PHARMAC
Pharmaceutical Management Agency

MEMORANDUM FOR CONSIDERATION BY CHIEF EXECUTIVE UNDER DELEGATED AUTHORITY

To: Steffan Crausaz, Chief Executive

From: Christine Chapman and Greg Williams

Date: 10 July 2012

Listing montelukast and ivermectin on the Pharmaceutical Schedule

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 exercise your delegated authority and:

resolve to create a new subheading in Section B of the Pharmaceutical Schedule named "Leukotriene Receptor Antagonists" in the Respiratory System and Allergies therapeutic group from 1 August 2012;

resolve to list Singulair (montelukast) in the Leukotrine Receptor Agonists subgroup of the Respiratory System and Allergies section in Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 August 2012 at a price and subsidy as follows (ex-manufacturer, excl. GST):

Chemical	Presentation	Product	Pack size	Price and subsidy
Montelukast	Tab 4 mg	Singulair	28	$18.48
Montelukast	Tab 5 mg	Singulair	28	$18.48
Montelukast	Tab 10 mg	Singulair	28	$18.48

resolve to apply the following Special Authority and prescribing guideline to the listing of montelukast in Section B of the Pharmaceutical Schedule from 1 August 2012:

Prescribing Guideline: Clinical evidence indicates that the effectiveness of montelukast is strongest when montelukast is used in short treatment courses.

Special Authority for subsidy

Initial application (Pre-school wheeze) from any relevant practitioner. Approvals valid for one year for applications meeting the following criteria:

All of the following:

1 To be used for the treatment of intermittent severe wheezing (possibly viral) in children under 5 years; and

2 The patient has trialled inhaled corticosteroids at a dose of up to 400µg per day beclomethasone or budesonide, or 200 µg per day fluticasone for at least one month; and

3 The patient continues to have at least three severe exacerbations at least one of which required hospitalisation (defined as in-patient stay or prolonged Emergency Department treatment) in the past 12 months.

Renewal (pre-school wheeze) **-** only from a relevant practitioner. Approvals valid for two years where the treatment remains appropriate and the patient is benefitting from treatment.

Initial application (exercise-induced asthma) from any relevant practitioner. Approvals valid without further renewal, unless notified, for applications meeting the following criteria:

Both:

1 Patient is being treated with maximal asthma therapy, including inhaled corticosteroids and long-acting beta-adrenoceptor agonists; and

2 Patient continues to experience frequent episodes of exercise-induced bronchoconstriction.

Initial application (aspirin desensitisation) only from a Clinical Immunologist or an Allergist. Approvals valid for one year, for applications meeting the following criteria:

1 All of the following:

1.1 Patient is undergoing aspirin desensitisation therapy under the supervision of a Clinical Immunologist or Allergist centre; and

1.2 Patient has moderate to severe aspirin-exacerbated respiratory disease or Samter's triad; and

1.3 Nasal polyposis, confirmed radiologically or surgically; and

1.4 Documented aspirin or NSAID allergy confirmed by aspirin challenge or a clinical history of severe reaction to aspirin or NSAID where challenge would be considered dangerous.

resolve to list Stromectol (ivermectin) 3 mg tablets in the Parasitical Preparations subgroup of the Dermatologicals section of Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 August 2012 at a price and subsidy of $17.20 per 4 tabs (ex- manufacturer, excl GST);

resolve to apply the following Special Authority criteria to the listing of ivermectin in Section B of the Pharmaceutical Schedule from 1 August 2012:

Special Authority for subsidy

Initial application (Scabies) from any relevant practitioner. Approvals valid for one month for applications meeting the following criteria

Applying clinician has discussed the diagnosis of scabies with a Dermatologist, Infectious Disease physician or clinical microbiologist; and

1. The patient is in the community; and
2. Either
   - 2.1. Patient has a severe scabies hyperinfestation (Crusted/ Norwegian scabies); or
   - 2.2. The community patient is physically or mentally unable to comply with the application instructions of topical therapy; or
   - 2.3. The patient has previously tried and failed to clear infestation using topical therapy

Or

3. The Patient is a resident in an institution and
4. All residents of the institution with scabies or at risk of carriage are to be treated for scabies concurrently; and

5. either
   5.1. Patient has a severe scabies hyperinfestation (Crusted/ Norwegian scabies); or
   5.2. The patient is physically or mentally unable to comply with the application instructions of topical therapy; or
   5.3. previous topical therapy has been tried and failed to clear the infestation

Renewal application (Scabies) from any relevant practitioner. Approvals valid for one month for applications meeting the following criteria

Applying clinician has discussed the diagnosis of scabies with a Dermatologist, Infectious Disease physician or clinical microbiologist; and
1. The patient is in the community; and
2. Either
   2.1. Patient has a severe scabies hyperinfestation (Crusted/ Norwegian scabies); or
   2.2. The community patient is physically or mentally unable to comply with the application instructions of topical therapy; or
   2.3. The patient has previously tried and failed to clear infestation using topical therapy
3. Or
4. The Patient is a resident in an institution and
5. All residents of the institution with scabies or at risk of carriage are to be treated for scabies concurrently; and
6. either
   6.1. Patient has a severe scabies hyperinfestation (Crusted/ Norwegian scabies); or
   6.2. The patient is physically or mentally unable to comply with the application instructions of topical therapy; or
   6.3. previous topical therapy has been tried and failed to clear the infestation

Note: Ivermectin is no more effective than topical therapy for treatment of standard scabies infestation.

Initial application (Other parasitic infections) from Infectious Disease Clinician, Clinical Microbiologist or Dermatologist. Approvals valid for one month for applications meeting the following criteria

Patient has either
1 Filaricides: or
2 Cutaneous larva migrans (creeping eruption); or
3 Strongyloidiasis

Renewal (Other parasitic infections) from Infectious Disease Clinician, Clinical Microbiologist or Dermatologist. Approvals valid for one month for applications meeting the following criteria

Patient has subsequent infection of either
1 Filaricides: or
2 Cutaneous larva migrans (creeping eruption); or
3 Strongyloidiasis

resolve to apply the following rule to Stromectol (ivermectin) as listed in Section B of the Pharmaceutical Schedule from 1 August 2012:

up to 100 tablets available on PSO

Note: PSO for institutional use only. Must be endorsed with the name of the institution for which the PSO is required and a valid Special Authority for patient of that institution

Note: Ivermectin available on BSO provided the BSO includes a valid Special Authority for a patient of the institution.

Note: for the purposes of subsidy of ivermectin, institution means age related residential care facilities, disability care facilities or penal institutions.

resolve to approve the 5 June 2012 agreement with Merck Sharp and Dohme (New Zealand) Limited.

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

SUMMARY OF PROPOSAL				
Market data	**Year ending**	**30 Jun 2013**	**30 Jun 2014**	**30 Jun 2015**
	Number of patients	17,911	19,988	21,341
	Number of Maori or PI people	1,480	1,707	1,980
Community Pharmaceuticals	Subsidy (gross)	$790,000	$890,000	$980,000
	Net cost to Schedule	$760,000	$780,000	$800,000
	Net present value	$3,560,000		
	Net distribution costs	s 9(2)(j)		
	Net cost to DHBs			
	Net present value			
Total	Total cost to DHBs			
	Net present value			

SUMMARY OF PHARMACEUTICAL			
Brand name	Singulair	**Chemical name**	Montelukast
Therapeutic Group	Leukotriene receptor antagonists	**Presentation**	4 mg chewable table, 5 mg chewable tablet, 10 mg tablet
Supplier	Merck Sharp and Dohme	**Proposal type**	New listing
MoH Restriction	Prescription medicine	**Application date**	01-Oct-1998
Section F	No	**Original pack**	No
Proposed restriction	0		

Brand - Formulation - Packsize	**Current subsidy**	**Proposed subsidy**	**Price**
Singulair - 4 mg chewable tab -28	NA	s 9(2)(j)	$18.48
Singulair - 5 mg chewable tab -28	NA		$18.48
Singulair - 10 mg tab -28	NA		$18.48

Market data	**Year ending**	**30 Jun 2013**	**30 Jun 2014**	**30 Jun 2015**
Number of patients		7,335	8,450	9,803
Number of Maori or PI people		1,480	1,707	1,980
Community Pharmaceuticals	Subsidy (gross)	$460,000	$530,000	$620,000
	Net cost to Schedule	s 9(2)(j)		
	Net present value			
	Net distribution costs			
	Net cost to DHBs			
	Net present value			
Total	Total cost to DHBs			
	Net present value			

Notes:
1. Subsidy (gross) and expenditure (gross) = forecast of spending at the proposed price and subsidy.
2. Net cost to DHBs = forecast of change in spending compared with status quo.
3. All pharmaceutical costs are ex-manufacturer.
4. All costs are ex-GST.
5. NPV is calculated over 5 years using an annual discount rate of 8%.
6. Calculations are in A502315.

SUMMARY OF PHARMACEUTICAL					
Brand name	Stromectol		**Chemical name**	Ivermectin	
Therapeutic Group	Anthelmintics (Infections - Agents for Systemic Use)		**Presentation**	Tab 3 mg	
Supplier	Merck Sharp and Dohme		**Proposal type**	New Listing	
MoH Restriction	Prescription medicine		**Application date**	May 2010	
Section F	No		**Original pack**	No	
Proposed restriction	Special Authority				
Brand - Formulation – Pack size	**Current subsidy**		**Proposed subsidy**	**Price**	
Stromectol - Tab 3 mg - 4		$0.00	$17.20	$17.20	
Market data	**Year ending**		**30 Jun 2013**	**30 Jun 2014**	**30 Jun 2015**
Number of patients			10,576	11,538	11,538
Community Pharmaceuticals	Subsidy (gross)		$330,000	$360,000	$360,000
	Net cost to Schedule		$300,000	$330,000	$330,000
	Net present value		$1,380,000		
	Net distribution costs		$12,000	$13,000	$13,000
	Net cost to DHBs		$310,000	$340,000	$340,000
	Net present value		$1,430,000		
Total	Total cost to DHBs		$310,000	$340,000	$340,000
	Net present value		$1,430,000		

Notes:
1. Subsidy (gross) and expenditure (gross) = forecast of spending at the proposed price and subsidy.
2. Net cost to DHBs = forecast of change in spending compared with status quo.
3. All pharmaceutical costs are ex-manufacturer.
4. All costs are ex-GST.
5. NPV is calculated over 5 years using an annual discount rate of 8%.
6. Calculations are in A46607.

Why proposal should be considered by the Chief Executive under Delegated Authority

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

- is consistent with previous Board decisions ; and
- is not considered contentious by PHARMAC's Chief Executive; and
- there are no potential long term financial risks.

Background and Analysis

- The proposal is to list montelukast under Special Authority for the treatment of pre-school wheeze, exercise-induced asthma and for use during aspirin desensitisation from 1 August 2012.

- The proposal also includes funding for ivermectin under a Special Authority for the treatment of crusted scabies or where topical treatment has failed or the patient is unable to comply with topical therapy, and for three parasitic infections which are currently funded by DHB hospitals through the discretionary community supply mechanism.

Montelukast

- Montelukast is an oral leukotriene receptor antagonist and is registered in New Zealand for the treatment of adult and paediatric patients 2 years and older for the prophylaxis and chronic treatment of asthma and relief of the symptoms of seasonal rhinitis.

- PTAC and the Respiratory Subcommittee of PTAC have assessed montelukast a number of times (relevant minutes attached in Appendix One). At their May 2011 meeting, PTAC recommended montelukast be listed in the Pharmaceutical Schedule under Special Authority with a low to medium priority.

- Montelukast is s 9(2)(j) on the priority list and is within the funding available for the financial year ending June 2013. The estimated QALY gain is s 9(2)(j) per $1 million by year three (See TAR 163 in Appendix Two).

- A confidential rebate would apply to montelukast in years two and three and subsidy and delisting protection would apply until 1 July 2014.

Ivermectin

- Ivermectin is an anthelmintic and is registered in New Zealand for the treatment of intestinal strongyloidiasis (anguillulosis), microfilaraemia in patients with lymphatic filariasis caused by Wuchereria bancrofti, and human sarcoptic scabies after prior treatment has failed.

- PTAC and the Anti-Infective Subcommittee have assessed ivermectin for the proposed indications and recommended that ivermectin be listed in the Pharmaceutical Schedule

with a high priority. The minutes are included in Appendix One.

- Ivermectin is s 9(2)(j) on the prioritisation list and is within the funding available for the financial year ending 30 June 2013. It is estimated to have a possible QALY gain of greater than 100 per $million (see TAR 188 Appendix two).

Agreement

- An agreement between Merck Sharp and Dohme (New Zealand) Ltd and PHARMAC is attached in Appendix Three. It contains subsidy and delisting protection until July 2014 for both products and a stepped rebate for Singular.

Clinical Effects

Montelukast

- Pre-school wheeze and exercise-induced asthma.
  Wheezing in preschool children is mostly associated with viral upper respiratory tract infections which can occur frequently and are not usually associated with any underlying inflammation between episodes. Exercise-induced asthma occurs when the airways narrow as a result of exercise asthma.

  It is estimated that treatment of pre-school wheeze with montelukast will prevent on average 0.76 asthma exacerbations per patient per year and may prevent approximately 100 hospitalisations per year.

  The majority of patients with exercise-induced asthma can prevent exacerbations by the use of short acting beta-adrenoceptor agonists or long acting beta-adrenoceptor agonists in combination with inhaled corticosteroids prior to exercise. Options available for those patients who are unable to control their exercise-induced asthma with these therapies are limited and some of these patients may gain benefit from montelukast. Montelukast is not on the list of the World Anti-Doping Agency's list of drugs banned in sports.

Differences in proposal compared with PTAC recommendations

- PTAC recommended a restriction on the number of tablets dispensed per prescription as the efficacy evidence is strongest when montelukast is used intermittently. Recognising that the cost per tablet negotiated is s 9(2)(j) than when PTAC assessed montelukast (s 9(2)(j)), PHARMAC staff consider a prescribing guideline noting that intermittent use is more effective is more appropriate than restricting the number of tablets.

  The Respiratory Subcommittee of PTAC recommended montelukast be used only after nedocromil in the treatment of exercise-induced asthma. When the Subcommittee considered montelukast, its price was s 9(2)(j) and therefore we do not consider that nedocromil should be a prerequisite for montelukast use.

Aspirin desensitisation

Aspirin desensitisation was not included in the initial proposal nor was this small group of patients specifically addressed by PTAC or the Respiratory Subcommittee. During the consultation period, PHARMAC received a response from Dr Anthony Jordan, Immunology Department, Auckland DHB requesting that the listing of montelukast be

expanded to include aspirin desensitisation.

Aspirin-exacerbated respiratory disease accounts for approximately 21% of adult asthma and is characterised by difficult–to-control asthma amongst other symptoms. Desensitisation is undertaken in the most severe of cases and involves the graded administration of aspirin in a controlled setting. Pre-treatment with leukotriene modifier drugs enhances the safety of oral aspirin challenge by decreasing the degree of asthmatic responses. The procedure is carried out at Auckland, Wellington and Christchurch hospitals with an estimated 100 patients per year nationally.

- In February 2004 PTAC recommended montelukast be listed for two other indications – aspirin induced asthma and asthma refractory to high dose inhaled corticosteroids with a high priority (PTAC February 2004). The Respiratory Subcommittee in February 2010 did not support listing montelukast for refractory asthma citing changes in the access criteria to combination inhalers and LABAS in the interim period and the lack of evidence seen in published trials. The Subcommittee did recommended listing montelukast for the treatment of aspirin induced asthma subject to appropriate targeting criteria which is not currently available nationwide. These two indications have not been included in this proposal however PHARMAC staff will continue to review access to this treatment.

Ivermectin

- Treatments for filaricides, cutaneous larva migrans and strongyloidiasis are currently available from DHB hospitals under discretionary community supply. As a result there is unlikely to be any change to the clinical effect from this portion of the proposal for patients seen in hospital. However in the community and particularly institutional settings a treatment in a tablet form is expected to increase the chance of infestation clearance.

- PTAC considers that scabies outbreaks are a significant problem in institutional settings due to the difficulties and time involved in applying topical treatments and isolating residents, particularly in institutions with elderly residents and dementia patients. An oral treatment in this setting would aid in ensuring treatment could be provided to all patients at a similar time and increase the chance of clearance of any infestation.

- PTAC also noted that there are likely to be unrecognised cases of crusted scabies in institutional settings, particularly amongst residents that are immunocompromised, and that this is likely to be a major source of re-infestation.

- Patients in the community with crusted scabies who cannot comply with topical therapy, or where it has been ineffective, would also be able to access a tablet treatment which may increase compliance and the chance of clearance of infestation.

Fiscal Effects

- Montelukast is forecast to cost the Community Pharmaceutical Budget s 9(2)(j) in Year one with an NPV of s 9(2)(j) (5 years,8%).

- This cost estimate is based on all children between the ages of two and five who have had at least one admission to hospital as a result of a respiratory exacerbation being prescribed montelukast for three months to twelve months depending on the number of

exacerbations they have as well as 2,000 patients with exercise induced asthma being prescribed three months treatment per year. Figures from the Immunology Department at Auckland DHB indicate that 100 patients may also undergo aspirin desensitisation in any one year and would take montelukast for an average of ~16 weeks. (Montelukast BIA reference A502315).

- The fiscal risk of listing montelukast is considered to be low as the patent expires in 2012 and a generic supplier is already registered in New Zealand (for 2 out of the 3 strengths). PHARMAC are aware of at least three other companies with generic montelukast and anticipate including it in the 2013/14 tender.

- The counterfactual to this proposal for montelukast is to run an RFP. This would mean deferring a listing until this is resolved, with the loss of any health benefit in the interim, and may not mean lower pricing. We note that there are at least three other companies with generic montelukast, although none have all strengths registered. Apotex indicated pricing of s 9(2)(j) Under the current agreement there is also no restriction on PHARMAC listing a second or third product at a lower price with wider access should the opportunity arise.

- Ivermectin is anticipated to cost the Community Pharmaceutical Budget $300,000 for the year ending 30 June 2013 and be a cost to DHBs of $1.43 million NPV (5 years, 8%).

- Cost estimates for ivermectin are based on current permethrin prescription data. We have estimated that 10% of patients using permethrin would require ivermectin therapy for treatment failure (10,000 patients per annum) and a further 1,500 patients per annum would be unable to comply with topical therapy. Crusted scabies is relatively rare with approximately 50 cases per annum. The costs also assume a dose of 5 tablets with two doses required per patient. Full working can be found in ivermectin BIA (objective reference A46607).

- The forecast total cost of the proposal (montelukast and ivermectin) is expected to be s 9(2)(j) (5 year, 8%) with an annual expenditure of s 9(2)(j)

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 15 June 2012. The consultation letter and all responses received by 29 June 2012 are attached as Appendix Five.

Sixteen responses were received; responders included MOHSS, Mylan New Zealand Ltd and other groups/individuals.

Summaries of what PHARMAC staff believe are the significant matters raised in these responses are provided in the table below. Most responders were supportive of the proposal.

Montelukast		
Stakeholder group	**Theme**	**PHARMAC Staff Comment**
Clinician	Clinical Immunologist requesting expansion of use to include aspirin desensitisation	On receipt of clinical information PHARMAC, with the agreement of MSD, propose to include aspirin desensitisation in the proposal.
Clinicians	Four general practitioners responded positively to the listing of montelukast. Two would like to see the Special Authority widened to include those patients whose asthma is refractory to inhaled corticosteroids.	This area has been assessed a number of times but PTAC and by the Respiratory Subcommittee of PTAC which see little or no therapeutic benefit to using montelukast in patients refractory to inhaled corticosteroids.

Clinicians from Starship Children's Hospital	1) Support the proposal but suggest that the prescriber be changed to read General Practitioner or Paediatrician for preschool wheeze and for severe asthma it should only be a Paediatrician. 2) Considered that prescribing decisions would be easier if the clinical thresholds for access were the same as internationally accepted evidence based guidelines. 3) The prescribing guideline should allow daily use if it would be clinically beneficial for an individual patient. 4) Citing listed Seretide prices the clinicians conclude that fluticasone plus montelukast is cheaper than a combination inhaler and should be able to continue to be used if the child is showing benefit. 5) Exercise induced asthma should not be a diagnostic category in children. 6) Clinical guidelines recommend that if there is no improvement after a trial of inhaled corticosteroids and LABAs, then the LABA should be stopped and montelukast commenced. They do not suggest adding montelukast to LABAs as the current proposal suggests. 7) They suggest that a child who has a poor response to ICS and LABAs should be reviewed by a Paediatric specialist before commencing montelukast.	1) PTAC considered the issue of restrictions on the prescribers and recommended that any relevant practitioner is appropriate. It is not proposed that Montelukast is funded for severe asthma at this time. 2) PTAC and the Respiratory Subcommittee of PTAC have assessed montelukast at a number of meetings and have recommended Special Authority criteria that best reflects the areas where most clinical benefits can be gained. 3) The prescribing guideline does not prevent daily use but notes that the greatest clinical gain occurs when it is used intermittently for a period of 2 to 4 weeks. 4) Montelukast is being listed for the treatment of children up to the age of five who have preschool wheeze as this is the area defined by PTAC and the Respiratory Subcommittee as showing the greatest clinical benefit. A rebate applies to Seretide. We would be happy to consider an application for other uses of montelukast. 5) The term exercise induced refers to patients of all ages with this form of asthma not specifically for children. 6) The intention of the proposed Special Authority is that montelukast be funded for exercise induced asthma only after other treatments have been tried. There is no requirement under the proposed Special Authority criteria that patients continue with some or all of these treatments. 7) Under the current proposal, montelukast is being funded for three indications only: children with preschool wheeze, patients who continue to experience frequent episodes of exercise-induced bronchoconstriction even after receiving maximal therapy and asthma desensitisation. The patient group noted in the consultation response is not eligible for treatment under this proposal, however we will continue to review access to this treatment over time.

Supplier	1)The supplier questioned the commercial fairness and the logic of listing a pharmaceutical for which the patent has expired without a competitive process and noted that generic companies will be shut out of the market for a year beyond what they may have otherwise expected. 2) The supplier objected to the use of a confidential rebate, commenting that it was difficult to bid competitively when there was a confidential rebate and that inflated list prices necessarily increase costs to DHBs via wholesaler mark-ups. 3) The supplier commented that if PHARMAC is to continue to use confidential rebates beyond patent expiry then it is reasonable for suppliers to see a justification, on a case by case basis in the consultation letters.	1) Under the current proposal, there are no restrictions to listing other supplier's brands of montelukast on the Pharmaceutical Schedule. 2) Confidential rebates do not preclude a company from making a competitively priced proposal. PHARMAC took into account the cost to the DHBs when assessing the proposal. 3) Confidential rebates are sometimes used in agreements if they result in lower net expenditure than could be achieved otherwise. PHARMAC staff are willing to consider listing another suppliers product if pricing can be agreed. We do not consider that justification of confidential rebates is required in consultation letters.
MoHSS and Pharmacy Guiild	The MoHSS did not see any technical issues with the proposal. The Pharmacy Guild supported the listing of montelukast but raised the concern that some age related residential care facilities are not certified to provide hospital care services and therefore would be unable to order ivermectin by a bulk supply order.	Sector Services do not see any technical or resource impacts as a result of this proposal. The special authority has been changed to include the ability for institutions to order up to 100 tabs under PSO.

Ivermectin responses		
Stakeholder group	**Theme**	**PHARMAC Staff Comment**
Dermatologists	Those eligible to apply for Special Authorities under the "other parasitic infections" criteria should include dermatologists, as they are the specialist most likely to see patients with cutaneous larva migrans	The Special Authority has been amended to include Dermatologists.
Dermatologists	It would be nice to see a strengthening of the statement: "The patient has previously tried and failed to clear infestation using topical therapy",	Clinicial advice was that ivermectin is no more effective than topical therapy and clinicians would use appropriate judgement in determining failure of topical therapy.
Dermatologists and Pharmacy Guild	It would be almost impossible to treat a whole ward or rest-home as they would be caught out by individual requirements. BSO is fine for hospital level care but many Age related residential care (ARRC) facilities cannot access BSO.	The ability for ivermectin to be sourced by rest homes allows for treatment of all patients who are contacts of an infection. We have included a PSO provision for non-hospital level ARRC facilitates
Clinician – Dermatologist	The proposal does not allow for the treatment of staff contacts	Staff should be able to comply with topical therapy and therefore would not require ivermectin unless they meet the entry criteria.
New Zealand Dermatology Society	Would like to see the Special Authority time period extended to three months as we recognise prolonged spread, reinfection and delayed diagnosis in institutions.	The length of one month for a Special Authority should allow the initial and repeat treatments (1 week apart). Should patients re-infect a new Special Authority application should be made.
New Zealand Dermatology Society	The dose ought not be restricted to 4 times 3 mg tablets.	There is no dose restriction proposed for ivermectin.
New Zealand Dermatology Society	Would like faster Special Authority application approvals to prevent delayed treatment or consideration of SA exemption for dermatologists	The current electronic Special Authority system provides a response in less than 1 minute. Paper based applications can take longer due to manual processing requirements.

Legal advisors' view

Legal advisors' view has not been sought in relation to this proposal.

Implementation

- Notify Merck Sharp and Dohme
- Clinicians - letter
- Pharmacy - Dispatch
- Reporting requirements - Ministerial report

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;*

   Listing montelukast would help to address the health needs of children under the age of five who continue to have severe exacerbations and patients who are limited in the amount of exercise that they can do because their current therapy does not fully control their asthma symptoms when they are participating in exercise. Patients who are undergoing aspirin desensitisation would have access to a fully funded treatment which is anticipated to help prevent or reduce the severity of respiratory reactions.

   Patients who have a scabies infestation who are unable to comply with topical therapy, or where topical therapy has failed, or have crusted scabies would have access to a treatment which is anticipated to result in clearance of the infestation.

2. *The particular health needs of Maori and Pacific peoples;*

   Maori and Pacific Island peoples have higher rates of asthma than non-Maori (22%, 20% and 15% respectively) and admissions to hospital of Maori and Pacific Island children due to respiratory disorders is significantly higher than for Europeans. Maori and Pacific Island peoples would receive a higher benefit from this proposal compared to all eligible people.

   PHARMAC does not have information on the particular need amongst Maori and Pacific Island people with scabies with respect to failure of permetherin however they would receive the same benefit as all eligible people.

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

   There are a wide range of proven, effective, fully funded inhaler treatments for patients with asthma and these provide relief for most patients however, there are a some areas, such as pre-school wheeze and exercise-induces asthma where the currently listed therapies do not provide sufficient relief for all patients. Montelukast would offer an alternative for these patients.

   The currently funded permetherin cream is as effective as ivermectin for the treatment of scabies (excluding crusted scabies) however there is some resistance developing to this pharmaceutical. In addition the cream is required to be topically applied to the entire body of the patient and all close contacts and many patients are unable to comply such as those in rest homes.

4. *The clinical benefits and risks of pharmaceuticals;*

   Evidence of the benefits of montelukast in the treatment of asthma is poor however there are some identifiable areas in which treatment may be beneficial. Montelukast has been shown a benefit in some children with preschool wheeze and the oral administration of a chewable tablet should make it easier for parents to ensure their

under-five year old children are getting the correct dose. Montelukast has also shown some benefit in the prevention of asthma exacerbations in patients whose symptoms are not fully controlled by inhaled therapy when they do exercise and for the prevention of exacerbations in patients undergoing aspirin desensitisation.

In June the FDA requested manufacturers of leukotriene inhibitors include information on neuropyschiatric events that have been reported in patients using these products. The reported neuropyschiatric events include post market cases of agitation, aggression, anxiousness, dream abnormalities and hallucinations, depression, insomnia, irritability, restlessness, suicidal thinking and behaviour (including suicide) and tremor.

Ivermectin is no more effective than topical therapy however it is an oral therapy and can be used to ensure compliance in patients who are unable to comply with topical therapy, such as those patients in age related residential facilities in which application of topical therapy may not be feasible.

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

   The QALYs per $1 million for montelukast is estimated to be 27 per $1 million increasing to 53 by year three due to agreed price reductions and the QALYs gained per $1 million for ivermectin is estimated to be greater than 100.

6. *The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule;*
   It is estimated that the cost to the community pharmaceutical budget would be $0.76 million for the year ending 30 June 2013, $3.56 million NPV (5 years, 8%), and a cost to DHBs of $3.71 million NPV (5 years, 8%).

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

   Patients and care facilities that are currently self-funding montelukast and ivermectin would have reduced direct costs.

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*

   No such objectives are relevant to assessing this proposal.

9. *Such other criteria as PHARMAC thinks fit.*
   No other criteria are relevant to assessing this proposal.

CHECKLIST FOR BOARD PAPERS

Paper: Listing montelukast and ivermectin on the Pharmaceutical Schedule

Consultation:

The following parties were consulted with during the development of this paper: [Note: leave box blank in respect of parties who were not consulted and indicate where all relevant comments received from the following parties as a result of consultation have been included in this paper or are attached]

Party	Consulted	Comments
Minister of Health	☐	☐
Ministry of Health	☐	☐
DHBs	☐	☐
PTAC	☐	☐
Consumer Advisory Committee	☐	☐
Affected health professionals (refer to attached distribution list)	☐	☐
Affected patient/consumer groups (refer to attached distribution list)	☐	☐
Affected suppliers (refer to attached distribution list)	☐	☐
Other affected public, groups and/or individuals (specify)	☐	☐

The Author(s) confirm that appropriate processes were followed for the development of this paper, including appropriate consultation and consideration of consultation responses.

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Other Authors: Greg Williams

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Peter Moodie
Andrew Davies

Approved: Andrew Davies

Relevant Manager

Record of the ANTI-INFECTIVE SUBCOMMITTEE OF PTAC Meeting held on 22 February 2012

Ivermectin

1.1 Members noted the PTAC minute relating to ivermectin for crusted scabies and use in institutional settings (e.g. rest homes). Members considered that the PTAC recommendation that ivermectin was no more effective than creams and lotions was appropriate. Members considered that if appropriate restrictions were not in place then institutions would use ivermectin rather than topical therapy as it was easier than applying the cream or lotion.

1.2 Members noted that ivermectin was more expensive than topical scabies therapy.

1.3 The Subcommittee noted that many community institutions had multiple general practitioners responsible for its patients and that if treatment with ivermectin was to be provided this would need to be co-ordinated. Members noted that many institutions had a charge nurse who should be able to co-ordinate care provision.

1.4 The Subcommittee noted that patients with Crusted scabies (also called 'Norwegian scabies') are very likely to benefit from ivermectin. Members noted that crusted scabies usually occurred in the immunocompromised. Patients with crusted scabies usually had a hyperinfestation of the scabies mite.

1.5 The Subcommittee considered that the following restriction may be appropriate:

1) Applying clinician has discussed the diagnosis of scabies with a Dermatologist, Infectious Disease physician or clinical microbiologist; and
2) The patient is in the community; and

Either

- a. Patient has a severe scabies hyperinfestation (Crusted/ Norwegian scabies); or
- b. The community patient is physically or mentally unable to comply with the application instructions of topical therapy; or
- c. The patient has previously tried and failed to clear infestation using topical therapy

Or

3) The Patient is a resident in an institution and
   - a. All residents of the institution with scabies or at risk of carriage are to be treated for scabies concurrently; and either
     - i. Patient has a severe scabies hyperinfestation (Crusted/ Norwegian scabies); or
     - ii. The patient is physically or mentally unable to comply with the application instructions of topical therapy; or
     - iii. previous topical therapy has been tried and failed to clear the infestation; or

Note: Ivermectin is no more effective than topical therapy for treatment of standard scabies infestation.

2 *Antiparasitics (minutes relating to Hospital formulary)*

2.1 With respect to ivermectin the Subcommittee considered that this is restricted to Infectious Disease physicians, Dermatologists and Clinical Microbiologists. The Subcommittee noted its previous recommendation regarding ivermectin for scabies in the community.

2.2 With respect to ivermectin the Subcommittee considered that this should be available in the community under Special Authority or on discharge for short term treatment of filariasis, cutaneous larva migrans (creeping eruption) and strongyloidiasis.

February 2011 PTAC minute

3 Ivermectin for crusted scabies

Application

3.1 The Committee considered a request from a clinician to list ivermectin tablets for first line treatment of crusted scabies outbreaks in institutional settings.

Recommendation

3.2 The Committee **recommended** that ivermectin be funded for the treatment of crusted scabies and in those for whom it is not possible to use lotions or creams.

3.3 The Committee further **recommended** that PHARMAC staff discuss with the Ministry of Health the possibility of making outbreaks of scabies in institutional settings a notifiable disease. If this were possible the decision to allow funded access would be made by the Medical Officer of Health. Under this scenario a Special Authority would be unnecessary; therefore, the Committee deferred making a final recommendation until further information was available.

The Decision Criteria particularly relevant to this recommendation are: *(i) The health needs of all eligible people within New Zealand; (iii) The availability and suitability of existing medicines, therapeutic medical devices and related products and related things; (iv) The clinical benefits and risks of pharmaceuticals; and (vii) The direct cost to health service users*

Discussion

3.4 The Committee noted that scabies outbreaks were a significant problem in institutional settings due to the difficulties and time involved in applying topical treatments and the difficulty in isolating residents, and this was particularly so in institutions with elderly residents and dementia patients. The Committee also noted that there are more likely to be unrecognised cases of crusted scabies in institutional settings, particularly amongst residents that may be immunocompromised and this is a major source of re-infestation.

3.5 The Committee noted that ivermectin is registered by Medsafe for the treatment of human sarcoptic scabies after prior treatment has failed. The recommended dosage is a single oral dose to provide ivermectin 200mg/kg of body weight. In the heavily infected forms of profuse or crusting scabies, a second dose within eight to 15 days of ivermectin and/or concomitant topical therapy may be necessary to obtain recovery. The Committee noted that the application was for use of ivermectin as a first line treatment for crusted scabies and for the treatment of residents in institutional settings with scabies infections or probable scabies infections. The applicant was requesting the use of two doses of ivermectin for each patient to ensure eradication of scabies in all residents. The applicant had suggested that more than two doses of ivermectin along with topical treatment may be required to eradicate scabies in people with crusted scabies.

3.6 The Committee noted that evidence of efficacy for this indication is limited and is mostly comprised of expert opinion supported by small uncontrolled studies. The Cochrane Review (Interventions for treating scabies, the Cochrane Library 2010 Issue 10) gives a comprehensive review of all topical and oral agents used for treating scabies. This reviewed 21 studies with treatment failure as the outcome measure. The review concluded that topical permethrin appears to be the most effective treatment for scabies and that ivermectin appears to be an effective oral treatment. The review further stated that more research is needed especially for the management of scabies in institutions.

3.7 The Committee also noted the results of an RCT comparing ivermectin with permethrin (Usha V et al. A comparative study of oral ivermectin and topical cream in the treatment of scabies. J.Am.Acad Dermatol 2000; 42:236-40) of 85 patients (40 receiving ivermectin; 45 receiving a single dose of permethrin) with follow-ups at one, two, four and eight weeks. A single dose of ivermectin gave a cure rate of 70% which increased to 95% with two doses at a two week interval. A single dose of permethrin was effective in 97.8% of patients with an additional patient responding to a second application. The two patients who did not respond to ivermectin were crossed over to the permethrin group and were cured after a single application. No major side effects were observed in either group. The authors concluded that a single application of permethrin is superior to a single dose of ivermectin and similar to two doses of ivermectin taken two weeks apart.

3.8 The Committee noted that in terms of safety ivermectin has been widely used and even with repeated doses serious adverse effects have been rare (Cochrane Review 2010). A letter to the Lancet (Barkwell R, Shields S. Deaths associated with ivermectin treatment in scabies. Lancet 1997; 349(9059):1144-5) reported an increased number of deaths amongst dementia care patients who had been unsuccessfully treated with up to three topical agents. 15 of the 47 patients died over a six month period compared to five in a “matched” control group. Whether this was due to ivermectin or to interactions with other scabicides, including lindane and permethrin, or other treatments such as psychoactive drugs was not clear, and there was considerable discussion in the Lancet of the validity of the report at that time. The Committee noted veterinary reports that collie dogs are known to be particularly prone to ivermectin neurotoxicity. There is speculation that increased crossing of the blood brain barrier by ivermectin could account for an increase in side-effects in the elderly.

3.9 The Committee considered that there was a public health dimension to outbreaks of scabies in institutions. Elderly and immunocompromised patients are more likely to have crusted scabies and there may be issues with the capacity for patients to give informed consent, particularly the elderly, dementia and intellectually disabled patients. The Committee considered that crusted scabies may need to be a notifiable disease and have a team approach to treatment involving the local Medical Officer of Health, a dermatologist, and medical, nursing and ancillary staff at the institution.

3.10 The Committee noted that ivermectin should be available for treatment but there were a number of areas that needed clarification prior to listing on the Pharmaceutical Schedule. These include, among others, the definition of institution in which treatment with ivermectin may be appropriate; definition of ‘outbreak’ in an institution, whether only individuals with crusted scabies should be treated or whether all residents and staff should also be treated. The Committee considered that guidelines could be developed in discussion with the Ministry of Health, dermatologists and infectious disease specialists.

3.11 The Committee noted that, currently, the cost of treatment with ivermectin is significantly higher than topical treatment and is carried by the patient, the institution or the family. The Committee recognised that there is considerable time required for staff to treat patients topically. The Committee noted that restrictions on the use of ivermectin may be required to contain costs.