# Anti-Infective Subcommittee of PTAC

# Meeting held 13 December 2012

# (minutes for web publishing)

Anti-Infective Subcommittee minutes are published in accordance with the *Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and PTAC Subcommittees 2008*.

Note:

- that this document is not necessarily a complete record of the Anti-Infective Subcommittee meeting; only the relevant portions of the minutes relating to Anti-Infective Subcommittee discussions about an Application or PHARMAC staff proposal that contain a recommendation are generally published.
- that any part of the minutes relating to hospital pharmaceuticals and the establishment of a national Preferred Medicines List (PML) will be released, in a complete publication with the original Hospital Pharmaceuticals Subcommittee minutes and final recommendations made by PTAC, once PTAC have reviewed each therapeutic group.

The Anti-Infective Subcommittee may:

(a) recommend that a pharmaceutical be listed by PHARMAC on the Pharmaceutical Schedule and the priority it gives to such a listing;
(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or
(c) recommend that PHARMAC decline to list a pharmaceutical on the Pharmaceutical Schedule.

These Subcommittee minutes were reviewed by PTAC at its meeting on 14 & 15 February 2013, the record of which will be available in April 2013.

# 1 Clinically recommended action points

1.1 The Subcommittee recommended that PHARMAC:

1.1.1 Fund moxifloxacin for Mycoplasma genitalium under Special Authority;

1.1.2 seek the advice of the Ophthalmology Subcommittee as to the appropriate wording of a restriction for moxifloxacin in penetrating eye injury;

1.1.3 remove the treatment naïve indication initiation from lamivudine as this was no longer clinically appropriate;

1.1.4 widen funded access to lamivudine with a medium priority to include prophylaxis for HBsAg +ve patients receiving anti-TNF therapy;

1.1.5 fund nitazoxanide with a medium priority under a Special Authority for refractory giardiasis or cryptosporidiosis;

1.1.6 widen access to tenofovir for treatment naïve hepatitis B patients with advanced fibrosis/cirrhosis only if cost neutral to entecavir;

1.1.7 widen access to tenofovir with a high priority for patients with decompensated cirrhosis under Special Authority;

1.1.8 fund, with a high priority, either boceprevir or telaprevir for treatment naïve hepatitis C genotype 1 patients with cirrhosis or advanced fibrosis who do not have the IL-28 genotype CC;

1.1.9 fund, with a high priority, either boceprevir or telaprevir for treatment-experienced hepatitis C genotype 1 patients regardless of fibrosis stage, who were responder relapsers or partial responders; and

1.1.10 fund, with a low priority, either boceprevir or telaprevir for hepatitis C genotype 1 patients who were treated with standard or pegylated interferon and ribavirin prior to 2004 who did not achieve an SVR but for whom early on treatment responses are not available.

# 2 Matters Arising and Therapeutic Group review

2.1 The Subcommittee noted its previous advice relating to cefazolin and recommended this be amended to the following (additions in **bold**):

> Only if prescribed for cellulitis in accordance with a DHB **approved** protocol and the prescription is endorsed accordingly.

2.2 The Subcommittee considered that cefazolin should be available on Practitioner Supply Order to facilitate appropriate usage in General Practice.

2.3 The Subcommittee noted that cefazolin would also be the appropriate prophylactic antibiotic for compound fractures in penicillin allergic patients.



Chair

*Moxifloxacin*

2.4 The Subcommittee noted the Named Patient Pharmaceutical Applications (NPPA) received for moxifloxacin for two indications, use in pseudomonas meningitis and penetrating eye injury, and a request for consideration of funding for use in mycoplasma genitalia.

2.5 The Subcommittee considered that moxifloxacin should not be a first line agent for the indication of pseudomonas meningitis. The Subcommittee noted that if microbiological confirmation of highly resistant isolates sensitive only to moxifloxacin was demonstrated, then moxifloxacin could be applied for under NPPA

2.6 The Subcommittee noted its previous advice regarding moxifloxacin usage. The Subcommittee noted that the minute was open to interpretation and recommended amending the restriction as follows (addition in bold):

> pneumococcal pneumonia or other invasive **pneumococcal** disease highly resistant to other antibiotics.

2.7 The Subcommittee noted that NPPA may remain appropriate for certain very specialised patients.

2.8 The Subcommittee considered the applications for use of moxifloxacin in penetrating eye injuries. The Subcommittee considered that this could represent a large group of patients who would be able to access this treatment. The Subcommittee noted that for the paediatric population, moxifloxacin dosing was not well elucidated as yet and that intravenous ceftazidime with or without vancomycin was available for penetrating eye injuries.

2.9 The Subcommittee considered that in most penetrating eye injury situations patients would be monitored very closely by Ophthalmologists and in these situations an intravenous antibiotic should be considered. The Subcommittee noted that delivery of eye care in New Zealand would be variable around the country due to the availability of Ophthalmologists.

2.10 Members noted that moxifloxacin was an appropriate oral antimicrobial agent for use in penetrating eye injuries but the definition of a penetrating eye injury would be important. The Subcommittee considered that the definition should define penetrating eye injury as one that penetrates to the aqueous humour. The Subcommittee considered a Special Authority with a 5 day approval and renewal may be appropriate.

2.11 The Subcommittee **recommended** seeking the advice of the Ophthalmology Subcommittee as to the appropriate wording of a restriction for moxifloxacin in penetrating eye injury.

2.12 The Subcommittee noted the request from Auckland District Health Board for consideration of funding of moxifloxacin for Mycoplasma genitalium. The Subcommittee noted that polymerise chain reaction (PCR) testing had been established in New Zealand and this was leading to an increase in diagnosis of

Mycoplasma genitalium in patients. Members noted that PCR testing was usually undertaken in patients with recurrent urethritis who had failure of first line agents.

2.13 The Subcommittee considered that the first line agents for treatment of mycoplasma genitalia were doxycycline or azithromycin. Members noted that if patients failed to clear Mycoplasma genitalium following adequate azithromycin therapy then it was unlikely that doxycycline would be effective. Members noted that testing should occur two weeks after therapy to ensure the treatment has had time to be effective. Members noted that some patients may re-infect but this would be hard to determine.

2.14 The Subcommittee noted that there was no resistance testing available in New Zealand at this time. The Subcommittee considered that moxifloxacin should not be used as a first line agent for Mycoplasma genitalium.

2.15 The Subcommittee **recommended** that moxifloxacin be funded for Mycoplasma genitalium under the following Special Authority:

Approval valid for 7 days for patients meeting the following criteria

1) Has polymerase chain reaction (PCR) confirmed Mycoplasma genitalium; and

2) has tried and failed to clear infection using azithromycin.

2.16 The Subcommittee considered that there was no evidence for treating the partner of a patient with Mycoplasma genitalium with moxifloxacin at this time.

2.17 The Subcommittee considered that the Special Authority should remain in place for lamivudine. The Subcommittee noted that lamivudine should not be used as a first line agent as resistance to lamivudine could confer some resistance to other antivirals.

2.18 The Subcommittee **recommended** removing the treatment naïve indication initiation from lamivudine as this was no longer clinically appropriate. The Subcommittee recommended that the renewal remain at 2 years as patients should be regularly reviewed to ensure there was no virological escape. The Subcommittee further recommended removing all of the contraindications in part 2 of the current Special Authority applying to lamivudine as these were no longer clinically relevant.

2.19 The Subcommittee noted that hepatitis B surface antigen positive (HBsAg+ve) patients who were receiving anti tumour necrosis factor (TNF) treatment were immunosuppressed and at risk of reactivation. The Subcommittee noted that all patients should be tested for hepatitis B and tuberculosis prior to initiation on anti-TNF agents.

2.20 The Subcommittee **recommended** widening funded access with a medium priorty to lamivudine to include prophylaxis for HBsAg +ve patients receiving anti-TNF therapy. Members recommended that the Special Authority criteria applying to lamivudine funding be amended as follows (additions in bold, deletions in strikethrough, note includes previous recommendations):

Initial application only from a gastroenterologist, infectious disease specialist, paediatrician or general physician. Approvals valid for 1 year for applications meeting the following criteria:
Both:
1 Any of the following:
~~1.1 All of the following:~~
~~1.1.1 HBsAg positive for more than 6 months; and~~
~~1.1.2 HBeAg positive or HBV DNA positive defined as > 100,000 copies per ml by quantitative PCR at a reference laboratory; and~~
~~1.1.3 ALT greater than twice upper limit of normal or bridging fibrosis or cirrhosis (Metavir stage 3 or 4 or equivalent) on liver histology or clinical/radiological evidence of cirrhosis;~~
~~or~~
1.~~2~~**1** HBV DNA positive cirrhosis prior to liver transplantation; or
1.~~3~~**2** HBsAg positive and have had a liver, kidney, heart, lung or bone marrow transplant; or
**1.4~~3~~ Hepatitis B virus naïve patient who has received a liver transplant from an anti-HBc (Hepatitis B core antibody) positive donor; or**
1.4 Hepatitis B surface antigen (HbsAg) **positive** patient who is receiving chemotherapy for a malignancy, or high dose steroids (at least 20mg/day for at least 7 days) or who has received such treatment within the previous two months; **or**
**1.5 Hepatitis B surface antigen positive patient who is receiving anti tumour necrosis factor treatment**
**1.6 Hepatitis B core antibody (anti-HBc) positive patient who is receiving rituximab plus high dose steroids (e.g. R-CHOP).**

~~2 All of the following:~~
~~2.1 No continuing alcohol abuse or intravenous drug use; and~~
~~2.2 Not coinfected with HCV or HDV; and~~
~~2.3 Neither ALT nor AST greater than 10 times upper limit of normal; and~~
~~2.4 No history of hypersensitivity to lamivudine; and~~
~~2.5 No previous lamivudine therapy with genotypically proven lamivudine resistance.~~

Renewal only from a gastroenterologist, infectious disease specialist, paediatrician or general physician. Approvals valid for 2 years for applications meeting the following criteria:
Either:
Renewal for patients who have maintained continuous treatment and response to lamivudine
1 All of the following:
1.1 Have maintained continuous treatment with lamivudine; and
1.2 Most recent test result shows continuing biochemical response (normal ALT); and,
1.3 HBV DNA < 100,000 copies per ml by quantitative PCR at a reference laboratory.
Renewal when given in combination with adefovir dipivoxil for patients with cirrhosis and resistance to lamivudine
2 All of the following
2.1 lamivudine to be used in combination with adefovir dipivoxil; and
2.2 patient is cirrhotic; and
Documented resistance to lamivudine, defined as:
2.3 patient has raised serum ALT (> 1 x ULN); and
2.4 patient has HBV DNA greater than 100,000 copies per mL, or viral load = 10 fold over nadir; and
2.5 detection of M204I or M204V mutation.

Renewal when given in combination with adefovir dipivoxil for patients with resistance to adefovir dipivoxil
1 All of the following
1.1 lamivudine to be used in combination with adefovir dipivoxil; and
Documented resistance to adefovir, defined as:
1.2 patient has raised serum ALT (> 1 x ULN); and
1.3 patient has HBV DNA greater than 100,000 copies per mL, or viral load = 10 fold over nadir; and
1.4 detection of N236T or A181T/V mutation.



Chair

2.21 The Subcommittee noted its previous recommendation regarding the restriction applying to vancomycin. The Subcommittee **recommended** the wording could be amended for clarity as pseudomembranous colitis was commonly caused by Clostridium difficile as follows (deletions in ~~strikethrough~~, additions in **bold**):

> Only if prescribed for a dialysis or cystic fibrosis patient or ~~in the treatment of pseudomembranous colitis or~~ for prophylaxis of endocarditis or for **treatment of Clostridium difficile following metronidazole failure** and the prescription is endorsed accordingly.

2.22 The Subcommittee noted that internationally hyper-virulent strains of Clostridium difficile were developing and patients may require combinations of metronidazole and/or first line oral vancomycin therapy. Members noted that this should be monitored and that the restriction may need to be amended into the future.

# 3 Quinacrine

3.1 The Subcommittee noted the PHARMAC-generated application for consideration of quinacrine for treatment of refractory giardiasis. The Subcommittee noted that there had only been five applications under PHARMAC's exception scheme (Exceptional Circumstances or Named Patient Pharmaceutical Assessment) in the last five years.

3.2 The Subcommittee noted that this treatment would only be applied for if the clinician could not access nitazoxanide and there was no need to consider this for a listing on the Pharmaceutical Schedule.

3.3 The Subcommittee considered that nitazoxanide would be the preferred community treatment for refractory giardiasis. The Subcommittee **recommended** funding nitazoxanide with a medium priority under a Special Authority as follows:

> Application from any prescriber for patients meeting any of the following criteria:
>
> 1. Patient has confirmed giardiasis and has failed to clear infection following two courses of nitroimidazole therapy; or
>
> 2. Patient has confirmed cryptosporidiosis and is immunocompromised.

3.4 The Subcommittee considered that PHARMAC should confirm patient numbers with community microbiology laboratories.

# 4 Tenofovir

*Tenofovir for treatment naïve hepatitis B patients with advanced fibrosis/cirrhosis*

4.1 The Subcommittee considered an application from Gilead for widening of access to tenofovir for treatment naïve hepatitis B patients with advanced fibrosis/cirrhosis.

4.2 The Subcommittee noted the key evidence supplied was the follow-up open label study from the two seminal studies of tenofovir, study 102 and 103. This study



Chair

followed 650 patients who were involved in the phase III trial over a period of 6 years. Members noted that 75% of the patients with an Ishak score of 4-6 (equivalent to metavir stage F3 or F4) at baseline showed an improvement of liver histology after 5 years.

4.3 Members noted the CALM study of lamivudine vs placebo which showed that reduction in viral load reduced the risk of hepatocellular carcinoma in patients with chronic hepatitis B. Members noted the recently published study in the Lancet (Marcellin et al. Regression of cirrhosis during treatment with tenofovir for chronic hepatitis B: a 5 year open-label follow-up study. Lancet on-line December 2012) which noted that there was currently no evidence to answer the question 'if complete viral suppression is achieved does this remove the risk of liver cancer?' however there is evidence complete viral suppression would reduce the risk. Members noted that if complete virological suppression was obtained then liver remodelling would occur.

4.4 The Subcommittee noted that there were no long term studies of entecavir for this indication at this time. Members noted that while there was no evidence that entecavir caused this histological change there was no evidence that this effect would not been seen. Members considered it was likely that if virological suppression occurred it was likely that histological remodelling would occur.

4.5 Members **recommended** widening access to tenofovir for treatment naïve hepatitis B patients with advanced fibrosis/cirrhosis only if cost neutral to entecavir.

*Tenofovir for patients with decompensated cirrhosis*

4.6 The Subcommittee noted that patients with decompensated cirrhosis are at risk of lactic acidosis if treated with entecavir. Members noted that patients with a Mayo score >20 were at particular risk of lactic acidosis.

4.7 Members considered there would be approximately 10 patients per annum who would access tenofovir under this indication.

4.8 The Subcommittee **recommended** with a high priority widening access to tenofovir for patients with decompensated cirrhosis under Special Authority as follows (additions in bold):

Initial application - (Chronic Hepatitis B) Only from a gastroenterologist, infectious disease specialist or general physician. Approvals valid without further renewal, unless notified, for applications meeting the following criteria:
Both
1 Patient has confirmed Hepatitis B infection (HBsAg positive for more than 6 months); and
2 Any of the following
2.1 All of the following
2.1.1 Patient has had previous lamivudine, adefovir or entecavir therapy; and
2.1.2 HBV DNA greater than 20,000 IU/mL or increased = 10 fold over nadir; and
2.1.3 Any of the following:
2.3.1 Lamivudine resistance - detection of M204I/V mutation; or



Chair

2.3.2 Adefovir resistance - detection of A181T/V or N236T mutation; or
2.3.3 Entecavir resistance - detection of relevant mutations including I169T, L180M T184S/A/I/L/G/C/M, S202C/G/I, M204V or M250I/V mutation; or

2.2 Patient is either listed or has undergone liver transplantation for HBV; **or**

**2.3 Patient has decompensated cirrhosis with a Mayo score >20.**

# 5 Protease Inhibitors for Hepatitis C – boceprevir and telaprevir

5.1 The Subcommittee noted the applications from Janssen-Cilag (telaprevir) and Merck Sharp and Dohme (boceprevir) for funding of their protease inhibitors for the treatment of patients with hepatitis C genotype 1 in combination with pegylated interferon with ribavirin (PGR).

5.2 The Subcommittee noted the August 2012 PTAC minute for telaprevir and boceprevir.

5.3 The Subcommittee noted that these were the first generation direct acting antiviral agents (DAAs) for the treatment of hepatitis C genotype 1. Members noted that they had a minimal effect in genotypes 2 and 4 and no effect on genotype 3. Members noted that 55% of hepatitis C patients were genotype 1 in New Zealand.

5.4 The Subcommittee noted that these products had to be given in combination with pegylated interferon and ribavirin. Members noted that if the protease inhibitors were given in isolation that resistance rapidly developed.

5.5 The Subcommittee noted that both products increased the sustained virological response rate in treatment naïve genotype 1 patients from 45% to 75%. Members noted that in the trials boceprevir had a slightly lower cure rate in both arms (placebo versus active) due to the included patient population. Members noted that there were more patients of African American descent in the boceprevir trial and this patient group had a lower response rate. Members noted that the SVR achieved in the New Zealand population would be an estimated 5% lower than in the trials, due to the higher fraction of HCV genotype 1a, which is more difficult to treat.

5.6 The Subcommittee considered that approximately 1% of the eligible population of hepatitis C patients had been treated with pegylated interferon so there was only a small population of treatment experienced patients. Members noted that responder relapsers had the most significant improvement in response rate with the addition of a DAA having an SVR of 75-80% compared to 20% on PGR alone. Partial responders also showed an improvement but it was lower than responder relapsers. Null responders only had a 20% chance of achieving SVR with the addition of a DAA to pegylated interferon.

5.7 The Subcommittee noted that telaprevir was only given for 12 weeks of therapy in combination with PGR followed by 12 or 36 weeks of PGR as per response guided therapy. Members noted that while Phase III trials tested an 8 week course of telaprevir in first line and a lead-in period in second line, these

alternative treatment algorithms were not proposed by Janssen-Cilag. Members noted that the major adverse event for patients on telaprevir was rash which could be severe and life threatening. Members noted that 5-10% of patients would have to cease telaprevir due to this rash.

5.8 The Subcommittee noted that boceprevir had a four week PGR initial phase followed by combination boceprevir and PGR from week four to week 28, then complete PGR as per response guided therapy, either to week 28, 36 or 48 as appropriate. The Subcommittee noted that the major adverse event associated with boceprevir was anaemia. Members noted that reducing the dose of ribavirin resolved this issue in most cases and erythropoietin was not usually required. Members considered that telaprevir and boceprevir were probably similar in terms of tolerability and safety profile.

5.9 Members noted reports from usage in the global early access programs had identified an issue in cirrhotic patients. Patients with cirrhosis and an increase in portal hypertension had a significantly higher rate of serious events and increased mortality. Members noted that the mortality rate in this patient group was 2-3%. Members considered that patients with cirrhosis should be screened to ensure there was no significant portal hypertension, varices or decompensation.

5.10 The Subcommittee noted that the IL-28 genotype was an important indicator of likely success of PGR and therefore the need for addition of a DAA. There are two inherited alleles – C which carries favourable response and T which is unfavourable. Members noted that patients with the homozygous CC genotype had a 75% chance of achieving SVR on PGR alone and the addition of a DAA did not significantly improve this rate. Members noted that where the genotype was TC or TT there was a lower rate of response to PGR with likely SVR of 30% and addition of a DAA for this group would increase the likelihood of SVR to around 75%.

5.11 The Subcommittee noted that the incidence of the favourable C allele is related to ethnicity. Members noted that there were high rates of the C allele in Asian populations and Maori and Pacific peoples. Members noted that Caucasians had a lower rate of the C allele.

5.12 The Subcommittee noted that Phase II trials for use of telaprevir and boceprevir in patients with advanced fibrosis showed similar rates of SVR.

5.13 The Subcommittee noted that if a patient had a very rapid virological response and had undetectable viral load at 4 weeks then there was no benefit in the addition of boceprevir. Members noted that in practice there was a two week delay in getting laboratory results. Members noted that between 10 and 15% of patients would have an undetectable load at 4 weeks.

5.14 Members noted that triple oral therapy for hepatitis C were undergoing phase III trials and were likely to be registered in 2015/16. Members noted that the development of resistance to the current DAAs was unlikely to cause a resistance issue for future products as there appeared to be no archiving of mutations in the hepatitis C virus.



Chair

5.15 Members noted that there were no phase III trials using DAAs in patients co-infected with HIV. Members noted that the phase II trials showed significant drug interactions for patients receiving anti-retroviral therapy with the addition of DAAs. Members noted that boceprevir appeared to cause greater interactions than telaprevir.

5.16 The Subcommittee noted that the DAAs could not be used in the post liver transplant due the increased risk of complications and lack of evidence at this time.

5.17 The Subcommittee noted that patients with a hepatitis C lymphoma could have resolution of the lymphoma if an SVR could be achieved. Members noted that there would be approximately 10 patients per annum who may have a hepatitis C lymphoma that would benefit from DAA and PGR combination therapy.

5.18 The Subcommittee considered that the group that would benefit most from treatment would be Hepatitis C genotype 1 patients with cirrhosis (excluding patients with portal hypertension and significant varices or decompensation), or advanced fibrosis (defined as F3 or F4 on fibroscan).

5.19 The Subcommittee considered that hepatitis C genotype 1 patients with non CC allele IL-28 genotype had a lower rate of response to pegylated interferon and ribavirin. Members noted that this group had a significant improvement in efficacy of achieving SVR with the addition of a DAA to PGR than PGR alone.

5.20 The Subcommittee considered that PGR responder relapse patients would benefit from retreatment with PGR and a DAA as they had a 75% chance of achieving an SVR. Members considered that partial responders would also benefit from retreatment with PGR and a DAA.

5.21 The Subcommittee noted that prior to 2004 the testing available did not allow clinicians to differentiate between partial responders and null responders. Members noted that this would represent a small patient group. Members noted that only 5% of patients have a partial response to PGR and it may not be cost effective to treat this group.

5.22 The Subcommittee considered that null responders to PGR had a very low chance of achieving SVR with combination PGR and a DAA and that it was unlikely to be cost effective to treat this group.

5.23 The Subcommittee **recommended** that either telaprevir or boceprevir would be an appropriate agent to fund as the products produced the same or similar in efficacy.

5.24 The Subcommittee **recommended,** with a high priority, funding either boceprevir or telaprevir for hepatitis C genotype 1 patients with cirrhosis or advanced fibrosis who are pegylated interferon and ribavirin treatment naïve, under the following Special Authority:



Chair

Application from gastroenterologist, Infectious disease specialist or General physician. Approvals valid for 12 or 24 weeks (as appropriate) for applications meeting the following criteria:

1 All of the following
- 1.1 Patient has hepatitis C genotype 1; and
- 1.2 Patient has IL-28B genotype CT or TT; and
- 1.3 Patient has severe fibrosis (F3) or cirrhosis (F4) or on fibroscan or equivalent; and both
  - 1.3.1 Patient does not have significant portal hypertension or varices; and
  - 1.3.2 Patient does not have decompensated liver disease
- 1.4 Patient has an approved Special Authority for pegylated interferon and ribavirin; and
- 1.5 Boceprevir/telaprevir is to be used in combination with pegylated interferon with ribavirin.

5.25 The Subcommittee **recommended,** with a high priority, funding retreatment with pegylated interferon and ribavirin in combination with boceprevir or telaprevir for hepatitis C genotype 1 patients who were either responder relapsers or partial responders to prior treatment with pegylated interferon and ribavirin. Members noted that a Special Authority would be required and offered to develop this if required.

5.26 The Subcommittee **recommended,** with a low priority, funding retreatment with pegylated interferon and ribavirin in combination with boceprevir or telaprevir for hepatitis C genotype 1 patients treated prior to 2004 with either standard interferon or pegylated interferon and ribavirin who did not achieve an SVR and in whom early on-treatment responses were not available.

5.27 The Subcommittee **recommended** funding boceprevir or telaprevir for either responder relapsers or partial responders (high priority) or patients treated prior to 2004 who did not achieve an SVR (low priority), under the following Special Authority:

Application from gastroenterologist, Infectious disease specialist or General physician. Approvals valid for 12 or 24 weeks (as appropriate) for applications meeting the following criteria:

1 All of the following
- 1.1 Patient has hepatitis C genotype 1; and
- 1.2 Patient has an approved Special Authority for pegylated interferon and ribavirin; and
- 1.3 Boceprevir/telaprevir is to be used in combination with pegylated interferon with ribavirin; and

2 Patient has previously been treated with pegylated interferon and ribavirin; and
- 2.1 either
  - 2.1.1 relapsed following a virological response on pegylated interferon and ribavirin; or
  - 2.1.2 had a partial response to pegylated interferon and ribavirin; or



Chair

2.1.3 received pegylated interferon and ribavirin prior to 2004 and did not achieve a sustained virological response; and

3 Patient has not received previous treatment with a protease inhibitor.

5.28 The Subcommittee **recommended** funding for DAAs for treatment naïve patients or Il-28 TC or TT allele patient groups with a low priority, The Subcommittee noted that the budget impact of funding these groups should be considered.

5.29 Members noted that if the DAAs were funded for treatment naïve patients or Il-28 TC or TT allele patient groups that the Special Authorities for advanced fibrosis or cirrhosis and previous partial responders or responder relapsers or those who received therapy prior to 2004 who did not achieve an SVR would still be required, alongside retreatment with pegylated interferon with ribavirin.

5.30 The Subcommittee noted the stopping rules provided by Janssen-Cilag with respect to telaprevir and from Merck Sharp and Dohme with respect to boceprevir. Members considered these stopping criteria to be appropriate.

5.31 The Subcommittee noted that there were an estimated 45,000-55,000 people with hepatitis C in New Zealand. Members noted that incidence of hepatitis C was estimated to have halved in the last decade, but that the proportion with cirrhosis would double by 2030. Members noted that less than 25% of the hepatitis C population had been diagnosed and less than 10% have been treated.

5.32 Members noted there are approximately 1000 hepatitis C patients per annum who has undergone antiviral treatment and of these approximately 500 were genotype 1. Of those patients, currently >90% were DAA treatment naïve.

5.33 The Subcommittee estimated that the availability of telaprevir or boceprevir will increase treatment uptake in patients with hepatitis C genotype 1. They estimated that there will be a pool of almost 500 hepatitis C genotype 1 patients who were either responder relapsers or partial responders to PGR who would benefit from retreatment with boceprevir or telaprevir. In addition there would be approximately 100 new treatment naive hepatitis C genotype 1 patients with severe fibrosis (F3) or compensated cirrhosis (F4) requiring treatment per annum.