Hospital Pharmaceuticals Review

PTAC, Hospital Pharmaceuticals Subcommittee & Respiratory Subcommittee minutes for web publishing

Respiratory System and Allergies therapeutic group

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This document contains minutes relevant to the consultation document of 25 September 2012 relating to products in the Respiratory System and Allergies therapeutic group.

Note that this document is not a complete record of the relevant PTAC and Subcommittee meetings; only the relevant portions of the minutes relating PTAC and its Subcommittees advice on the review of Hospital Pharmaceuticals are included.

Contents

Hospital Pharmaceuticals Subcommittee – 5 July 2011

1 Antiallergy Preparations

1.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Antiallergy Preparations heading.

1.2 The Subcommittee noted that the following pharmaceuticals are commonly used in DHB hospitals and/or are fully subsidised in the Pharmaceutical Schedule and recommended they be included in a national preferred medicines list (PML) without need for further prioritisation:

- Bee venom allergy treatments
  - Maintenance kit - 6 vials 120 µg freeze dried venom, 6 diluent 1.8 ml
  - Treatment kit - 1 vial 550 µg freeze dried venom, 1 diluent 9 ml, 3 diluent 1.8 ml
- Wasp venom allergy treatment
  - Treatment kit (paper wasp venom) - 1 vial 500 µg freeze dried polister venom, 1 diluent 9 ml, 1 diluent 1.8 ml
  - Treatment kit (yellow jacket venom) - 1 vial 550 µg freeze dried vespula venom, 1 diluent 9 ml, 1 diluent 1.8 ml
- Beclomethasone dipropionate
  - Aqueous nasal spray 50 µg per dose
  - Aqueous nasal spray 100 µg per dose
- Budesonide
  - Aqueous nasal spray 50 µg per dose
  - Aqueous nasal spray 100 µg per dose
- Fluticasone propionate
  - Aqueous nasal spray 50 µg per dose
- Ipratropium bromide
  - Aqueous nasal spray 0.03%
- Sodium cromoglycate
  - Aqueous nasal spray 4%
- Cetirizine hydrochloride
  - Oral liq 1 mg per ml
  - Tab 10 mg
- Chlorpheniramine maleate
  - Inj 10 mg per ml, 1 ml ampoule
  - Oral liq 2 mg per 5 ml
- Cyproheptadine hydrochloride
  - Tab 4 mg
- Fexofenadine hydrochloride
  - Tab 60 mg
  - Tab 120 mg
  - Tab 180 mg
- Loratadine
  - Oral liq 1 mg per ml
  - Tab 10 mg
- Promethazine hydrochloride
  - Inj 25 mg per ml, 2 ml ampoule

- Oral liq 5 mg per 5 ml
- Tab 10 mg
- Tab 25 mg

- Trimeprazine tartrate
  - Oral liq 30 mg per 5 ml

1.3 The Subcommittee recommended that the listing of bee and wasp venom allergy kits in a national PML be subject to restrictions on their use that are in line with the Special Authority restrictions for them in the Pharmaceutical Schedule.

1.4 The Subcommittee noted that allergen desensitisation kits for substances other than bee or wasp venom were not widely used in DHB hospitals, and were not subsidised in the Pharmaceutical Schedule, and recommended that they not be included in a national PML. Members noted that separate to the issue of desensitisation kits are allergy testing kits, and considered that these should remain available in hospitals.

1.5 The Subcommittee noted that omalizumab is not widely used in DHB hospitals, and noted that the Respiratory Subcommittee had previously recommended against its listing in the Pharmaceutical Schedule. The Subcommittee recommended that it not be included in a national PML.

1.6 The Subcommittee noted that there is some use of adrenaline auto-injectors by DHB hospital staff, such as district nurses and carers in children's wards. The Subcommittee considered that as these are not funded in the Pharmaceutical Schedule, listing in a national PML could not be justified, as inclusion in a national PML would result in de facto community funding. The Subcommittee recommended that adrenaline auto-injectors not be included in a national PML, and considered that current use by hospital staff could be replaced by ampoules or prefilled syringes and adequate training.

2 Anticholinergic Agents

2.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Anticholinergic Agents heading.

2.2 The Subcommittee noted that the following pharmaceuticals are commonly used in DHB hospitals and/or are fully subsidised in the Pharmaceutical Schedule and recommended they be included in a national preferred medicines list (PML) without need for further prioritisation:

- Ipratropium bromide
  - Aerosol inhaler 20 µg per dose
  - Nebuliser soln 250 µg per ml, 1 ml
  - Nebuliser soln 250 µg per ml, 2 ml
- Tiotropium bromide
  - Powder for inhalation 18 µg per dose
- Salbutamol with ipratropium bromide
  - Aerosol inhaler 100 µg with ipratropium bromide 20 µg per dose
  - Nebuliser soln 2.5 mg with ipratropium bromide 0.5 mg per 2.5 ml vial

2.3 The Subcommittee recommended that the listing of tiotropium in a national PML be subject to restrictions on its use that are in line with the Special Authority restriction for it in the Pharmaceutical Schedule.

3 Beta-Adrenoceptor Agonists

3.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Beta-Adrenoceptor Agonists heading.

3.2 The Subcommittee noted that the following pharmaceuticals are commonly used in DHB hospitals and/or are fully subsidised in the Pharmaceutical Schedule and recommended they be included in a national preferred medicines list (PML) without need for further prioritisation:

- Salbutamol
  - Aerosol inhaler, 100 µg per dose
  - Infusion 1 mg per ml, 5 ml ampoule
  - Inj 500 µg per ml, 1 ml ampoule
  - Nebuliser soln 1 mg per ml, 2.5 ml
  - Nebuliser soln 2 mg per ml, 2.5 ml
  - Oral liq 2 mg per 5 ml
- Terbutaline sulphate
  - Powder for inhalation 250 µg per dose
  - Inj 0.5 mg per ml, 1 ml amp

3.3 Members noted that one DHB had reported using terbutaline nebuliser solution for a patient with salbutamol allergy. The Subcommittee considered that this use should be managed through an exceptions mechanism, rather than by listing on a national PML.

4 Cough Suppressants

4.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Cough Suppressants heading.

4.2 The Subcommittee considered that there was limited evidence in support of cough suppressants, and noted that none are subsidised in the Pharmaceutical Schedule. Members noted that in the palliative care setting it was likely that strong opioids would be used for this purpose rather than using lower strength over-the-counter opioid containing cough suppressants.

4.3 The Subcommittee considered that excluding all cough suppressants from a national PML could be difficult, and recommended that the most commonly used product, pholcodine oral liq 1 mg per ml, be included in a national PML.

4.4 The Subcommittee recommended that dextromethorphan, diphenhydramine, opiate squill and 2 mg per ml and 3 mg per ml strengths of pholcodine be excluded from a national PML.

4.5 The Subcommittee noted that there may be some use of dextromethorphan in the surgical setting, and requested that the view of anaesthetists be sought on its exclusion.

5 Decongestants

5.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Decongestants heading.

5.2 The Subcommittee noted that the following pharmaceuticals are commonly used in DHB hospitals and/or are fully subsidised in the Pharmaceutical Schedule and recommended they be included in a national preferred medicines list (PML) without need for further prioritisation:

- Oxymetazoline hydrochloride
  - Aqueous nasal spray 0.25 mg per ml
  - Aqueous nasal spray 0.5 mg per ml
- Pseudoephedrine hydrochloride
  - Tab 60 mg
- Sodium chloride
  - Aqueous nasal spray 6.5 mg per ml
- Sodium chloride with sodium bicarbonate
  - Soln for nasal irrigation
- Xylometazoline hydrochloride
  - Aqueous nasal spray 0.05%
  - Aqueous nasal spray 0.1%
  - Nasal drops 0.05%
  - Nasal drops 0.1%

5.3 Members noted that sodium chloride nasal spray is generally used for compounding with other products, not as a therapeutic product in its own right. The Subcommittee considered that it was not necessary for the other strength of this product (7.4 mg per ml) to be included in a national PML.

5.4 Members noted that different packs of sodium chloride with sodium bicarbonate nasal irrigation (NeilMed Sinus Rinse) are available, and that the starter kit is the one that is predominantly used and should be listed.

5.5 The Subcommittee noted that while xylometazoline is more widely used than oxymetazoline, and is also a less expensive agent, having both agents on a national PML would provide a backup in the event of long-term supply issues, which have occurred previously.

5.6 The Subcommittee considered that, as menthol capsules are not widely used in DHB hospitals, and are not subsidised in the Pharmaceutical Schedule, they did not need to be included in a national PML

5.7 The Subcommittee considered that, as dexchlorpheniramine maleate is not widely used in DHB hospitals, and is not fully subsidised in the Pharmaceutical Schedule, it did not need to be included in a national PML.

6 Inhaled Corticosteroids

6.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Inhaled Corticosteroids heading.

6.2 The Subcommittee noted that the following pharmaceuticals are commonly used in DHB hospitals and/or are fully subsidised in the Pharmaceutical Schedule and recommended they be included in a national preferred medicines list (PML) without need for further prioritisation:

- Beclomethasone dipropionate

- Aerosol inhaler 50 µg per dose
- Aerosol inhaler 100 µg per dose
- Aerosol inhaler 250 µg per dose

- Budesonide
  - Powder for inhalation 100 µg per dose
  - Powder for inhalation 200 µg per dose
  - Powder for inhalation 400 µg per dose
- Fluticasone
  - Aerosol inhaler 50 µg per dose
  - Aerosol inhaler 125 µg per dose
  - Aerosol inhaler 250 µg per dose
  - Powder for inhalation 50 µg per dose
  - Powder for inhalation 100 µg per dose
  - Powder for inhalation 250 µg per dose

6.3 The Subcommittee noted that there is some use of nebulised budesonide in DHB hospitals, and recommended that the 500 µg in 2 ml nebuliser solution should be included in a national PML, but that there was no need for the other presentation (1 mg in 2 ml) to also be included. The Subcommittee requested that the view of the Respiratory Subcommittee be sought on the need for budesonide nebuliser solution in a national PML.

7 Inhaled Long-Acting Beta-Adrenoceptor Agonists

7.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Inhaled Long-Acting Beta-Adrenoceptor Agonists heading.

7.2 The Subcommittee noted that the following pharmaceuticals are commonly used in DHB hospitals and/or are fully subsidised in the Pharmaceutical Schedule and recommended they be included in a national preferred medicines list (PML) without need for further prioritisation:

- Eformoterol fumarate
  - Powder for inhalation 6 µg per dose
  - Powder for inhalation 12 µg per dose
- Salmeterol
  - Aerosol inhaler 25 µg per dose
  - Powder for inhalation 50 µg per dose
- Budesonide with eformoterol
  - Aerosol inhaler 100 µg with eformoterol fumarate 6 µg
  - Aerosol inhaler 200 µg with eformoterol fumarate 6 µg
  - Powder for inhalation 100 µg with eformoterol fumarate 6 µg
  - Powder for inhalation 200 µg with eformoterol fumarate 6 µg
  - Powder for inhalation 400 µg with eformoterol fumarate 12 µg
- Fluticasone with salmeterol
  - Aerosol inhaler 50 µg with salmeterol 25 µg
  - Aerosol inhaler 125 µg with salmeterol 25 µg
  - Powder for inhalation 100 µg with salmeterol 50 µg
  - Powder for inhalation 250 µg with salmeterol 50 µg

7.3 The Subcommittee recommended that the listing of budesonide with eformoterol and fluticasone with salmeterol in a national PML be subject to restrictions on their use that are in line with the Special Authority restriction for them in the Pharmaceutical Schedule.

7.4 The Subcommittee considered that, because the higher dose products of fluticasone with salmeterol (aerosol inhaler 250 µg with salmeterol 25 µg, powder for inhalation 500 µg with salmeterol 50 µg) were not subsidised in the Pharmaceutical Schedule, they should not be included in a national PML.

8 Leukotriene Receptor Antagonists

8.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to montelukast.

8.2 The Subcommittee recommended that, as montelukast is not subsidised in the Pharmaceutical Schedule, and as it does not have a unique use within hospitals, that it not be included in a national PML.

9 Mast Cell Stabilisers

9.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Mast Cell Stabilisers heading.

9.2 The Subcommittee noted that the following pharmaceuticals are commonly used in DHB hospitals and/or are fully subsidised in the Pharmaceutical Schedule and recommended they be included in a national preferred medicines list (PML) without need for further prioritisation:

- Nedocromil
  - Aerosol inhaler 2 mg per dose
- Sodium cromoglicate
  - Aerosol inhaler 5 mg per dose
  - Powder for inhalation 20 µg per dose

10 Methylxanthines

10.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Methylxanthines heading.

10.2 The Subcommittee noted that the following pharmaceuticals are commonly used in DHB hospitals and/or are fully subsidised in the Pharmaceutical Schedule and recommended they be included in a national preferred medicines list (PML) without need for further prioritisation:

- Aminophylline
  - Inj 25 mg per ml, 10 ml
- Theophylline
  - Oral liq 80 mg per 15 ml
  - Tab long-acting 250 mg

10.3 The Subcommittee noted that one DHB had reported using aminophylline tablets. The Subcommittee recommended that, as these are not widely used in DHB hospitals, and as they are not subsidised in the Pharmaceutical Schedule, that they not be included in a national PML.

11 Mucolytics and Expectorants

11.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Mucolytics and Expectorants heading.

11.2 The Subcommittee noted that the following pharmaceuticals are commonly used in DHB hospitals and/or are fully subsidised in the Pharmaceutical Schedule and recommended they be included in a national preferred medicines list (PML) without need for further prioritisation:

- Bromhexine hydrochloride
  - Tab 8 mg
  - Oral liq 8 mg per 5 ml
- Dornase alfa
  - Nebuliser soln 2.5 mg per 2.5 ml ampoule
- Sodium chloride
  - Nebuliser soln 7%

11.3 The Subcommittee requested that the view of the Respiratory Subcommittee be sought on the benefits of bromhexine hydrochloride, and on the need for its inclusion in a national PML.

11.4 The Subcommittee recommended that the listing of dornase alfa in a national PML be subject to restrictions on its use that are in line with the restrictions for it in the Pharmaceutical Schedule.

11.5 The Subcommittee noted that one DHB had reported using a lower strength of bromhexine oral liquid (12 mg per 15 ml), but considered that this did not need to be included in a national PML.

11.6 The Subcommittee recommended that as guaifenesin and guaifenesin with bromhexine hydrochloride were not widely used in DHB hospitals, and as they are not subsidised in the Pharmaceutical Schedule, they not be included in a national PML.

12 Pulmonary Surfactants

12.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Pulmonary Surfactants heading.

12.2 The Subcommittee noted that the following pharmaceuticals are commonly used in DHB hospitals and/or are fully subsidised in the Pharmaceutical Schedule and recommended they be included in a national preferred medicines list (PML) without need for further prioritisation:

- Beractant
  - Soln 200 mg per 8 ml vial

- Poractant alfa
  - Soln 120 mg per 1.5 ml vial
  - Soln 240 mg per 3 ml vial

12.3 The Subcommittee noted that having two agents included would be useful from a supply security perspective, and also that some patients may be unable to take one or the other for religious reasons.

13 Respiratory Stimulants

13.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Respiratory Stimulants heading.

13.2 The Subcommittee noted that the following pharmaceuticals are commonly used in DHB hospitals and/or are fully subsidised in the Pharmaceutical Schedule and recommended they be included in a national preferred medicines list (PML) without need for further prioritisation:

- Caffeine citrate
  - Inj 20 mg per ml, 2.5 ml ampoule (caffeine base 10 mg per ml)
  - Oral liq 20 mg per ml (caffeine base 10 mg per ml)
- Doxapram
  - Inj 20 mg per ml, 5 ml vial

13.3 The Subcommittee noted that doxapram was an older product that was not widely used, and requested the view of anaesthetists and of the Respiratory Subcommittee on the use of it and the need for its inclusion in a national PML.

14 Sclerosing Agents

14.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to talc.

14.2 The Subcommittee noted that most DHB hospitals used sterile talc as a sclerosing agent, either as a powder or as a slurry (soln 100 mg per ml, 50 ml), and recommended that both be included in a national PML.

15 Tumour Necrosis Factor (TNF) Inhibitors

15.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to the use of infliximab for sarcoidosis.

15.2 The Subcommittee noted that infliximab is funded in Auckland DHB for use in treatment-resistant sarcoidosis, but not a formulary item in any other DHBs for this indication.

15.3 The Subcommittee noted that treatment of sarcoidosis is not an approved indication for infliximab, and that the evidence for its use is mostly limited to case reports. However, the Subcommittee noted the information that had previously been considered by the Auckland DHB Hospital Medicines Committee, and considered that in the case of life-threatening refractory disease, treatment with infliximab appeared to be reasonable.

15.4 The Subcommittee recommended that infliximab be included in a national PML for the treatment of life-threatening sarcoidosis that is refractory to other treatments.

Respiratory Subcommittee – 16 February 2012

16 Hospital Pharmaceuticals

16.1 The Subcommittee noted a paper and presentation by PHARMAC staff outlining the developments and future initiatives planned in regards to PHARMAC finalising a national Preferred Medicines List (PML) and eventually taking responsibility for funding and procurement of DHB hospital medicines. The Subcommittee did not raise any concerns or issues in regards to this project.

16.2 The Subcommittee reviewed a series of recommendations by the Hospital Pharmaceuticals Subcommittee in regards to which pharmaceuticals relevant to respiratory medicine should be included on a national PML. The Subcommittee noted that PHARMAC had invited feedback from relevant colleges and professional societies, and noted the responses that were received.

Anticholinergic agents

16.3 The Subcommittee noted and agreed with the recommendations in relation to anticholinergic agents. The Subcommittee commented that combination products such as salbutamol with ipratropium bromide are rarely used in hospitals, with prescribing of separate inhalers being preferred

Beta-adrenoceptor agonists

16.4 The Subcommittee noted and agreed with the recommendations in relation to beta-adrenoceptor agonists. The Subcommittee noted that while there is little evidence to support the use of salbutamol oral liquid in asthma, there appears to be some benefit from its use in children with neuromuscular disease as a strengthening agent.

Cough suppressants

16.5 The Subcommittee noted that the Hospital Pharmaceutical Subcommittee had recommended that pholcodine oral liquid 1 mg per ml should be included in the PML. The Subcommittee considered that more than one product would not be required. The Subcommittee noted that cough preparations had been delisted from the Section B of the Pharmaceutical Schedule in 2003. The Subcommittee noted that other agents, such as codeine and morphine, can also be used as cough suppressants in appropriate circumstances.

Decongestants

16.6 The Subcommittee noted and agreed with the recommendations in relation to decongestants.

Inhaled corticosteroids

16.7 The Subcommittee noted the recommendations in relation to inhaled corticosteroids.

16.8 The Subcommittee noted that the Hospital Pharmaceuticals Subcommittee had recommended that one form of budesonide nebuliser solution (250 mcg per ml, 2 ml) be included in a national PML, but that a higher strength (500 mcg per ml, 2 ml) not be included. The Subcommittee considered that the nebulising solution was used in

the treatment of croup and in the intensive care setting post extubation as an alternative to parenteral steroids.

16.9 The Subcommittee noted that clinicians may need to administer doses of up to 2 mg of nebulised budesonide, which would require 8 ml of the lower dose solution to be used, and as such having the both strengths of this product available would be an advantage.

16.10 Members noted that nebulised steroids would likely only be used if the treating physician was unable to administer parental dexamethasone (or other steroids) in a patient unable to tolerate oral preparations, this may be a problem in smaller hospitals with les specialised skill sets.

Leukotriene receptor agonists

16.11 The Subcommittee noted and agreed with the recommendations in relation to leukotriene receptor antagonists.

Long-acting beta-adrenoceptor agonists

16.12 The Subcommittee noted and agreed with the recommendations in relation to long-acting beta-adrenoceptor agonists.

Mast cell stabilisers

16.13 The Subcommittee noted and agreed with the recommendations in relation to mast cell stabilisers.

Methylxanthines.

16.14 The Subcommittee noted and agreed with the recommendations in relation to methylxanthines.

Mucolytics and expectorants

16.15 The Subcommittee noted the recommendations in relation to mucolytics and expectorants.

16.16 The Subcommittee noted that the Hospital Pharmaceuticals Subcommittee had recommended that some formulations of bromhexine hydrochloride be included in a national PML. The Subcommittee considered that there was insufficient evidence to support the inclusion of bromhexine in a national PML and that a Cochrane review shows that it has little or no benefit, and recommended that it not be included at this time. The Subcommittee noted that the product could be re-assessed at a later date if there were requests for it.

16.17 The Subcommittee noted the recommendation that dornase alfa should be listed in a national PML subject to the same access criteria that apply in the community. The Subcommittee noted that dornase alfa is sometime used in hospital to treat children experiencing a semi-acute cystic fibrosis exacerbation and may be used for up to 2 to 4 weeks.

16.18 Members considered that it would be important to provide access to dornase alfa in this acute situation, but that there would need to be established national criteria for

such use. The Subcommittee recommended this issue be referred to the Cystic Fibrosis Panel for discussion, including a review of the evidence, and comment.

Pulmonary surfactants

16.19 The Subcommittee noted and agreed with the recommendations in relation to pulmonary surfactants.

Respiratory stimulants

16.20 The Subcommittee noted and agreed with the recommendations in relation to respiratory stimulants.

16.21 The Subcommittee noted that doxapram is reserved for infants born at more extreme prematurity who have been extubated and continue to have central apnoeas, despite continuous positive airway pressure and maximal caffeine, in whom neonatologists believe reventilation would represent a major setback. The Subcommittee considered that doxapram should be listed in a national PML with a high priority as it is used in tertiary units around the country and perhaps also in the higher-level secondary units such as Hawke's Bay.

Sclerosing agents

16.22 The Subcommittee noted and agreed with the recommendations in relation to respiratory stimulants.

16.23 The Subcommittee noted that talc had been recommended for inclusion, but that other agents were also used as sclerosing agents, such as bleomycin, doxycycline and tetracycline.

Tumour necrosis factor (TNF) inhibitors

16.24 The Subcommittee noted that the Hospital Pharmaceuticals Subcommittee has recommended that infliximab be funded for the treatment of life-threatening pulmonary sarcoidosis that is refractory to other treatments. The Hospital Pharmaceuticals Subcommittee noted that infliximab is funded in Auckland DHB for use in treatment-resistant pulmonary sarcoidosis but is not used in any other DHB.

16.25 The Subcommittee noted a January 2005 application from [a clinician] to Auckland DHB's Hospital Medicines Committee for funding of infliximab in the treatment of pulmonary sarcoidosis. The outcome of the application was that infliximab be added to the Auckland DHB formulary for the treatment of resistant pulmonary sarcoidosis restricted to prescribing by [that clinician] and supply of a report on each patient treated. The Subcommittee noted that [the clinician] is an expert in the treatment of sarcoidosis[1].

16.26 The subcommittee noted five clinical trials supplied by PHARMAC:

- Brougham et al (Am J Respir Crit Care Med 2006;174:795-802) was a phase II double blind, multicentre, placebo-controlled randomised clinical trial. 138 patients with chronic pulmonary sarcoidosis were randomised to receive intravenous infusions infliximab 3 or 5 mg/kg or placebo at weeks 0, 2, 6, 12, 18 and 24 with follow up to week 52. The primary

[1] Name of clinician withheld under section 9(2)(a) of the Official information Act 1982

endpoint was the change from baseline to week 24 in percent of predicted FVC. There was a mean increase of 2.5% FVC in the combined infliximab groups at week 24 (statistically significant but of uncertain clinical significance). There was no change in functional secondary outcome such as SGRQ or Borg's dyspnea score at week 24. Pneumonia was more common in the infliximab patients at 7% vs 2%. *Post hoc* exploratory analysis suggested that patients with more severe disease tended to benefit more from infliximab treatment. A major criticism of the study is that patients were stable for at least one month prior to the initiation of treatment, potentially biasing a possible treatment effect, and had only moderate disease at best making extrapolation to severe treatment resistant patients difficult.

- Brougham et al (Chest 2009;136:526-535). This paper assessed the reproducibility of reading the chest roentgenogram from the 138 patients in the Am J Respir Crit Care Med 2006 study using three different evaluation methods: the Scadding staging system, the Muers scoring, and a global assessment of the changes with therapy. Chest roentgenograms were performed at specific time points during the study and reviewed by two radiologists with expertise in sarcoidosis. Baseline staging was only fair (k=0.43 (0.32 – 0.54)), while change in global assessment scores showed good agreement (k=0.61 (0.51 – 0.71)) as did components of the Muers score. Improvement in both scores correlated with improvement in FVC.

- Judson et al (Eur Respir J 2008;31:1189-1196) describes the development of a new scoring system for extrapulmonary sarcoidosis – extrapulmonary physician organ severity tool; (ePOST) with an adjustment for the number of organs involved (ePOSTadj) – using the patients in the Am J Respir Crit Care Med 2006 study. Changes were noted between placebo and inflixamib treated patients at 24 weeks but these did not persist at 52 weeks. The Committee noted that the results needed to be treated with caution as there has been no validation for this system and, importantly, no correlation with clinical outcome.

- Loza et al (Clinical and Vaccine Immunology 2011;18:931-939). Serum samples from the patients enrolled in the Am J Respir Crit Care Med 2006 study were tested for 92 inflammatory associated proteins, 29 of which were found to be significantly elevated in sarcoidosis. In a post hoc exploratory analysis, those with the highest levels of TNFα, with more severe disease, had greatest improvement in FVC.

16.27 Park et al Sarcoidosis Vasc Diffuse Lung Dis.2009;26(2):121-131. A randomised, double-blind, placebo-controlled trial. 27 patients with mild to moderate stable sarcoidosis were randomised to receive pentoxifylline (1200 – 2000 mg/day) or placebo for 10 months as prednisone was tapered. The study was terminated early due to poor recruitment – only 27 of a targeted 100 enrolled. Despite this the pentoxifylline showed a reduction in flares and a reduction in total cumulative prednisone dose for the duration of the 10-month trial. There was no difference in primary outcome or pulmonary function.

16.28 The Subcommittee noted that while there was weak/moderate evidence of minimal clinical benefit of infliximab in patients with mild to moderate, stable pulmonary sarcoidosis this was based on one clinical trial, and there was no evidence provided

for the effect of infliximab in the treatment of severe, resistant pulmonary sarcoidosis patients.

16.29 The Subcommittee noted that earlier case reports had indicated the potential for some patients to gain considerable benefit from this treatment.

16.30 The subcommittee considered that TNFs do have a role to play in the treatment of pulmonary sarcoidosis.

16.31 The Subcommittee considered that infliximab should be included in a national PML for the treatment of life threatening pulmonary sarcoidosis that is resistant to other treatment options, as previously recommended. The Subcommittee recommended that the listing restriction also include the requirement use in a particular patient is to have been recommended by a recognised expert in the treatment of pulmonary sarcoidosis.

17 Review of Respiratory System and Allergies Recommendations

17.1 The Subcommittee reviewed its previous recommendations in relation to products in the Respiratory System and Allergies group, feedback from other organisations, and recommendations from the Respiratory Subcommittee.

Antiallergy Preparations

17.2 The Subcommittee noted that it had previously recommended listing cyproheptadine in a national PML. The Subcommittee noted that use of this for psychiatric indications would likely be a long-term treatment and recommended that PHARMAC consider subsidising this in the community.

17.3 The Subcommittee noted that it had previously recommended against listing allergy desensitisation kits, other than those funded in the community, in a national PML. Members considered that a review of funded allergy desensitisation kits would be useful.

Inhaled Corticosteroids

17.4 The Subcommittee noted the comments from the Respiratory Subcommittee in relation to budesonide nebuliser solution, and recommended that both strengths of this product be included in a national PML.

Leukotriene Receptor Antagonists

17.5 Members noted that it had previously recommended that montelukast not be included in a national PML, as it is not subsidised in the community. The Subcommittee noted that montelukast has a niche use in hospitals as part of aspirin desensitisation protocols, and recommended that it be included in a national PML, with prescribing restricted to use in aspirin desensitisation.

Mucolytics and Expectorants

17.6 The Subcommittee noted and agreed with the recommendation from the Respiratory Subcommittee to exclude bromhexine from a national PML.

17.7 The Subcommittee noted the comments from the Respiratory Subcommittee in relation to the use of dornase alfa in treating cystic fibrosis exacerbations. The Subcommittee noted that there did not appear to be a clear role for dornase alfa in the acute short-term situation, and members were unaware of evidence to support such use. The Subcommittee considered that this issue would need to be formally evaluated by PTAC and recommended that the Cystic Fibrosis Panel be asked to submit supporting evidence for this indication.

Respiratory Stimulants

17.8 The Subcommittee noted the feedback in relation to doxapram, and reaffirmed its recommendation to include this in a national PML.

Tumor Necrosis Factor Inhibitors

17.9 The Subcommittee noted that it had previously recommended that infliximab be included in a national PML for the treatment of pulmonary sarcoidosis, and noted that the Respiratory Subcommittee supported this recommendation. Members noted that evidence in support of this use that has been published since this indication was approved at Auckland DHB is relatively poor.

17.10 The Subcommittee noted that the Respiratory Subcommittee had recommended that prescribing of infliximab for pulmonary sarcoidosis be subject to recommendation by 'a recognised expert in the treatment of pulmonary sarcoidosis'; members noted that it could be difficult to define such an expert, and noted that most prescribing for this indication in New Zealand is done at Auckland DHB.

Pharmacology and Therapeutics Advisory Committee – 10 & 11 May 2012

18 Respiratory System and Allergies

18.1 The Committee considered a list of pharmaceuticals under consideration for use in DHB hospitals under the Respiratory System and Allergies heading, including advice from the Hospital Pharmaceuticals Subcommittee and the Respiratory Subcommittee. Except where indicated, the Committee agreed with the recommendations by the subcommittees.

18.2 The Committee noted that the subcommittees had recommended that pholcodine be included in a national PML. Members noted that there is little evidence in support of pholcodine, but that it may be practically difficult to exclude it from hospitals.

18.3 The Committee noted that the subcommittees had recommended that montelukast be included for aspirin desensitisation, but that as this had recently become subsidised in the community, it would now be included in a national PML for wider use.

18.4 The Committee noted the comments by the Respiratory Subcommittee in relation to semi-acute use of dornase alfa. Members agreed that it would be useful for the Cystic Fibrosis Panel to consider this issue and provide evidence for PTAC to consider.

18.5 The Committee noted that dornase alfa is also used in treating pleural effusions after failure of other agents, and recommended that this indication be included.