consideration and may attribute different significance to each of the Factors from that attributed by PHARMAC staff



Footnotes

[1] The person receiving the medicine or medical device must be an eligible person, as set out in the Health and Disability Services Eligibility Direction 2011 under Section 32 of the New Zealand Public Health and Disability Services Act 2000

[2] The current Māori health areas of focus are set out in PHARMAC's Te Whaioranga Strategy.

[3] Government health priorities are currently communicated to PHARMAC by the Minister of Health's Letter of Expectations.

[4] Pharmaceutical expenditure includes the impact on the Combined Pharmaceutical Budget (CPB) and / or DHB hospital budgets (as appropriate).

5. Please note PHARMAC's Factors for Consideration schematic currently does not explicitly refer to the health needs of family, whānau and wider society, but this factor should be considered alongside those depicted in the schematic.

PHARMACEUTICAL MANAGEMENT AGENCY (PHARMAC)

MINUTE OF THE DIRECTOR OF OPERATIONS DECISION UNDER DELEGATED AUTHORITY

JUNE 2017

The Director of Operations, exercising the authority delegated by the Chief Executive under the Financial Delegations Policy has made the following decision to:

resolve to expand funded access to ledipasvir with sofosbuvir (Harvoni) tab 90 mg with sofosbuvir 400 mg from 9 June 2017 by changing the current access criterion for patients with decompensated cirrhosis to reduce the MELD score from 15 or greater to 12 or greater;

resolve to amend the restriction for ledipasvir with sofosbuvir (Harvoni) tab 90 mg with sofosbuvir 400 mg in Section B of Pharmaceutical Schedule from 1 July 2017 to as follows (additions in bold, deletions in strikethrough):

Access criteria:
Chronic hepatitis C – Advanced disease– where ribavirin is not contraindicated. Applications from any relevant practitioner Approvals valid for 12 weeks for applications meeting the following criteria:
All of the following:
1. Patient has chronic hepatitis C (any genotype); and
2 Ribavirin treatment is not contraindicated; and
3. Any of the following:
    3 1 Patient has decompensated cirrhosis with a MELD score of ~~15~~ **12** or greater; or
    3.2 Patient has been accepted onto a list for a liver transplant or has received a liver transplant; or
    3.3 Patient has essential mixed cryoglobulinaemia with associated purpuric skin rash and; Either
        3.3.1 Cryoglobulinaemic glomerulonephritis; or
        3 3 2 Systemic vasculitis

Chronic hepatitis C – Advanced disease where ribavirin is contraindicated Applications from any relevant practitioner. Approvals valid for 24 weeks for applications meeting the following criteria:
All of the following:
1 Patient has chronic hepatitis C (any genotype); and
2. Ribavirin treatment is contraindicated; and
3. Any of the following:
    3.1 Patient has decompensated cirrhosis with a MELD score of ~~15~~ **12** or greater; or
    3 2 Patient has been accepted onto a list for a liver transplant or has received a liver transplant; or
    3.3 Patient has essential mixed cryoglobulinaemia with associated purpuric skin rash and; Either
        3.3.1 Cryoglobulinaemic glomerulonephritis; or
        3.3.2 Systemic vasculitis.

note no restriction change is required for Part II of Section H of the Pharmaceutical Schedule as hospital access requires patients to have a valid Special Authority approval according to the criteria set out in Section B of the Schedule;

note that widening of access to ledipasvir with sofosbuvir (Harvoni) tablets as detailed above would appear in the printed and online Pharmaceutical Schedule from 1 July 2018;

note that funded access from 9 June 2017 would be possible to implement without a change to the printed or online Pharmaceutical Schedule because the funding and distribution of ledipasvir with sofosbuvir (Harvoni) is managed by PHARMAC and the application form is not a standard Special Authority;

note that updated application forms would be distributed to relevant clinicians along with notification of the decision;

resolve that consultation on this proposal was appropriate, and no further consultation is required

PHARMAC
Pharmaceutical Management Agency

MEMORANDUM FOR BOARD TELECONFERENCE MEETING OF 13 DECEMBER 2018

To: PHARMAC Directors

From: Chief Executive

Date: December 2018

Proposal to list glecaprevir with pibrentasvir (Maviret) for the treatment of chronic hepatitis C and amend the listing terms for paritaprevir with ritonavir and ombitasvir with dasabuvir +/- ribavirin (Viekira Pak +/- RBV) and adalimumab (Humira, HumiraPen)

Recommendations

It is recommended that, having regard to the decision making framework set out in PHARMAC's Operating Policies and Procedures, you:

resolve to approve the resolutions outlined in Appendix One of this Board paper;

resolve to approve the 2 October 2018 agreement with AbbVie Ltd relating to the listing of glecaprevir with pibrentasvir (Maviret);

resolve to approve the 28 November 2018 amendment to the 20 April 2016 agreement with AbbVie Ltd relating to the listing of paritaprevir with ritonavir and ombitasvir with dasabuvir (Viekira Pak) and paritaprevir with ritonavir and ombitasvir with dasabuvir with ribavirin (Viekira Pak-RBV);

resolve to approve the 28 November 2018 amendment to the 21 October 2015 agreement with AbbVie Ltd relating to the listing of adalimumab (Humira, HumiraPen);

resolve that the consultation on this proposal was appropriate, and no further consultation is required;

note that Maviret would be distributed to pharmacies under a mechanism that would be funded by the supplier, AbbVie Ltd; and

note the implementation plan that would support this proposal.

SUMMARY OF PROPOSAL OVERALL						
Market data	**Year ending**	**30 Jun 2019**	**30 Jun 2020**	**30 Jun 2021**	**30 Jun 2022**	**30 Jun 2023**
Community Pharmaceuticals	Subsidy (gross)	Withheld	Withheld	Withheld	Withheld	Withheld
	Net cost to Community Pharmaceuticals	Withhel	Withheld	Withhel	Withhel	Withheld
	Net present value	Withheld				
Hospital Pharmaceuticals	Expenditure (gross)	$0	$0	$0	$0	$0
	Net cost to Hospital Pharmaceuticals	$0	$0	$0	$0	$0
	Net present value	$0				
Total CPB impact	Expenditure (gross)	Withheld	Withheld	Withheld	Withheld	Withheld
	Net pharmaceutical cost	Withhel	Withheld	Withhel	Withhel	Withheld
	Net present value	Withheld				
Other DHB costs	Net cost to DHBs	$0	$0	$0	$0	$0
DHB distribution costs	Net distribution costs	$0	$0	$0	$0	$0
Total	Total cost to DHBs	Withhel	Withheld	Withhel	Withhel	Withheld
	Net present value	Withheld				

SUMMARY OF MAVIRET PROPOSAL						
Market data	**Year ending**	**30 Jun 2019**	**30 Jun 2020**	**30 Jun 2021**	**30 Jun 2022**	**30 Jun 2023**
Number of patients		1732	1580	1080	660	660
Number of Māori or PI people		363	331	226	138	138
Community Pharmaceuticals	Subsidy (gross)	Withheld	Withheld	Withheld	Withheld	Withheld
	Net cost to Community Pharmaceuticals	Withheld	Withhel	Withhel	Withhel	Withheld
	Net present value	Withheld				
Hospital Pharmaceuticals	Expenditure (gross)	$0	$0	$0	$0	$0
	Net cost to Hospital Pharmaceuticals	$0	$0	$0	$0	$0
	Net present value	$0				
Total CPB impact	Expenditure (gross)	Withheld	Withheld	Withheld	Withheld	Withheld
	Net pharmaceutical cost	Withheld	Withhel	Withhel	Withhel	Withheld
	Net present value	Withheld				
Other DHB costs	Net cost to DHBs	$0	$0	$0	$0	$0
DHB distribution costs	Net distribution costs	$0	$0	$0	$0	$0
Total	Total cost to DHBs	Withheld	Withhel	Withhel	Withhel	Withheld
	Net present value	Withheld				

SUMMARY OF HARVONI OFFSETS						
Market data	**Year ending**	**30 Jun 2019**	**30 Jun 2020**	**30 Jun 2021**	**30 Jun 2022**	**30 Jun 2023**
Number of patients		55	50	45	40	35
Community Pharmaceuticals	Subsidy (gross)	Withhel	Withhel	Withhel	Withhel	Withhel
	Net cost to Community Pharmaceuticals	Withheld	Withheld	Withheld	Withheld	Withheld
	Net present value	Withheld				
Hospital Pharmaceuticals	Expenditure (gross)	$0	$0	$0	$0	$0
	Net cost to Hospital Pharmaceuticals	$0	$0	$0	$0	$0
	Net present value	$0				
Total CPB impact	Expenditure (gross)	Withhel	Withhel	Withhel	Withhel	Withhel
	Net pharmaceutical cost	Withheld	Withheld	Withheld	Withheld	Withheld
	Net present value	Withheld				
Other DHB costs	Net cost to DHBs	$0	$0	$0	$0	$0
DHB distribution costs	Net distribution costs	$0	$0	$0	$0	$0
Total	Total cost to DHBs	Withheld	Withheld	Withheld	Withheld	Withheld
	Net present value	Withheld				

SUMMARY OF HUMIRA/HUMIRAPEN PROPOSAL						
Market data	**Year ending**	**30 Jun 2019**	**30 Jun 2020**	**30 Jun 2021**	**30 Jun 2022**	**30 Jun 2023**
		5116	5014	5248	5369	5387
Community Pharmaceuticals	Subsidy (gross)	Withheld	Withheld	Withheld	Withheld	Withheld
	Net cost to Community Pharmaceuticals	Wi	Withheld	Wi	Wi	Wi
	Net present value	Withheld				
Hospital Pharmaceuticals	Expenditure (gross)	$0	$0	$0	$0	$0
	Net cost to Hospital Pharmaceuticals	$0	$0	$0	$0	$0
	Net present value	$0				
Total CPB impact	Expenditure (gross)	Withheld	Withheld	Withheld	Withheld	Withheld
	Net pharmaceutical cost	Wi	Withheld	Wi	Wi	Wi
	Net present value	Withheld				
Other DHB costs	Net cost to DHBs	$0	$0	$0	$0	$0
DHB distribution costs	Net distribution costs	$0	$0	$0	$0	$0
Total	Total cost to DHBs	Withheld	Withheld	Withheld	Withheld	Withheld
	Net present value	Withheld				

Notes:

1. Subsidy (gross) = forecast of spending on the proposed chemical at the proposed subsidy
2. Net cost to Community Pharmaceuticals = forecast of change in total net spending on pharmaceuticals listed on the Schedule compared with status quo, including offsets from replacing the Viekira Pak agreement. Note that the proposal results in savings versus the status quo from year 5 onwards
3. Other DHB costs = service impacts Minimal incremental costs as majority of patients expected to be treated via primary care with existing funding.
4. DHB distribution costs = There are no pharmaceutical mark-up or dispensing fee costs associated with this proposal due to the distribution method for Maviret Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) .
5. All costs are expressed ex manufacturer, excluding GST
6. NPV is calculated over 5 years using an annual discount rate of 8%.
7. The proposal is expected to minimally affect DHBs' income from patient co-payments and distribution costs met by the DHBs as all of these costs are Withheld under .
8. Calculations: A1214735

Executive Summary

- The proposal is to approve agreements with AbbVie Limited (AbbVie) to:
    - fund glecaprevir with pibrentasvir (Maviret), a pangenotypic direct acting antiviral (DAA) treatment for chronic hepatitis C[1] (HCV), from 1 February 2019;
    - delist paritaprevir, ritonavir and ombitasvir with dasabuvir +/ ribavirin (Viekira Pak/Viekira Pak RBV), a DAA for patients with genotype 1 HCV, from 1 February 2019; and
    - amend the pricing and contractual terms applying to adalimumab (Humira).
- There would be no change to the listing of sofosbuvir with ledipasvir (Harvoni), a pangenotypic DAA for patients with HCV with severe liver disease.
- This proposal would provide a potential cure for up to 21,500 additional HCV infected patients (patients with genotype 2 to 6 who do not have severe liver disease). These patients currently have no funded DAA treatment option; therefore, this proposal offers significant opportunity to continue to reduce the burden of HCV infection in New Zealand. Should this proposal be approved, all treatment naïve people with HCV (estimated as 50,000) would have access to a potentially curative treatment.
- The long term benefits to patients of curing HCV is the reduction of liver disease progression, reduction of the development of hepatocellular carcinoma and avoidance of the need for liver transplant. The long-term benefits to the health system would include reductions in the demand for services to manage patients with end stage liver disease care, the need for hepatocellular carcinoma support and the need for liver transplantation. We note that Maviret offers significant suitability benefits for primary care and patients compared with currently funded treatment options, including a more straightforward tablet regimen, reduced duration of treatment and no monitoring required by primary care for most patients.
- The fiscal impact of listing Maviret would be a cost of Withheld under section 9(2)(b) over 5 years (NPV, 8% discount rate) to the CPB; however, this cost would be offset by a reduction of Harvoni expenditure (Withheld under NPV) and Withheld under section 9(2)(b) on Humira (Withh Withheld NPV) meaning the net fiscal impact of the proposal would be a savings of Withh Withhel over 5 years (NPV). Due to uncertainty of overall patient numbers, there is a small risk that the overall impact of this proposal would be a cost of Withheld under over 5 years (NPV, 8%) to the CPB
- The proposal for Maviret is ranked number Wit on our Options for Investment priority list, with a likely range of Withhel QALYs per $1 million to cost saving P rogressing this proposal would not prevent higher ranked proposals from being progressed, mainly because this proposal would not incur any additional expenditure in this or the next financial year and would be cost saving overall.
- The alternative to this proposal for Maviret would be to run a commercial process for sole supply of one pangenotypic agent However, given the current commercial landscape (limited competition, uncertainty of patient numbers, the complexity of distribution arrangements and current contractual requirements around subsidy and delisting protection), the high health need of patients currently receiving no treatment and our ability to leverage the adalimumab market, PHARMAC staff consider that, on balance, this proposal would provide better value in the short medium term and earlier access to treatment for patients.

[1] The chronic from of hepatitis C is referred to as an abbreviated 'HCV' for the purpose of this document.

- An alternative distribution mechanism is proposed for Maviret, because distributing the proposed new treatments through DHB funded community pharmacy dispensing would otherwise result in a distribution cost of [redacted] (5yr NPV) for DHBs. Under this alternative distribution mechanism there would be no prescription co payment payable for Maviret [redacted]
- Significant activity to support the uptake of DAA treatment has occurred with the sector since 2016 The implementation plan (Appendix Five) to support this proposal outlines what we consider would be the key challenges and PHARMAC's response to those should this proposal be progressed

Why Proposal Not Decided Under Delegated Authority

The proposal outlined in this Board paper has not been dealt with by the Chief Executive under delegated authority because:

- the estimated total NPV of financial movements (savings and spend) for this proposal is [redacted] of the Pharmaceutical Budget; and
- we propose not to use standard distribution and dispensing arrangements of pharmaceuticals already in place with DHBs and pharmacy.

The Financial Impact (NPV) is calculated on the basis of the net present value of the proposed subsidy (ex-manufacturer exclusive of GST) over 5 years at a discount rate of 8% to be paid by the funder for the product(s) and the forecast demand, taking into account any effect of the change/decision on that demand, versus the status quo

The Proposal

The proposal involves listing a new treatment for HCV (Maviret), amendment of listing terms for an existing funded HCV treatment (Viekira Pak) and amendment of listing for adalimumab (Humira), as detailed below. All three treatments are supplied by AbbVie.

HCV treatments

In July 2016 PHARMAC listed Viekira Pak +/ ribavirin (supplied by AbbVie), for genotype 1 patients without severe liver disease, and Harvoni (supplied by Gilead) for patients with any genotype who have severe liver disease

Harvoni would remain listed subject to restrictions for patients with any genotype with severe liver disease We expect the volume of patients accessing Harvoni to reduce as a result of this proposal; details regarding these assumptions are in Appendix Three.

Under this proposal, Maviret would be listed in the Pharmaceutical Schedule at a price of $24,750 per pack of 84 tablets from 1 February 2019 and Viekira Pak and Viekira Pak-RBV would be delisted at the same time.

Maviret would replace Viekira Pak +/- ribavirin and would treat all genotypes without severe liver disease, noting that Maviret cannot be used in patients with severe liver disease.

No patients would be required to change treatments because any patients presenting with a prescription for Viekira Pak prior to 1 February 2019 would be dispensed their full 12 week course of treatment Viekira Pak would also remain funded (albeit not listed in the Schedule) until 31 March 2019 for those patients who present with a prescription after 1 February 2019.

PHARMAC has entered into a provisional agreement with AbbVie dated 2 October 2018 for Maviret to be open listed with no restrictions on funded access, conditional on consultation and PHARMAC Board approval. This agreement differs from a standard listing agreement as it contains:

- Withheld under section 9(2)(b)(ii) confidential rebates to minimise financial risk;
- Withheld under section 9(2)(b)(ii) and 9(2)(j)
- Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)
- subsidy and delisting protection for three years from the date of listing (i.e. to 1 February 2022);
- Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)
- provisions for an alternative distribution arrangement

The alternative distribution arrangement would see Maviret distributed outside of the standard community pharmacy supply chain. Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j) Withheld under section 9(2)(b)(ii) the provision of the dispensing and patient counselling service would be managed by AbbVie. PHARMAC staff note that the proposed mechanism is similar to the current Viekira Pak distribution arrangements which involves the pharmacy being provided with product free of charge to dispense to patients. However, some improvements have been negotiated to closer align with standard dispensing mechanisms and remove the need for PHARMAC managing the prescriptions and logistics in house. Prescriptions for Maviret would be processed through pharmacy dispensing software so that dispensing data can be captured in Pharmhouse (the database that collects data on dispensings of funded medicines); this will mean that PHARMAC will no longer need to receive and store patient data. We note that under this arrangement there would be no prescription co-payment payable for Maviret

Adalimumab (Humira)

PHARMAC has entered into an agreement with AbbVie dated 28 November 2018, conditional on consultation and PHARMAC Board approval, to amend the existing agreement with AbbVie for the listing of Humira in the Pharmaceutical Schedule. In summary, the amendments would:

- Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)
- provide an additional year of protection from subsidy reduction and delisting for Humira, from the current end date of 30 June 2019 to a new end date of 30 June 2020.
- provide an additional year of protection from changes to the Special Authority criteria and Hospital Restrictions applying to Humira, from the current end date of 30 June 2019 to a new end date of 30 June 2020.

- widen access to adalimumab in the indication of plaque psoriasis, to bring the criteria in line with those that apply to another funded biologic treatment, secukinumab This is expected to have negligible financial or clinical impact given that there is already a similarly priced biologic treatment available funded subject to the same criteria as the proposed changes for adalimumab Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j) Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)

These amendments would have no significant clinical impacts. Note that we have not consulted on the proposed amendments to the Humira agreement; our reasoning for this is discussed in the Consultation section of this paper

Note that all but the commercial considerations and budget impact sections of the remainder of this paper will focus on Maviret, as the adalimumab component of the proposal would have no significant clinical impacts.

PHARMAC staff can provide the provisional agreement for Maviret, the amendment to the agreement for Viekira Pak and the amendment to the Humira agreement to any Board member who wishes to review them in detail.

Commercial considerations

PHARMAC staff note that this section is more detailed than the Board might usually see in other Board papers for Pharmaceutical Schedule funding decisions. We consider that this is warranted due to the market complexities for HCV treatments and consultation feedback provided by Gilead. Gilead is a competitor to AbbVie in the HCV market segment and its Epclusa brand is the only other pangenotypic DAA registered in New Zealand.

The table below summarises DAAs currently funded or under assessment by PHARMAC:

Brand	Chemical name	Supplier	PHARMAC status
Viekira PAK +/- RBV	paritaprevir with ritonavir, ombitasvir and dasabuvir +/- ribavirin	AbbVie	Listed – delisted as proposed
Harvoni	sofosbuvir with ledipasvir	Gilead	Listed
Maviret	glecaprevir with pibrentasvir	AbbVie	Ranked – listed as proposal
Sovaldi	sofosbuvir	Gilead	Under assessment – awaiting a commercial proposal
Epclusa	sofosbuvir with velpatasvir	Gilead	Ranked – awaiting a commercial proposal
Vosevi	sofosbuvir with velpatasvir and voxilaprevir	Gilead	Under assessment – To be considered by PTAC February 2019

HCV treatments

The current agreements for Viekira Pak and Harvoni include subsidy and delisting protection until 1 July 2019. This provides a level of complexity with respect to a competitive process because it effectively prevents PHARMAC from being able to award sole supply for the entire market to a pangenotypic HCV treatment prior to 1 July 2019. Although it may have been possible to devise a competitive process where the market was split by genotype, which could have allowed the incumbent supplier/s to bid for sole supply of part of the market prior to the end of subsidy protection, or that involved non-exclusive listings prior to the end of subsidy protection, we considered that this would be complex to implement, could potentially unfairly advantage the incumbent suppliers and may not result in the best pricing We consider that the simplest, fastest and most commercially viable option to make a pangenotypic DAA available for patients before 1 July 2019 is direct negotiation with a supplier of a pangenotypic product

PHARMAC staff have considered the relative benefits of delaying listing a new pangenotypic product and running a competitive process now for a listing commencing on 1 July 2019, versus listing a pangenotypic product now and running a competitive process in the future (for sole supply from 1 February 2022). While it may be possible to achieve better net pricing than the current proposal via a competitive process, Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j) Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j). Further, this proposal would allow earlier patient access to a pangenotypic DAA, with significant associated health benefits whilst also being cost saving versus the status quo

This proposal would not prevent PHARMAC from listing a second pangenotypic DAA. However, any proposal for another product would need to offer a competitive/comparable price/budget impact for listing, which would include consideration of distribution costs. We have considered whether the rebate structure negotiated with AbbVie would have a negative financial impact if another product were listed and have determined that this would be unlikely.

On balance, we consider that this proposal would provide a favourable balance of financial risk and earlier patient access to this highly effective treatment. More detail about the approach is provided in the following section

Rationale for direct contracting with AbbVie

The listing agreement for Maviret has been secured by direct contracting with the supplier rather than a competitive process. We note that the process followed by PHARMAC has been one of parallel negotiations with the only two registered suppliers of pangenotypic DAAs in the New Zealand market. The discussions occurred within a context of the status quo listing arrangements where AbbVie already has the bulk of the HCV DAA market with its Viekira Pak product

While the two suppliers' products (Maviret for AbbVie and Epclusa for Gilead) are different in a number of ways, clinical advice confirms that they are similar for the treatment naïve patients, and it appears appropriate to consider them as representing a single market within which either, or both, products could be listed.

In these circumstances, one approach to ensuring we achieve the best health outcomes within available funding would be to run a Request for Proposals (RFP) or other formal competitive process for either sole supply or non-exclusive listings. A more flexible approach would be to initiate discussions with both suppliers, recognising their different circumstances, different levels of willingness and different timeframes, in order to secure one or more listings at the earliest opportunity, but without sole supply. PHARMAC staff adopted the latter approach.

Commencing in early 2017 PHARMAC staff sought proposals from both suppliers, although not via an RFP process. Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j) Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j) Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j) Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j) Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)

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Withheld under section 9(2)(h)

Adalimumab (Humira)

We have considered whether the proposed extended protections for Humira would limit our ability to make savings, noting that annual net expenditure on adalimumab is currently approximately Withheld under section 9(2)(h)(ii). There are two key activities that the proposed contract amendments for Humira would prevent us from considering during the extended protection period; running a competitive process for adalimumab and restricting access to adalimumab.

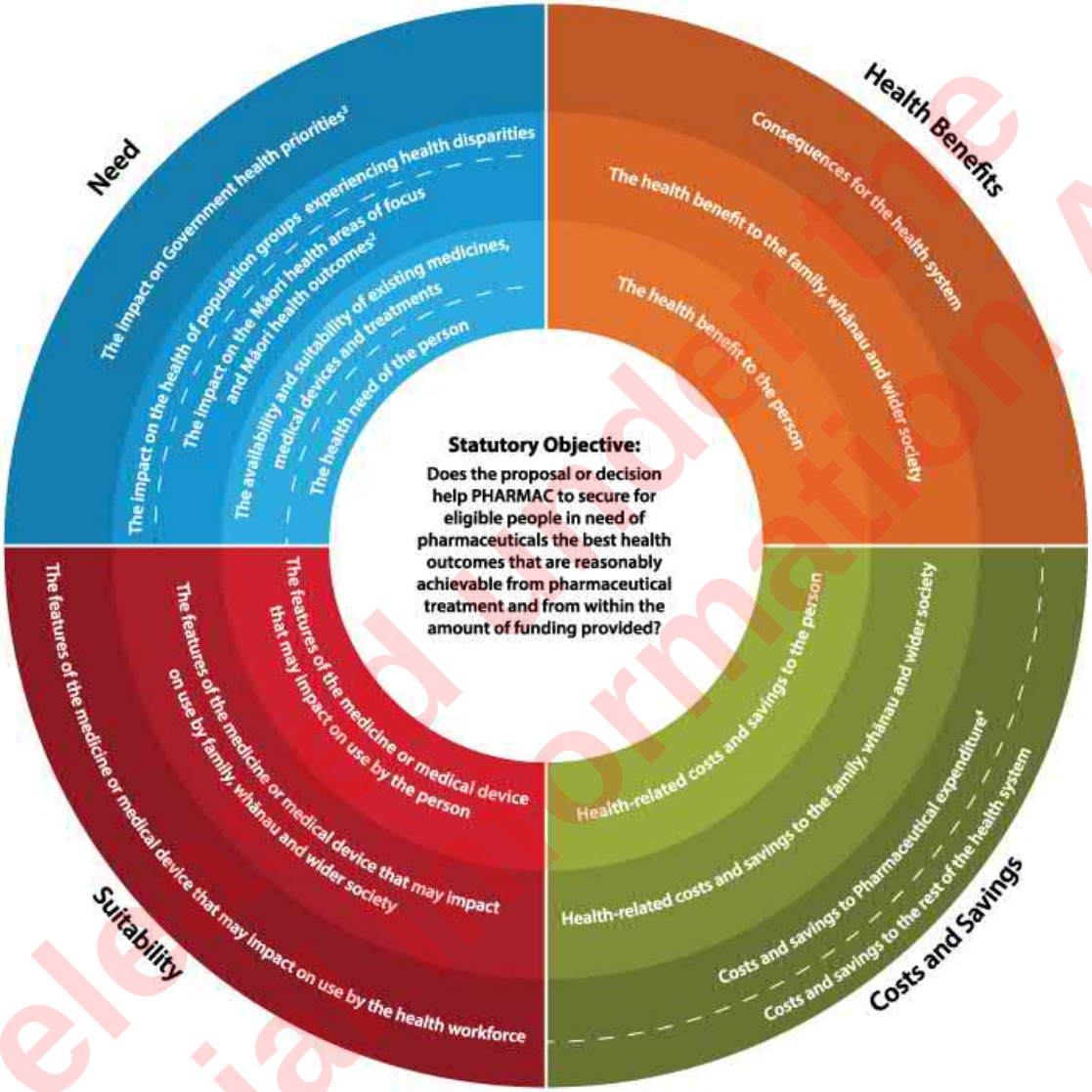
With regards to the possibility of a competitive process, we understand that although the base patent on adalimumab has expired, there are multiple additional patents that do not expire until 5 June 2022. Withheld under section 9(2)(h)
Withheld under section 9(2)(h)
Withheld under section 9(2)(h)
Withheld under section 9(2)(h)

There is one biosimilar product submitted to Medsafe, supplied by Amgen. AbbVie has advised that there is a global settlement agreement between Amgen and AbbVie for this product, although it is not clear to us what this entails From reports in Australia it appears that the global agreement limits entry of Amgen's product into several international markets until 2023. This may or may not include New Zealand If Amgen's product was able to enter the New Zealand market ahead of patent expiry, we consider that this would be unlikely to occur quickly, taking into account Medsafe registration timelines and the need for New Zealand supply/patent issues to be resolved

We note that there is a current RFP for etanercept due to close on 17 December 2018 and there are some indications that are shared by etanercept and adalimumab Our strong preference is to take a staggered approach to biologic markets, the timing of which would not be significantly hindered by the proposed extension to subsidy, delisting and criteria protection for adalimumab We note that there is nothing in the current proposal that would prevent us from listing Amgen's biosimilar product alongside Humira, potentially with differential (wider) access if the pricing was better

Factors for Consideration

This paper sets out PHARMAC staff's assessment of the proposal using the Factors for Consideration in the Operating Policies and Procedures Some Factors may be more or less relevant (or may not be relevant at all) depending on the type and nature of the decision being made and, therefore, judgement is always required The Board is not bound to accept PHARMAC staff's assessment of the proposal under the Factors for Consideration and may attribute different significance to each of the Factors from that attributed by PHARMAC staff.



Footnotes

[1] The person receiving the medicine or medical device must be an eligible person, as set out in the Health and Disability Services Eligibility Direction 2011 under Section 32 of the New Zealand Public Health and Disability Services Act 2000

[2] The current Māori health areas of focus are set out in PHARMAC's Te Whaioranga Strategy.

[3] Government health priorities are currently communicated to PHARMAC by the Minister of Health's Letter of Expectations.

[4] Pharmaceutical expenditure includes the impact on the Combined Pharmaceutical Budget (CPB) and / or DHB hospital budgets (as appropriate).

[5] Please note PHARMAC's Factors for Consideration schematic currently does not explicitly refer to the health needs of family, whānau and wider society, but this factor should be considered alongside those depicted in the schematic

Health need

Health need of the person

Infection with the hepatitis C virus can cause both acute and chronic hepatitis; the acute process usually leads to chronic infection. HCV often follows a progressive course over many years and can ultimately result in cirrhosis, hepatocellular carcinoma, and the need for liver transplantation. HCV is now the most common indication for liver transplant in New Zealand.

The most frequent complaint for patients with HCV infection is fatigue; other less common manifestations include nausea, anorexia, myalgia, arthralgia, weakness, and weight loss. In early stages of the infection the symptoms are rarely incapacitating and may be difficult to ascribe to liver disease alone

A person's expected health loss depends on how far the condition has progressed. It takes about 20-40 years from infection to develop cirrhosis, and prior to cirrhosis many patients are asymptomatic. However, once cirrhosis develops, disease progression is more rapid. We estimate that the mean life expectancy of a patient with decompensated cirrhosis is approximately three years.

Availability and suitability of existing treatments

PHARMAC currently funds two DAA treatments for HCV: Viekira Pak[2] and Harvoni.

Viekira Pak is only suitable for patients with the genotype 1 virus (about 55% of cases in New Zealand) and is unsuitable for patients with decompensated cirrhosis or similarly severe conditions It is given as a 12 to 24 week course including two or three different tablets that are taken as one dose in the morning and a different dose at night. Evidence indicates more than 90% of patients receive a sustained virological response, which is equivalent to being free of the virus or 'cured', on completion of a course of treatment

Harvoni can be used in all genotypes[3]. It is currently only funded for patients with the most severe disease: patients with decompensated cirrhosis, post liver transplant, or cryoglobulinemia. This targeting of funding is due to the high cost of Harvoni and the high health need of these patients

In addition to the above DAAs, PHARMAC also funds one other treatment for HCV: pegylated interferon with ribavirin However, this treatment is almost never used now, even where other funded agents aren't suitable, due to the poor efficacy, contraindications, severe adverse effects and long treatment time.

In some patients, DAA treatment may not result in a cure; this has been seen in 3% of Viekira Pak treated patients (n=90) and in 10 Harvoni treated patients in New Zealand to date. We note that evidence indicates this is only seen in 0 5% of Maviret treated patients Depending on the reasons for the lack of response (related to adherence or virologic failure) some patients can be re-treated with the same regimen while others may require a different treatment due to viral resistance

[2] Some patients will require co-administration with ribavirin
[3] In most cases, will depend on treatment history, genotype and cirrhosis (some scenarios will require co-administration with ribavirin)

Patients who have viral resistance to current DAAs require a DAA treatment regimen that includes sofosbuvir (Sovaldi), which is supplied by Gilead [redacted] We are aware that sofosbuvir has a patent expiring in May 2030 and, therefore, generic entry into this market is unlikely in the near future. We plan to continue assessing our options for this patient group.

We plan to seek further advice on any treatment options for patients with viral resistance at the next Anti infective Subcommittee of PTAC meeting.

Health need of others

HCV infection mainly occurs through exposure to infected blood or body fluids Current HCV infections most commonly occur from shared needles during illicit drug use. In New Zealand, perhaps 1% of the total population are active intravenous illicit drug users, and 52% of intravenous illicit drugs users accessing Needle Exchange Services are HCV antibody positive. An annual ESR report from 2012 showed that 82% of individuals notified with an acute HCV infection indicated a history of intravenous drug use

Impact on Māori health areas of focus and health outcomes

From data on patients accessing treatment with Viekira Pak and Harvoni since June 2016, it appears that there is a slight overrepresentation of Māori patients compared with the New Zealand population as a whole We do not know if this correlates to an over representation of Māori in terms of HCV infection prevalence.

Any other populations experiencing health disparities

The same data show that Pacific peoples are accessing funded HCV treatments at a similar rate to other patients, while Asian people have lower rates of access

Government health priorities

The Government has a priority to reduce transmission of infectious diseases and to minimise harm from alcohol and drug dependence, which could apply to this proposal as hepatitis C infections most often come from illicit drug use.

In May 2016, the World Health Assembly endorsed the Global Health Sector Strategy (GHSS) on viral hepatitis 2016–2021. The GHSS calls for the elimination of viral hepatitis as a public health threat by 2030 (reducing new infections by 90% and mortality by 65%). New Zealand was one of 194 countries that adopted this Strategy which set the goal of eliminating viral hepatitis by 2030.

Health Benefit

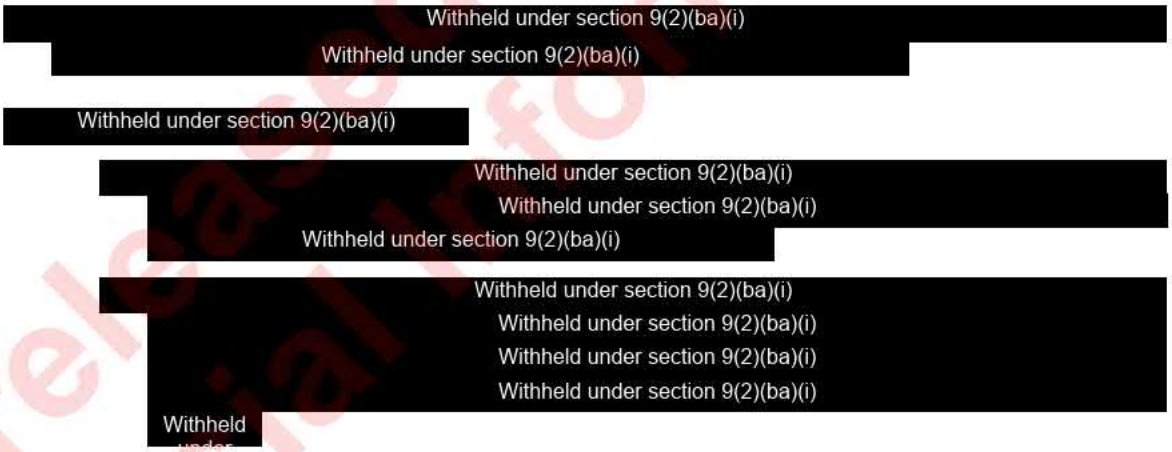
This proposal would mean that all HCV treatment-naive patients with any genotype (currently funded treatments cover 57% of this cohort) would potentially be able to be cured from the disease It is considered that patients who are cured before they develop cirrhosis would be able to be discharged from frequent ongoing monitoring. They would have significantly reduced risk of developing cirrhosis, liver cancer, liver failure requiring liver transplant and eventually dying compared to someone who has not been cured Patients who are cured also do not spread the virus which is a significant health benefit to others.

The Pharmacology and Therapeutics Advisory Committee (PTAC) considered that the safety and efficacy of Maviret was excellent, and that its efficacy was better than Viekira Pak. PTAC recommended that Maviret be funded with medium priority pending Medsafe registration and publication of clinical evidence, both of which have now occurred PTAC noted that since Maviret is not used with ribavirin, this would reduce the number of side effects and complexity of treatment, and noted that it has significantly less drug drug interactions and has a reduced treatment duration compared with Viekira Pak.

This proposal would provide a potential cure for up to 21,500 additional HCV infected patients, offering significant advantages to continue reducing the burden of HCV in New Zealand.

A full copy of PTAC minutes relating to Maviret are available in Appendix Two

Advisor Conflicts of Interest



Consequences for the health system

It is estimated that 95% of treatment naïve patients are non-cirrhotic and, therefore, the majority of patients can be managed in primary care. Currently the treatment pathway in primary care for HCV involves genotype testing, as Viekira Pak only treats genotype 1. Patients are also required to complete a liver elastography scan[4] to assess whether cirrhosis is present and, if present, to stage the level of severity. Patients with cirrhosis are referred to secondary care for management and receive treatment either with Viekira Pak (if cirrhosis is not severe) or Harvoni (if severe)

[4] Note that the term liver elastography scans used within this document includes mobile and fixed Fibroscan machines and Shear Wave machines being used in radiology departments.

There are both long and short term possible impacts to the health system as a result of this proposal

In the short term, as this proposal would provide a treatment option for patients who do not currently have access to a funded DAA, there may be additional requirements for HCV diagnostic testing and staging in primary care as well as prescribing in both primary and secondary care However, we consider the impact of this may be limited in the absence of a Ministry of Health led initiatives as patients known to secondary care are staged and ready for treatment, we do not expect there to be an influx of new patients requesting treatment from to our experience with the first DAA listings in 2016

We note that staging of disease has previously been reliant on access to liver elastography scans and that this service is currently capacity constrained PHARMAC staff are aware that a new National HCV Guidance and Clinical Pathway has recently been developed with recommendations to use the AST Platelet Ratio Index APRI[5] score from blood testing to determine an indicator of cirrhosis and around 20% are then referred to have a liver elastography scan follow up. We note that APRI blood tests are available at all community diagnostic laboratories PHARMAC staff have been working with the Ministry of Health to ensure that this Guidance and Clinical Pathway are ready for distribution amongst DHBs around the time of notification of this decision.

Unlike Viekira Pak, Maviret is a pangenotypic treatment and therefore pre-treatment genotype testing would not be necessary in treatment-naïve or newly presenting patients. Treatment duration with Maviret is likely to be shorter than with Viekira Pak or Harvoni These advantages would likely result in some small savings for the health system.

With regards to long term impacts, given that there is a high cure rate, there would be a significant reduction of any ongoing health resource required for management of the HCV (e.g. clinic visits, monitoring for cirrhosis, blood tests, liver transplants, management of symptoms etc) Information from the New Zealand Liver Transplant Unit indicates that up to 50 liver transplants are performed each year, with the most common reason being HCV related cirrhosis It is considered that the availability of a DAA treatment to patients before cirrhosis develops would reduce the number of HCV infected patients requiring liver transplants.

Funding for GP service impacts, which is outside of PHARMAC's remit, was raised in consultation responses and it was also raised in 2016 when the Board considered the listing of Viekira Pak. This feedback has been provided to the Ministry of Health, which considers that these services in primary care still remain covered via existing capitated funding PHARMAC staff note that while more clinic appointments may be required to monitor patients when receiving current HCV treatments, monitoring requirements would be far less for Maviret than for Viekira Pak (our clinical advice considered that there was no monitoring required during Maviret treatment for most patients).

We note there may be difficulties for primary care to identify people with potential HCV infection who could benefit from treatment. Therefore, PHARMAC staff have been working on a process to match HCV laboratory result data to Primary Health Organisations (PHOs) enrolment data; with the aim of sharing this matched data with PHOs so people who, based on laboratory testing, may benefit from DAA treatment can be followed up.

[5] AST Platelet Ratio Index (http://www.hepatitisc.uw.edu/page/clinical-calculators/apri)

With regards to the impact on pharmacy, we note that Viekira Pak is distributed by an alternative mechanism to standard prescription items, in that the distribution of Viekira Pak is managed by a coordinator at PHARMAC and the product is supplied free of charge to registered pharmacy where it is dispensed to the patient without a co payment. This was put in place due to the high cost that would be incurred by DHBs for distribution via the standard wholesale chain (estimated at an incremental cost of Withheld under per annum). Currently there are 350 registered "Viekira Pak AbbVie Care Pharmacies" able to provide Viekira Pak (only 270 have done this) If this proposal is progressed, Maviret would similarly be provided free of charge to pharmacies who register to provide this product but, in contrast to Viekira Pack, ordering and management of stock would be managed directly between the pharmacy and AbbVie (without the need for a PHARMAC intermediary) AbbVie aims to have a minimum 250 pharmacies accredited (via a 2 hour learning module) to provide Maviret by the time of listing (should this proposal be approved).

The Ministry of Health is aware of the potential resource impacts involved with managing projected patient numbers and the additional patients required to meet WHO elimination targets. A Health Report has been drafted by the Ministry of Health and is currently with the Director General of Health for review before being presented to the Minister of Health for consideration

Suitability

Maviret is a fixed dose combination tablet which includes all components of the treatment. Dosage is once daily with food; each dose is three tablets. This is a significantly simpler dosage regimen than the currently funded Viekira Pak which is a complex mix of multiple tablets, with a different dose in the morning from the evening.

PTAC considered that because Maviret has fewer drug-drug interactions than Viekira Pak, no monitoring is required and treatment duration is reduced, then it should be more straightforward for general practitioners to prescribe.

Costs and Savings

Health related costs and savings to the person

Maviret costs and savings to the person would be identical to those that they would currently experience if being treated by currently funded HCV treatments In this unique situation we have arranged for there be no prescription co-payment payable for Maviret. We note that the decisions to waive co-payments are normally made by the Ministry of Health.

Health related costs and savings to the family, whānau and wider community

No significant costs to the patient or others are noted

Cost and savings to Pharmaceutical expenditure

Based on the most recent expenditure report (November 2018), there are currently no available funds for new investment in the 2018/19 financial year [redacted]

The fiscal impact of listing, based on widened funded access for genotype 2 to 6 patients, would be a cost of [redacted] over 5 years (NPV, 8% discount rate) to the CPB; however, this cost would be offset by a reduction of Harvoni expenditure [redacted] and [redacted] on Humira ([redacted]) meaning the net fiscal impact of the proposal would be a savings of [redacted] over 5 years (NPV, 8% discount rate) to the CPB.

Due to uncertainty of overall patient numbers, there is a small risk that the overall impact of this proposal would be a cost of [redacted] over 5 years (NPV, 8%) to the CPB.

There is a financial risk that if the Ministry of Health rapidly pursues WHO targets for elimination then this would increase the cost of widened access to [redacted] over 5 years (NPV, 8% discount rate)[6]. International experience has shown that this is dependent on a screening strategy and a registry, which has financial and ethical barriers to overcome The Ministry of Health is working through these elements and are awaiting direction from the Minister of Health on some aspects.

Further detail about PHARMAC staff's summary of [redacted] and patient assumptions is set out in Appendix Three.

Costs and savings to the rest of the health system

Treatment for HCV infection currently requires several support services, including GP visits, specialist time and diagnostic tests. We estimate that, depending on the patient's circumstance and who is managing the treatment, these costs could be about $1,000 to $2,000 per person to the DHB. However, we have not included these costs in our budget impact assessment for this proposal for the following reasons:

- We consider that those patients who would be likely treated in secondary care (e.g. have known cirrhosis) would likely be seen regularly; therefore, the addition of prescribing a DAA would likely happen alongside one of the regular clinic visits
- There is a new diagnostic blood test which reduces the need for a liver elastography scan, therefore we do not anticipate listing of an additional DAA would be likely to have a large impact on the need for liver elastography scans.
- Patients prescribed Maviret are not required to have regular blood test monitoring; unlike Viekira Pak which requires blood tests at weeks 2, 4 and 8 weeks of treatment
- Genotype testing is not required prior to treatment initiation with Maviret.

[6] This assumes treating 7% of the HCV prevalent pool and that the prevalent patient pool in New Zealand is 50,000 There is doubt that the true prevalent pool is 50,000 and work is being done in the sector to further investigate this number.

- Our understanding, from the Ministry of Health, is that the funding for care of HCV patients in primary care would remain covered by existing capitated funding

The achievement of a cure would significantly reduce health service costs as patients would not progress to more severe health states, consequently reducing ongoing patient monitoring, testing and disease management costs Based on modelling conducted by the CDA Foundation[7], it is estimated that approximately 92 percent of patients with chronic HCV in New Zealand are non cirrhotic Analysis by PHARMAC staff estimates that annual health costs for HCV patients double when a patient becomes cirrhotic, then increases again approximately 13 fold should they progress to decompensated cirrhosis. These offsets are not realised within a five-year period and, therefore, PHARMAC staff have also not included these in our budget impact assessment.

The Dynamics of the Market for HCV

When the DAAs (Viekira Pak and Harvoni) were first listed in 2016, there was a rapid treatment uptake PHARMAC staff consider that these were 'warehoused patients' who were identified in secondary care and many were treated in the first six months of listing. Like Australia, New Zealand has seen a rapid decline in treatment numbers after the initial surge in patient treatment

Patients treated with subsidised DAAs to date total 3200 and, based on 1000 new cases each year, treatment numbers are only just ahead of estimated new infections We note that the total patient pool is poorly understood in New Zealand and the less severe patients (those not already under care) are less likely to identify themselves for testing unless they present to their GP with symptoms that correlate with disease. Internationally, it is recognised that screening and a patient registry is the most cost-effective way to find these patients. This is something that the Ministry of Health is currently working on. We are also aware that the Health Promotion Agency is intending to launch a social marketing campaign to encourage people to be tested for HCV. It is planned that this would be launched around the same time as any pangenotypic was funded, but timing is yet to be confirmed.

We are aware that many patients treated to date are those that have existing liver cirrhosis or further declining liver condition and have been treated through secondary care. We would expect the trend to start to favour general practice when Maviret is listed due to the treatment being easier to prescribe and monitor.

Future pharmaceutical considerations

AbbVie and Gilead are the global market leaders of pangenotypic DAAs. As noted earlier in this paper, Gilead is the supplier of the only other registered pangenotypic DAAs (Epclusa and Harvoni). There is currently one other product, supplied by Gilead, in the process of being registered, Vosevi, which is a fixed dose combination sofosbuvir with velpatasvir and voxilaprevir. PHARMAC has received a funding application for this product and it will be considered by PTAC at its February 2019 meeting; we note that its indication is for patients who have not cleared the virus with existing DAAs containing an Non structural protein 5A (NS5A) inhibitor

[7] A not for profit organisation which has provided epidemiological modelling to many of the countries signed up to the WHO elimination targets.

Merck, BMS and Janssen have all had non pangenotypic products registered or in development; however, these have either be considered and recommended for decline by PTAC or have not yet been registered in New Zealand We note that none of these three suppliers have a pangenotypic product and we consider there is no clinical advantages to pursuing applications for non pangenotypic formulations

PHARMAC staff are not aware of other DAAs in development that are being considered for registration in New Zealand.

International Prices for Maviret

Comparative pricing in international jurisdictions is noted below We consider it likely that both the UK and Australia would have negotiated rebates on this product and, therefore, the list price is unlikely to be an indication of relative price.

Table 1 International price comparison for Maviret

Country	Source	Strength	Pack Size	Local Price	Exchange Rate (xe.com October 2018)	Gross Price ($NZ)
Proposal		100 mg / 40 mg	84	-	-	$24,750
United Kingdom	BNF	100 mg / 40 mg	84	£12,994	1.93	$25,106
Australia	PBS	100 mg / 40 mg	84	$18,667	1 09	$20,395

Cost-Effectiveness

The overall cost effectiveness of funding Maviret is estimated to be cost saving.

On average, a patient who does not take a HCV treatment would require $27,000 of health care support over their lifetime (discounted at 3.5% pa), while the current net cost of cure with Viekira Pak for genotype 1 patients (based on the tiered commercial arrangement) is between Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j) per course of treatment.

Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)
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Withheld under section 9(2)(b)(ii), 9(2)(ba)(i) and 9(2)(j)

As such, the estimated cost-effectiveness of both these scenarios is cost-saving (i.e., patients getting additional QALYs at less overall cost). Genotype 2 to 6 patients would gain an average of W QALYs, coming from improved quality of life and prevention of progression into worse disease states and to death.

Comments from Interested Parties

Section 49(a) of the New Zealand Public Health and Disability Act 2000 (the Act) requires PHARMAC to consult, when it considers it appropriate to do so, on matters that relate to the management of pharmaceutical expenditure with any sections of the public, groups or individuals that, in the view of PHARMAC, may be affected by decisions on those matters

Accordingly, a consultation letter was circulated on 20 July 2018 to all suppliers and other parties that, in the view of PHARMAC, may be affected by the recommendations contained in this paper.

We note that the proposal consulted on was for a list date as soon as practicable following regulatory approval by Medsafe, but no earlier than 1 October 2018. Following receipt of consultation feedback, we notified on 27 August 2018 that we require additional time to consider the issues raised and a 1 October 2018 listing date would not occur

Note that we have not consulted on the proposed amendments to the Humira agreement. We consider that such consultation is not necessary at this point because it is our view that there are no additional impacts that would affect patients, clinicians, DHBs or suppliers that we would need to consider as part of this proposal. Of note:

- our assessment is that there will not be viable competition for adalimumab within the extended subsidy and delisting period;
- even if there was viable competition, the proposed terms would not prevent the listing of another adalimumab biosimilar if a commercial proposal was provided to us; and
- although there are proposed changes to the Humira access criteria, the changes would result in widening access to a level of a similar funded agent (secukinumab) and we have received previous feedback supportive of similarly widening access to TNF alpha inhibitors (such as adalimumab) when consulting on secukinumab.

The consultation letter, the distribution list, and all responses received by the end of 13 August are attached as Appendix Four.

The table below summarises the responses received and PHARMAC staff comment on these

Issue	Responder(s)	Staff comment
Supportive		
Fully supportive without further comments on listing	John Perry, gastroenterologist Frank Weilert, clinician Allan Moffitt, Clinical Director at ProCare CCDHB Addiction Services (Oliver & Patel) Jo Scott Jones, Medical Director at Pinnacle Midlands Health Network Karl Schmidt, Southern DHB Aaron Kim, pharmacist of Unichem Medi-Centre Pharmacy Addiction Practitioner's Association Aotearoa New Zealand (Paton) Jennifer Irvine, Hepatitis C Nurse Community Alcohol & Drug Services (Pooley) CDHB (Dalrymple & Doogue) Pharmacy Guild (Rickman) Anna Meuli, GP Liaison for Hauora Tairāwhiti	Noted

Feedback regarding dispensing and distribution arrangements		
Considered potential issues around distribution mechanism, including location of pharmacies, number of pharmacies, and accessibility of information about pharmacies that are able to dispense Maviret. NB: Some consult responders specifically supported the Maviret AbbVie Care Pharmacy Programme eg the Pharmacy Guild	Northern Region Hepatitis C Steering Group (Gane et al) Seed the Change (also separate responses from members) Kwee Goh, Pharmacist Whanganui Regional Health Network (MacDonald) Ed Gane, Chief Hepatologist at NZ Liver Transplant Unit	Any pharmacy can be part of the AbbVie Care Pharmacy programme. Details of pharmacies that choose to be part of the programme would be available on the following website www maviret co nz PHARMAC staff note that the proposed programme is very similar to the current arrangement for Viekira Pak. PHARMAC staff would work with AbbVie and pharmacies to ensure appropriate locations, distribution etc. of pharmacies. Prisons would be served as per current arrangements. Pharmacies that provide medication to prisons can provide Maviret as long as they are registered with AbbVie to do so.
How is the handling fee being paid?	Fiona Morris, Operations Analyst at Ministry of Health	Any fee for service, paid to pharmacies, would be paid for by AbbVie directly to the pharmacy
Prescribing and patient management		
Allow nurse prescribers to prescribe Maviret	HFNZ & ASHM Ed Gane, Chief Hepatologist at NZ Liver Transplant Unit	The proposal is to list Maviret without restrictions Funded Maviret would be dispensed to any patient with a prescription written by any person (including nurse prescribers) lawfully able to prescribe it.
Treatment of treatment-experienced patients should be done in secondary care	McLaughlin et al, Christchurch Hospital	The Ministry of Health would update 'Health Pathways' or create a similar clinical decision-making tool to guide clinicians about which patients should be treated in primary care vs secondary care.
Questions the statement "patients with hepatic impairment would not receive the treatment". Notes Maviret is not contraindicated due to having cirrhosis.	Withheld patient	Maviret would be open-listed; however, as noted in the prescribing information on the Medsafe website, it is not recommended in patients with moderate hepatic impairment and is contraindicated for severe hepatic impairment. We are aware that cirrhotic patients are currently referred to secondary services for treatment. If this proposal is approved, these patients may be treated with either Maviret or Harvoni, at the treating specialist's discretion, depending on clinical circumstance.

Further treatments should be funded for patients that would still have suboptimal or no treatment options, as follows: 1. Patients for whom DAA treatment has failed should receive Maviret plus sofosbuvir (and possibly with ribavirin), or sofosbuvir / velpatasvir / voxilaprevir (Vosevi). 2. Patients with decompensated cirrhosis should receive sofosbuvir / velpatasvir (Epclusa) in place of Harvoni as responders consider this would be cheaper due to treatment duration and higher efficacy.	Specialists from Southern DHB (Fraser et al) New Zealand Society of Gastroenterology (Schultz) Stedman & Falvey, Gastroenterologists AbbVie (Easome et al) Bridget Faire, Auckland DHB Seed the Change (also separate responses from members) Hepatitis Foundation of New Zealand & Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine Ed Gane, Chief Hepatologist at NZ Liver Transplant Unit Northern Region Hepatitis C Steering Group (Gane et al)	We acknowledge that if this proposal is approved there would be small subgroups of patients with remaining unmet clinical need This proposal would not prevent PHARMAC from considering funding of other hepatitis C treatments for these patients. We intend to seek further advice on this at the next Anti-infective Subcommittee meeting. In the meantime, we have requested an updated commercial proposal from Gilead for these patient groups As yet we have not received a response.
Strongly supportive of the proposal Considered that the goal should be elimination of hepatitis C and suggested a 'test and treat' campaign.	Seed the Change (Claire Newman)	Noted. We note that funding of a pangenotypic treatment would be PHARMAC's direct contribution to an elimination strategy the Ministry of Health may lead.
1 Concerns that GPs are underfunded for the extended visits that hepatitis C support requires. 2 Concerned about inequity of access for Māori and disadvantaged groups and seek better funding to allow such patients to see GPs. 3. On discontinuing Viekira Pak simultaneously: most who commented on this were supportive. Northern Region Hepatitis C Steering Group (Gane et al) asked to delay the delisting of Viekira Pak for 2-4 weeks to allow for any delays in presenting with a script	Royal New Zealand College of General Practitioners (Thorn)	1. If this proposal is approved we will again pass this feedback onto the Ministry of Health, which is responsible for the funding of DHB Services. 2 PHARMAC is considering how we can optimally work with partners, including Ministry of Health, DHBs and Work and Income, to develop strategies to prevent inequities in access occurring We note also that there would be no pharmacy co-payments incurred by patients for dispensing Maviret prescriptions as part of the distribution arrangements for this treatment 3. Our advice indicates that once a positive decision is notified (assuming the proposal is approved), it is unlikely that there would be many new prescriptions written for Viekira Pak. However, AbbVie has agreed to supply Viekira Pak to pharmacies in the circumstance where a patient presents with a prescription post 1 December 2018, this would be made available up until the 31 January 2019

Commercial considerations		
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Summary of consultation feedback on implementation and education		
Various consultation feedback indicated that the following should be considered to support any implementation: - Presentations at national primary care meetings - Presentations at regional primary care CME meetings Provision of training sessions/webinars for the primary care team about treating hepatitis C - Provision of education materials, such as guidelines and written materials, on the place of Maviret in treatment - Updated National Pathways - National awareness campaign	PHARMAC staff have completed an implementation plan that involves working with the supplier and other agencies in the health sector to ensure that: • educational materials are produced in time for listing • National Pathways are updated in time for listing • there are a range of opportunities and methods for people to get information about Maviret, including at conferences and regional meetings. PHARMAC staff note that a national awareness campaign is in development, led by the Ministry of Health and Health Promotion Agency.	

Legal Advice

Where necessary, management will obtain legal advice on issues such as whether any proposal is consistent with PHARMAC's legislative and public law obligations, including those which may have specific relevance to the particular proposal eg human rights implications of a proposal. If the Board considers that further legal advice is required on any issue, this should be communicated to management in advance of the Board meeting. Management will then obtain the required advice

Legal Advisors' View

Confidential & Legally Privileged Advice from PHARMAC's General Counsel

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Implementation

Section 49(b) of the Act requires PHARMAC to take measures to inform the public, groups and individuals of PHARMAC's decisions concerning the pharmaceutical schedule. Accordingly, if the Board adopts the recommendations contained in this paper PHARMAC staff will take the measures outlined in the attached Engagement and Implementation Plan (Appendix Five). The plan builds on two years of implementation activity to support uptake of hepatitis C treatments and outlines how we propose to address implementation of the proposed funding of Maviret A focus of the plan is to ensure those in need of treatment for HCV access treatment.

Furthermore, should the proposal be progressed we would notify all interested parties through:

- the distribution of a notification letter to health professionals including gastroenterologists, infectious disease specialists, general practitioners and community and hospital pharmacists;
- a story included in the Pharmaceutical Schedule Update, and other newsletter and email networks; and
- directly notifying our key partners, including members of the Integrated Hepatitis Service Implementation Group.

The notification would include information about listing date, who would benefit from treatment, the benefits of the new treatment, and information on how PHARMAC would support healthcare professionals to provide Maviret to people who would benefit

We note that, should the Board approve this proposal, there would be a short time period between decision and listing date (proposed for 1 February 2019) PHARMAC staff have been working with the sector to ensure that implementation requirements that must be in place for a 1 February 2019 list date are able to be completed. This includes national Health Pathways updated, updated educational material for healthcare professionals, and pharmacies accredited for dispensing of Maviret. Further activities would be rolled out over the subsequent months to support uptake of this treatment.

Appendices

Appendix One: Resolutions

Appendix Two: PTAC Minutes

Appendix Three: Summary of Expenditure Tiers and Patient Assumptions

Appendix Four: Consultation Letter and Responses *(**note** some responses may fall under more than one category)*

Appendix Five: Engagement and Implementation Approach

MINUTES OF THE PHARMACEUTICAL MANAGEMENT AGENCY (PHARMAC)

BOARD MEETING BY TELECONFERENCE DECEMBER 2018

The meeting was held by teleconference, starting at 1.30pm, with the following attendees:

Board members

Steve Maharey	Chair
Jan White	Board Member
Ross Lawrenson	Board Member
Jens Mueller	Board Member

PHARMAC staff in attendance

Sarah Fitt	Chief Executive
Lisa Williams	Director of Operations
Alison Hill	Director of Engagement & Implementation
Michael Johnson	Director of Strategic Initiatives
John Wyeth	Medical Director
Mark Woodard	Director of Corporate Services/CFO
Lizzy Cohen	Board Secretary

Matthew Tyson, Geraldine MacGibbon, Janet Mackay (PHARMAC staff) attended for the Schedule and Funding item.

1. Apologies

Nicole Anderson, Board Member

2. Chair Report

3. Schedule and Funding

3.1 Proposal to list glecaprevir with pibrentasvir (Maviret) for the treatment of chronic hepatitis C and amend the listing terms for paritaprevir with ritonavir and ombitasvir with dasabuvir +/- ribavirin (Viekira Pak +/- RBV) and adalimumab (Humira, HumiraPen)

resolved to approve the resolutions outlined in Appendix One of this Board paper;

resolved to approve the 2 October 2018 agreement with AbbVie Ltd relating to the listing of glecaprevir with pibrentasvir (Maviret);

resolved to approve the 28 November 2018 amendment to the 20 April 2016 agreement with AbbVie Ltd relating to the listing of paritaprevir with ritonavir and ombitasvir with dasabuvir (Viekira Pak) and paritaprevir with ritonavir and ombitasvir with dasabuvir with ribavirin (Viekira Pak-RBV);

resolved to approve the 28 November 2018 amendment to the 21 October 2015 agreement with AbbVie Ltd relating to the listing of adalimumab (Humira, HumiraPen);

resolved that the consultation on this proposal was appropriate, and no further consultation is required;

noted that Maviret would be distributed to pharmacies under a mechanism that would be funded by the supplier, AbbVie Ltd; and

noted the implementation plan that would support this proposal.

Jens Mueller and Ross Lawrenson **(carried)**

Proposal to list glecaprevir-pibrentasvir (Maviret) for the treatment of chronic hepatitis C – resolutions

resolved to list glecaprevir-pibrentasvir (Maviret) in the Hepatitis C Treatment therapeutic subgroup of the Infections – agents for systemic use therapeutic group in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 February 2019, as follows (ex-manufacturer, excl. GST);

Chemical	Presentation	Brand	Pack size	Price and subsidy
Glecaprevir with pibrentasvir	Tab 100 mg with pibrentasvir 40 mg	Maviret	84 OP	$24,750.00

resolved to apply the following note to the listing of glecaprevir with pibrentasvir in Section B of the Pharmaceutical Schedule from 1 February 2019 as follows;

noted the supply of treatment is via PHARMAC's approved direct distribution supply. Further details can be found on PHARMAC's website https://www.pharmac.govt.nz/hepatitis-c-treatments/

resolved to apply Xpharm to the listing of glecaprevir with pibrentasvir in Section B of the Pharmaceutical Schedule from 1 February 2019;

resolved to apply the following note to the listing of glecaprevir with pibrentasvir in Part II of Section H of the Pharmaceutical Schedule from 1 February 2019;

noted the supply of treatment is via PHARMAC's approved direct distribution supply. Further details can be found on PHARMAC's website https://www.pharmac.govt.nz/hepatitis-c-treatments/

resolved to delist Viekira Pak (paritaprevir, ritonavir and ombitasvir with dasabuvir) from the Hepatitis C Treatment therapeutic subgroup of the Infections – agents for systemic use therapeutic group in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 February 2019 as follows:

Chemical	Presentation	Brand	Pack size
Paritaprevir, ritonavir and ombitasvir with dasabuvir	Tab 75 mg with ritonavir 50 mg, and ombitasvir 12.5 mg (56), with dasabuvir tab 250 mg (56)	Viekira Pak	1 OP

resolved to delist Viekira Pak-RBV (paritaprevir, ritonavir and ombitasvir with dasabuvir and ribavirin) from the Hepatitis C Treatment therapeutic subgroup of the Infections – agents for systemic use therapeutic group in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 February 2019 as follows:

Chemical	Presentation	Brand	Pack size
Paritaprevir, ritonavir and ombitasvir with dasabuvir and ribavirin	Tab 75 mg with ritonavir 50 mg, and ombitasvir 12.5 mg (56) with dasabuvir tab 250 mg (56) and ribavirin tab 200 mg (168)	Viekira Pak-RBV	1 OP

Jan White and Jens Mueller **(carried)**

The meeting closed at 2.05pm

Chair [signature] Date 1/2/18