Hospital Pharmaceuticals Review

PTAC, Hospital Pharmaceuticals Subcommittee, Haematology Subcommittee, Cardiovascular Subcommittee, Reproductive and Sexual Health Subcommittee and Cancer Treatments Subcommittee minutes for web publishing

Blood and Blood Forming Organs therapeutic group

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

This document contains minutes relevant to the consultation document of 25 February 2013 relating to products in the Blood and Blood Forming Organs 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.

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Hospital Pharmaceuticals Subcommittee – 5 April 2011

1 Antithrombotic Agents

1.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Antithrombotic Agents 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:

- Heparin sodium
  - Inj 1,000 iu per ml, 1 ml
  - Inj 1,000 iu per ml, 5 ml
  - Inj 1,000 iu per ml, 35 ml
  - Inj 5,000 iu per ml, 1 ml
  - Inj 5,000 iu per ml, 5 ml
  - Inj 25,000 iu per ml, 0.2 ml
- Phenindione
  - Tab 10 mg
  - Tab 25 mg
  - Tab 50 mg
- Protamine sulphate
  - Inj 10 mg per ml, 5 ml
- Rivaroxaban
  - Tab 10 mg
- Warfarin sodium
  - Tab 1 mg
  - Tab 2 mg
  - Tab 3 mg
  - Tab 5 mg
- Aspirin
  - Tab 100 mg
  - Suppos 300 mg
- Clopidogrel
  - Tab 75 mg
- Dipyridamole
  - Inj 5 mg per ml, 2 ml
  - Tab 25 mg
  - Tab long-acting 150 mg
- Ticlopidine
  - Tab 250 mg
- Alteplase
  - Inj 10 mg
  - Inj 50 mg
- Streptokinase
  - Inj 250,000 iu
  - Inj 1,500,000 iu
- Tenecteplase

- Inj 50 mg
- Urokinase
  - Inj 10,000 iu
  - Inj 50,000 iu
  - Inj 100,000 iu
  - Inj 500,000 iu

1.3 The Subcommittee noted that there is significant variation in the use of different formulations of heparin products between hospitals, however considered that it would not be necessary to try to standardise these.

1.4 The Subcommittee recommended that one or both of the heparin sodium IV bags (50 iu per ml, 500 ml and 100 iu per ml, 250 ml) be listed in a national PML, however were uncertain as to whether there was need for both to be available. Members noted that the Safe and Quality Use of Medicines (SQUM) group had done work on this area before, and recommended that PHARMAC review this information.

1.5 Members questioned the need for three different formulations of heparinised saline (10 iu per ml, 5 ml; 100 iu per ml, 2 ml and 100 iu per ml, 5 ml), and recommended that PHARMAC staff seek feedback on the relative utility of each of these. Members also recommended that PHARMAC staff seek feedback from renal physicians and district nurses on the need for more than one formulation of heparinised saline in the community for home dialysis patients.

1.6 The Subcommittee noted that four antithrombotic agents (abciximab, bivalirudin, eptifibatide and tirofiban) were periangiography treatment options. Members noted that the use of these varied, and that their use will relate to the availability of catheterisation laboratories.

1.7 The Subcommittee considered that further information was needed before making a recommendation on the availability of these, and recommended that PHARMAC staff seek cardiologist input into whether all four of these treatments are required, and on which of these should be widely available, and which should have more limited uses.

1.8 The Subcommittee noted that for heparin-induced thrombocytopenia (HIT), three antithrombotic treatments have been available (bivalirudin, danaparoid and lepirudin), although danaparoid has become difficult to obtain and future supplies are not certain.

1.9 The Subcommittee considered that further information was needed before making a recommendation on these treatments, and recommended that PHARMAC staff consult with haematologists on the use of these products for HIT.

1.10 The Subcommittee noted that lepirudin is an unregistered medicine, and members considered that as a general rule, registered products should be given preference over unregistered products in a national PML, providing that they had the same or similar therapeutic effect.

1.11 The Subcommittee noted that PHARMAC was intending to consult on the dabigatran in the Pharmaceutical Schedule shortly, and recommended that it be included in a national PML if it does become listed in the Pharmaceutical Schedule.

1.12 Members considered that the listing of dabigatran would reduce the use of warfarin and enoxaparin in the community, although would not completely replace either.

1.13 The Subcommittee recommended that at least one low molecular weight heparin (LMWH) be listed in a national PML, and recommended that feedback be sought on restricting a national PML to a single LMWH.

1.14 Members noted that while enoxaparin is subject to Special Authority restrictions in the Pharmaceutical Schedule, there should be no such restrictions on LMWH products in a national PML.

1.15 Members recommended that the listing of rivaroxaban in a national PML be subject to restrictions on its use that are in line with the Special Authority restrictions for it in the Pharmaceutical Schedule.

1.16 The Subcommittee considered that, as aspirin tab 75 mg and tab 150 mg were not subsidised in the Pharmaceutical Schedule, and as they did not have a unique use within hospitals, they should only be available within a hospital for continuation of care, not for initiation.

1.17 The Subcommittee noted the previous PTAC and Cardiovascular Subcommittee minutes for prasugrel, and recommended that prasugrel be listed in a national PML if it becomes subsidised in the Pharmaceutical Schedule, with restrictions in the PML being equivalent to any Special Authority restrictions.

1.18 The Subcommittee considered that reteplase was no longer in use in a majority of DHBs, and recommended that it not be included in a national PML.

1.19 Members noted that DHB hospitals had indicated that they do not use dextrose with sodium citrate and citric acid (ACD-A), but recommended that PHARMAC staff consult with the New Zealand Blood Service over the need for this in hospitals.

1.20 Members recommended that PHARMAC also seek feedback from the Haematology Society of Australia and New Zealand on all of the products under the Antithrombic Agents heading.

Cardiovascular Subcommittee – 23 September 2011

2 Antithrombotic Agents

2.1 In relation to aspirin, the Subcommittee considered that there was no evidence that a strength lower than 100 mg reduced bruising or abdominal discomfort and recommended that 100 mg enteric coated is the only low dose aspirin strength listed in a national PML. The Subcommittee noted that if a patient required an alternative to the 100 mg enteric coated strength then they could take a 100 mg enteric coated tablet on every second day or use the 300 mg soluble aspirin.

2.2 In relation to low molecular weight heparin, the Subcommittee considered that in cardiology, only enoxaparin was required. The Subcommittee considered that other practitioner groups should be consulted on the need for the inclusion of other low molecular weight heparins on the national PML.

2.3 In relation to heparin sodium infusions (infusion 50 iu per ml, 500ml and infusion 100iu per ml, 250ml), the Subcommittee noted that they are not used in cardiology and therefore could be excluded from a national PML.

2.4 In relation to prasugrel, the Subcommittee recommended that it be included in the PML in line with its recommendations that it be funded in Section B of the Pharmaceutical Schedule. The Subcommittee considered that even if prasugrel is not listed in Section B, it should be considered for inclusion on the PML for patients with STEMIs undergoing immediate PCI. In this scenario and for this patient group, the Subcommittee considered that it would be appropriate to switch patients back to clopidogrel, which is fully funded in Section B of the Pharmaceutical Schedule, prior to discharge.

Hospital Pharmaceuticals Subcommittee – 6 December 2011

BLOOD AND BLOOD FORMING ORGANS

3 Antianaemics

3.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Antianaemics 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 that they be included in a national preferred medicines list (PML) without need for further prioritisation:

- Erythropoietin alpha
  - Inj 1,000 iu, prefilled syringe
  - Inj 2,000 iu, prefilled syringe
  - Inj 3,000 iu, prefilled syringe
  - Inj 4,000 iu, prefilled syringe
  - Inj 5,000 iu, prefilled syringe
  - Inj 6,000 iu, prefilled syringe
  - Inj 10,000 iu, prefilled syringe
- Erythropoietin beta
  - Inj 2,000 iu, prefilled syringe
  - Inj 3,000 iu, prefilled syringe
  - Inj 4,000 iu, prefilled syringe
  - Inj 5,000 iu, prefilled syringe
  - Inj 6,000 iu, prefilled syringe
  - Inj 10,000 iu, prefilled syringe
- Folic acid
  - Oral liq 50 µg per ml
  - Tab 0.8 mg
  - Tab 5 mg

3.3 The Subcommittee recommended that the listing of erythropoietin alpha and erythropoietin beta 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.

3.4 The Subcommittee considered that a parenteral form of folic acid was required in a national PML, but noted that previously used presentations had been discontinued. The Subcommittee recommended that a national PML include a folic acid injection, and that PHARMAC determine which product to list based on availability.

4 Antifibrinolytics, Haemostatics and Local Sclerosants

4.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Antifibrinolytics, Haemostatics and Local Sclerosants heading.

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

- Sodium tetradecyl sulphate
  - Inj 3%, 2 ml
- Tranexamic acid
  - Inj 500 mg per 5 ml
  - Tab 500 mg
- Eptacog alfa (recombinant factor VIIa)
  - Inj 1 mg
  - Inj 2 mg
  - Inj 5 mg
- Moroctocog alfa (recombinant factor VIII)
  - Inj 250 iu
  - Inj 500 iu
  - Inj 1,000 iu
  - Inj 2,000 iu
- Nonacog alfa (recombinant factor IX)
  - Inj 250 iu
  - Inj 500 iu
  - Inj 1,000 iu
  - Inj 2,000 iu
- Octocog alfa (recombinant factor VIII)
  - Inj 250 iu
  - Inj 500 iu
  - Inj 1,000 iu
  - Inj 1,500 iu
  - Inj 2,000 iu
  - Inj 3,000 iu
- Phytomenadione
  - Inj 2 mg per 0.2 ml
  - Inj 10 mg per ml, 1 ml

4.3 The Subcommittee recommended that ferric subsulfate be included in a national PML, but considered that further advice was required before it could recommend a particular presentation. Members noted that most DHBs had reported using this, and used either a solution (500 ml) or gel form (259 mg per g, 8 g). The Subcommittee requested that the view of gynaecologists be sought on this issue.

4.4 The Subcommittee noted that a variety of presentations of recombinant blood factor products is required to cater for individual dosing needs, but requested the view of haematologists as to whether all of the above presentations are required.

4.5 The Subcommittee noted that drotrecogin alfa (recombinant activated protein C) has recently been discontinued internationally, and considered that this did not need to be included in a national PML.

4.6 The Subcommittee noted that eptacog alfa 1.2 mg, 2.4 mg and 4.8 mg injections had been discontinued and considered that they did not need to be included in a national PML.

4.7 The Subcommittee noted that there was very little use of ethanolamine oleate, ornipressin and polidocanol in DHB hospitals, and considered that these did not need to be included in a national PML.

4.8 The Subcommittee noted that while there was wide use of sodium tetradecyl sulphate 3% injection in DHB hospitals, there was little use of the 0.5% and 1% injections in either DHB hospitals or the community. The Subcommittee recommended that these strengths not be included in a national PML, and considered that it may be appropriate to delist these from the Pharmaceutical Schedule as well.

4.9 The Subcommittee noted that menadiol phosphate 10 mg tablet and phytometadione 10 mg tablet had been discontinued, and considered that they did not need to be included in a national PML. Members noted however that it would be useful to have an oral preparation of phytomenadione available.

5 Antithrombotics

5.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to fondaparinux. Members noted that other antithrombotic agents had been considered previously.

5.2 The Subcommittee recommended that fondaparinux sodium (inj 5 mg per ml, 0.5 ml and inj 12.5 mg per ml, 0.6 ml) be included in a national PML, and that its use should be restricted to heparin-induced thrombocytopaenia.

6 Colony-Stimulating Factors

6.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Colony-Stimulating Factors 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 that they be included in a national preferred medicines list (PML) without need for further prioritisation:

- Filgrastim
  - Inj 300 µg per ml, 1 ml
  - Inj 600 µg per ml, 0.5 ml prefilled syringe
  - Inj 960 µg per ml, 0.5 ml prefilled syringe
- Pegfilgrastim
  - Inj 10 mg per ml, 0.6 ml

6.3 The Subcommittee noted that lenograstim is not currently in use in DHB hospitals, and considered that this did not need to be included in a national PML.

6.4 The Subcommittee noted that only one DHB had reported using ancestim, and considered that there was not a need for this to be included in a national PML.

6.5 The Subcommittee noted that sargramostim is used in paediatric oncology trials, and considered that this should be available, either through PML listing or through an exceptions provision covering clinical trials.

6.6 The Subcommittee noted that while the Health Research Council is the primary funder of clinical trials in New Zealand, PHARMAC has a legislative function to undertake research also. Members noted that in determining the provisions of an exceptions scheme that relate to clinical trials, PHARMAC should ensure that the boundaries and relative roles of PHARMAC and the Health Research Council are clear.

7 Other Biologics

7.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to rituximab.

7.2 The Subcommittee noted that rituximab had already been recommended for inclusion in a national PML for use in rheumatology.

7.3 The Subcommittee recommended that prescribing restrictions for rituximab in a national PML be extended to include the following:

- haemophilia with inhibitors;
- idiopathic thrombocytopenic purpura; and
- autoimmune haemolytic anaemia.

8 Fluids and Electrolytes

8.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Fluids and Electrolytes heading.

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

- Calcium chloride dihydrate
  - Inj 1 g in 10 ml
- Compound sodium lactate (Hartmann's solution)
  - Inj sodium 131 mmol/L with potassium 5 mmol/L, calcium 2 mmol/L, bicarbonate 29 mmol/L, chloride 111 mmol/L, 500 ml
  - Inj sodium 131 mmol/L with potassium 5 mmol/L, calcium 2 mmol/L, bicarbonate 29 mmol/L, chloride 111 mmol/L, 1,000 ml
- Glucose
  - Inf 5%, 100 ml
  - Inf 5%, 250 ml
  - Inf 5%, 500 ml
  - Inf 5%, 1,000 ml
  - Inf 10%, 500 ml
  - Inf 10%, 1,000 ml
  - Inj 50%, 10 ml
  - Inj 50%, 90 ml
  - Inf 50%, 500 ml
- Glucose with potassium chloride
  - Inf 5% glucose with 20 mmol/L potassium chloride, 1,000 ml
- Glucose with sodium chloride

- Inf glucose 2.5% with sodium chloride 0.45%, 500 ml
- Inf glucose 4% with sodium chloride 0.18%, 1,000 ml
- Inf glucose 4% with sodium chloride 0.18%, 500 ml

- Potassium chloride
  - Inj 75 mg (1 mmol) per ml, 10 ml
- Potassium chloride with sodium chloride
  - Inf 20 mmol/L potassium chloride with 0.9% sodium chloride, 1,000 ml
  - Inf 30 mmol/L potassium chloride with 0.9% sodium chloride, 1,000 ml
  - Inf 40 mmol/L potassium chloride with 0.9% sodium chloride, 1,000 ml
- Potassium dihydrogen phosphate
  - Inj 1 mmol per ml, 10 ml
- Ringer's solution
  - Inj sodium 147 mmol/L with potassium 4 mmol/L, calcium 2.2 mmol/L, chloride 156 mmol/L, 1,000 ml
- Sodium bicarbonate
  - Inj 8.4%, 10 ml
  - Inj 8.4%, 50 ml
  - Inj 8.4%, 100 ml
- Sodium chloride
  - Inf 0.45%, 500 ml
  - Inj 0.9%, 5 ml
  - Inj 0.9%, 10 ml
  - Inj 0.9%, 20 ml
  - Inf 0.9%, 50 ml
  - Inf 0.9%, 100 ml
  - Inf 0.9%, 250 ml
  - Inf 0.9%, 500 ml
  - Inf 0.9%, 1,000 ml
  - Inf 3%, 1,000 ml
  - Inf 23.4% (4 mmol/ml), 20 ml
- Water
  - Purified for inj 5 ml
  - Purified for inj 10 ml
  - Purified for inj 20 ml
  - Purified for inf 1,000 ml
- Calcium polystyrene sulphonate
  - Powder
- Compound electrolytes
  - Powder for oral soln
- Compound electrolytes with glucose
  - Soln with electrolytes
- Potassium bicarbonate
  - Tab eff 315 mg with sodium acid phosphate 1.937 g and sodium bicarbonate 350 mg
- Potassium chloride
  - Tab eff 548 mg (14 mmol) with chloride 285 mg (8 mmol)
  - Tab long-acting 600 mg (8 mmol)
  - Oral liq 2 mmol/ml 25 ml
- Sodium bicarbonate
  - Cap 840 mg
- Sodium chloride

- Tab 600 mg
- Oral liq 2 mmol/ml 25 ml

- Sodium polystyrene sulphonate
  - Powder
- Hydroxyethyl starch 130/0.4
  - Inf 6%, 500 ml
- Succinylated gelatine
  - Inf 4%, 500 ml

8.3 The Subcommittee noted that the following pharmaceuticals were not widely used in DHB hospitals, but considered that they were important treatment options, and should be included in a national PML:

- Compound electrolytes
  - Inf calcium chloride 1.29 g with lactic acid 1.35 g and magnesium chloride 508 mg in 250 ml (1) and sodium bicarbonate 14.68 g with sodium chloride 30.64 g in 4750 mL (1) [Haemosol B0]
  - Inj sodium 140 mmol/L with potassium 5 mmol/L, magnesium 1.5 mmol/L, chloride 98 mmol/L, acetate 27 mmol/L and gluconate 23 mmol/l, 500 ml [Plasma-Lyte 148 in Water]
  - Inj sodium 140 mmol/L with potassium 5 mmol/L, magnesium 1.5 mmol/L, chloride 98 mmol/L, acetate 27 mmol/L and gluconate 23 mmol/l, 1,000 ml [Plasma-Lyte 148 in Water]
- Compound electrolytes with glucose
  - Inf glucose 50 g with 140 mmol sodium, 5 mmol potassium, 1.5 mmol magnesium, 98 mmol chloride, 27 mmol acetate and 23 mmol gluconate, 1,000 ml [Plasma-Lyte 148 in Glucose]
- Compound sodium lactate with glucose
  - Inj sodium 131 mmol/L with potassium 5 mmol/L, calcium 2 mmol/L, bicarbonate 29 mmol/L, chloride 111 mmol/L and glucose 5%, 1,000 ml
- Glucose
  - Inf 5%, 50 ml
  - Inf 70%, 500 ml
  - Inf 70%, 1,000 ml
- Glucose with potassium chloride and sodium chloride
  - Inf 4% glucose with potassium chloride 20 mmol/L and sodium chloride 0.18%, 1,000 ml
  - Inf 4% glucose with potassium chloride 30 mmol/L and sodium chloride 0.18%, 1,000 ml
- Glucose with sodium chloride
  - Inf glucose 5% with sodium chloride 0.2%, 500 ml
  - Inf glucose 5% with sodium chloride 0.45%, 1000 ml
- Potassium chloride
  - Inj 225 mg (3 mmol) per ml, 20 ml
- Sodium acetate
  - Inj 4 mmol per ml, 20 ml
- Sodium chloride
  - Inf 1.8%, 500 ml
- Sodium dihydrogen phosphate (sodium acid phosphate)
  - Inj 1 mmol per ml, 20 ml
- Water
  - Purified for inf 250 ml

- Purified for inf 500 ml

8.4 The Subcommittee noted that there was little use of the Plasma-Lyte range of electrolyte replacement products, and requested that the view of anaesthetists be sought on the need for these in a national PML.

8.5 The Subcommittee noted that there are a variety of safety issues regarding solutions of potassium chloride with sodium chloride, and recommended that PHARMAC staff seek the view of the Health Quality & Safety Commission for further information on this.

8.6 The Subcommittee noted that some DHBs had rationalised use of water for injection and of sodium chloride 0.9% to only using 10 ml ampoules, rather than 5 ml, 10 ml and 20 ml ampoules, and recommended that PHARMAC consider making such a change for all DHB hospitals, and for the community, in the future.

8.7 The Subcommittee noted that the pack sizes for calcium polystyrene sulphonate and sodium polystyrene sulphonate were large, and considered that individual dose sachets would be useful in hospitals.

8.8 The Subcommittee considered that further advice was required before making a recommendation on glucose prefilled syringe (50%, 50 ml). The Subcommittee noted that only a few DHBs had reported using this presentation, and requested the view of intensivists on the need for this to be included in a national PML.

8.9 The Subcommittee considered that further advice was required before making a recommendation on the listing of sodium bicarbonate prefilled syringe (8.4%, 50 ml). Members noted that this would only be required if sodium bicarbonate was included in resuscitation protocols, and requested that PHARMAC staff obtain more information about these protocols.

8.10 The Subcommittee considered that further advice was required before making a recommendation on the listing of hydroxyethyl starch 200/0.5 in a national PML. The Subcommittee requested that the view of anaesthetists and intensivists be sought on the need for this in a national PML, and the benefits of it over hydroxyethyl starch 130/0.4.

8.11 The Subcommittee noted that gelatin-based plasma volume expanders were becoming much less used than starch-based products, and requested the view of anaesthetists and intensivists about the need for gelatin-based products in a national PML.

8.12 The Subcommittee considered that there may be benefit from having an oral liquid formulation of potassium chloride subsidised in the community, but considered that its use would need to be restricted to prevent overuse. The Subcommittee also considered that there would be benefit from having a sodium chloride tablet available in the community.

8.13 The Subcommittee noted that the following pharmaceuticals are not widely used in DHB hospitals and are not subsidised in the Pharmaceutical Schedule, and recommended that they not be included in a national PML:

- Compound electrolytes

- Inf glucose 50 g with 40 mmol sodium, 13 mmol potassium, 1.5 mmol magnesium, 40 mmol chloride and 16 mmol acetate, 1,000 ml [Plasma-Lyte 56 in Glucose]

- Glucose
  - Inf 5%, 10 ml
  - Inf 25%, 1,000 ml
- Glucose with potassium chloride and sodium chloride
  - Inf 2.5% glucose with potassium chloride 20 mmol/L and sodium chloride 0.45%, 500 ml
  - Inf 4% glucose with potassium chloride 20 mmol/L and sodium chloride 0.18%, 500 ml
- Glucose with sodium chloride
  - Inf glucose 5% with sodium chloride 0.45%, 500 ml
- Magnesium chloride
  - Inf 96 mg per ml, 5 ml
- Potassium acetate
  - Inj 0.49 g per ml, 5 ml
  - Inj 4 mmol per ml, 20 ml
- Potassium chloride
  - Inj 150 mg (2 mmol) per ml, 10 ml
- Sodium bicarbonate
  - Inj 5%, 500 ml
- Sodium hydrogen phosphate
  - Inj 3 mmol per ml, 1 ml
  - Inj 3 mmol per ml, 5 ml
- Water
  - Purified for inf 100 ml
- Compound electrolytes
  - Ice block 62.5 ml

8.14 The Subcommittee noted that dextran-based products had been discontinued, and considered that these did not need to be included in a national PML.

8.15 The Subcommittee noted that polygeline (inf 3.5%, 500 ml) is in use in a small number of DHBs, and is used less than succinylated gelatine (inf 4%, 500 ml). The Subcommittee considered that there was not a need for polygeline to be included in a national PML.

9 Minerals

9.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Minerals 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 that they be included in a national preferred medicines list (PML) without need for further prioritisation:

- Calcium carbonate
  - Tab 1.25 g (500 mg elemental)
  - Tab 1.5 g (600 mg elemental)

- Tab eff 1.75 g (1 g elemental)
- Calcium gluconate
  - Inj 10%, 10 ml
- Sodium fluoride
  - Tab 1.1 mg
- Ferrous fumarate
  - Tab 200 mg
- Ferrous fumarate with folic acid
  - Tab 310 mg with folic acid 350 µg
- Ferrous gluconate with ascorbic acid
  - Tab 170 mg with ascorbic acid 40 mg
- Ferrous sulphate
  - Oral liq 150 mg per 5 ml
  - Tab long-acting 325 mg
- Ferrous sulphate with ascorbic acid
  - Tab long-acting 325 mg with ascorbic acid 500 mg
- Ferrous sulphate with folic acid
  - Tab long-acting 325 mg with folic acid 350 µg
- Iron polymaltose
  - Inj 50 mg per ml, 2 ml
- Iron sucrose
  - Inj 20 mg per ml, 5 ml
- Magnesium sulphate
  - Inj 49.3%
- Zinc chloride
  - Inj 5 mg per 2 ml (76 µmol elemental)
- Zinc sulphate
  - Cap 220 mg (50 mg elemental)

9.3 The Subcommittee noted that four oral magnesium products were in use in DHB hospitals (magnesium amino acid chelate 250 mg tablet; magnesium hydroxide 311 mg tablet; magnesium oxide 400 mg tablet; magnesium oxide with magnesium orotate, magnesium phosphate and magnesium amino acid chelate 300 mg tablet). The Subcommittee recommended that an oral magnesium product be listed in a national PML, but did not consider that it had sufficient information to recommend one over another. The Subcommittee noted that there may be benefit from having an oral magnesium product subsidised in the community also.

9.4 The Subcommittee noted that there is a use for magnesium sulphate injection (100 mmol in 250 ml) within obstetrics, and recommended that this be included in a national PML.

10 Vitamins

10.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Vitamins 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 that they be included in a national preferred medicines list (PML) without need for further prioritisation:

- Multivitamins
  - Cap vitamin A 2500 units, betacarotene 3 mg, cholecalciferol 11 µg, alpha tocopherol 150 units, phytomenadione 150 mcg, folic acid 0.2 mg, ascorbic acid 100 mg, thiamine 1.5 mg, pantothenic acid 12 mg, riboflavin 1.7 mg, niacin 20 mg, pyridoxine hydrochloride 1.9 mg, cyanocobalamin 3 mcg, zinc 7.5 mg and biotin 100 mcg [vitABDECK]
  - Powder vitamin A 4200 mcg, 55.5 mcg vitamin D1, 21.4 mg vitamin E, 400 mg vitamin C, 166 mcg vitamin K1, 3.2 mg thiamin, 4.4 mg riboflavin, 35 mg niacin, 3.4 mg vitamin B6, 303 mcg folic acid, 8.6 mcg vitamin B12, 214 mcg biotin, 17 mg pantothenic acid, 350 mg choline and 700 mg inositol [Paediatric Seravit]
  - Tab (BPC cap strength)
- Vitamin A with vitamins D and C
  - Soln 1000 u with Vitamin D 400 u and ascorbic acid 30 mg per 10 drops
- Hydroxocobalamin
  - Inj 1 mg per ml, 1 ml
- Pyridoxine hydrochloride
  - Inj 100 mg per ml
  - Tab 25 mg
  - Tab 50 mg
- Thiamine hydrochloride
  - Tab 50 mg
  - Inj 100 mg per ml, 2 ml
- Vitamin B Complex
  - Tab, strong, BPC
- Ascorbic acid
  - Tab 100 mg
- Alfacalcidol
  - Cap 0.25 mcg
  - Cap 1 mcg
  - Oral drops 2 mcg per ml
- Calcitriol
  - Cap 0.25 mcg
  - Cap 0.5 mcg
  - Oral liq 1 mcg per ml
- Cholecalciferol
  - Tab 1.25 mg (50,000 iu)
- Alpha tocopheryl acetate
  - Water solubilised soln 156 iu/ml, with calibrated dropper

10.3 The Subcommittee recommended that the listing of multivitamins capsule [vitABDECK] and powder [Paediatric Seravit] be subject to restrictions on their use that are in line with the Special Authority criteria for them in the Pharmaceutical Schedule.

10.4 The Subcommittee recommended that the listing of alpha tocopheryl acetate be subject to restrictions on its use that are in line with the Special Authority criteria for it in the Pharmaceutical Schedule.

10.5 The Subcommittee noted that Ketovite and Ketovite Liquid brands of multivitamins had been discontinued, and considered that these products did not need to be included in a national PML.

10.6 The Subcommittee noted that hydroxocobalamin 2.5 g injection is not widely used, but is an important treatment for cyanide poisoning, and recommended that it be included in a national PML. Members noted that this product should be listed alongside other antidotes, rather than with vitamin preparations.

10.7 The Subcommittee noted that in cases of alcoholism or Wernicke's encephalopathy, patients are required to take high doses of thiamine hydrochloride, and considered that using the 50 mg preparation would create a sizeable pill burden. The Subcommittee recommended that thiamine hydrochloride 100 mg tablets also be included in a national PML. The Subcommittee noted that a 100 mg capsule was also available, but considered that this did not need to be included.

10.8 The Subcommittee noted that most DHBs reporting using at least one chewable vitamin C preparation. The Subcommittee considered that it would be useful to have at least one such presentation available, and recommended that ascorbic acid 250 mg chewable tablets be included in a national PML, but considered that it would not be necessary to list the 500 mg and 1 g preparations.

10.9 The Subcommittee also recommended that ascorbic acid powder be included in a national PML. Members noted that this should be listed as part of compounded preparations, rather than with vitamin preparations.

10.10 The Subcommittee noted that oral and parenteral preparations of retinol are not widely used, and are not subsidised in the Pharmaceutical Schedule, but noted that this is an important treatment option for patients with measles. The Subcommittee recommended that 10,000 iu tablets, 25,000 iu capsules and 150,000 iu per ml, 7.5 ml injection be listed in a national PML. The Subcommittee considered that it would not be necessary to list the 9,000 iu capsules.

10.11 The Subcommittee noted that three DHBs had reported previously using a parenteral form of ascorbic acid (500 mg per 5 ml injection). The Subcommittee recommended that this not be included in a national PML.

10.12 The Subcommittee noted that pyridoxine 50 mg injection is not in use in DHB hospitals, and recommended that it not be included in a national PML.

10.13 The Subcommittee noted that alfacalcidiol injection (2 mcg per ml, 1 ml) is not in use in DHB hospitals, and recommended that it not be included in a national PML.

10.14 The Subcommittee noted that calcitriol injection (1 mcg per ml, 1 ml) is not widely used in DHB hospitals, and recommended that it not be included in a national PML.

10.15 The Subcommittee noted that ergocalcferol (1.25 g tablet) is not in use in DHB hospitals, and recommended that it not be included in a national PML.

10.16 The Subcommittee noted that alpha tocopheryl acetate capsules (100 u, 200 u and 500 u) are in use in a number of DHB hospitals, but are not subsidised in the Pharmaceutical Schedule, and do not have a unique use within hospitals. The Subcommittee recommended that they not be included in a national PML.

10.17 The Subcommittee noted that a parenteral preparation of vitamins B and C was not currently in use in DHB hospitals, but considered that having this available would be of significant benefit for emergency departments in cases of alcoholism, and recommended that the following be listed in a national PML:

- Multivitamins
  - Inj thiamine hydrochloride 250 mg with riboflavin 4 mg and pyridoxine hydrochloride 50 mg, 5 ml ampoule (1) and ascorbic acid 500 mg with nicotinamide 160 mg, 2 ml ampoule (1) [Pabrinex IM]
  - Inf thiamine hydrochloride 250 mg with riboflavin 4 mg and pyridoxine hydrochloride 50 mg, 5 ml ampoule (1) and ascorbic acid 500 mg with nicotinamide 160 mg and glucose 1000 mg, 5 ml ampoule (1) [Pabrinex IV]
  - Inf thiamine hydrochloride 500 mg with riboflavin 8 mg and pyridoxine hydrochloride 100 mg, 10 ml ampoule (1) and ascorbic acid 1000 mg with nicotinamide 320 mg and glucose 2000 mg, 10 ml ampoule (1) [Pabrinex IV]

Reproductive and Sexual Health Subcommittee – 25 June 2012

11 Hospital Pharmaceuticals Review

11.1 The Subcommittee noted that the Hospital Pharmaceuticals Subcommittee had sought advice on the presentations of ferric subsulfate that should be included in a national PML. Members noted that solution and gel formulations were currently in use, and considered that both should remain available.

11.2 The Subcommittee noted that the Hospital Pharmaceuticals Subcommittee had sought advice on the need for more than one low molecular weight heparin (LMWH) to be included in a national PML. Members noted that some clinicians consider tinzaparin to be the preferred LMWH for prophylaxis of deep-vein thrombosis in pregnancy.

11.3 The Subcommittee noted that a recent publication on this topic (McLintock et al, Aust N Z J Obstet Gynaecol. 2012 Feb;52(1):14-22.) recommended the use of any LMWH for DVT prophylaxis in pregnancy. The Subcommittee considered that it was not necessary for tinzaparin to be included in a national PML.

Haematology Subcommittee – 6 August 2012

12 Hospital Pharmaceuticals Review

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

12.2 The Subcommittee noted that the Hospital Pharmaceuticals Subcommittee had recommended that the prescribing of erythropoietin in DHB hospitals be subject to restrictions that are in line with the Special Authority criteria in the community.

12.3 The Subcommittee noted that the use of erythropoietin as an alternative to blood transfusions for religious reasons is an on-going issue that is not covered by the community criteria.

12.4 Members noted that trials are underway investigating the use of erythropoietin in a pre-surgical setting, which may require consideration in the future.

12.5 The Subcommittee noted that the Hospital Pharmaceuticals Subcommittee had queried whether all currently available presentations of recombinant blood factor products were required in a national PML. The Subcommittee recommended that all of these presentations be included.

12.6 The Subcommittee noted that the Hospital Pharmaceuticals Subcommittee had requested advice on the need for more than one form of low molecular weight heparin to be available in DHB hospitals. The Subcommittee noted that many DHBs currently use enoxaparin only, and that a few use dalteparin. Members noted that historically tinzaparin was used preferentially in obstetrics, but that this was no longer the majority view and that tinzaparin is now not commonly used in DHB hospitals.

12.7 The Subcommittee considered that having more variants of low molecular weight heparin available increased the risk of confusion and therefore overdose.

12.8 The Subcommittee considered that it would be preferable just to list enoxaparin in a national PML, and to exclude dalteparin and tinzaparin. However, the Subcommittee considered that it would be acceptable to include dalteparin also. The Subcommittee recommended that tinzaparin not be included in a national PML.

12.9 The Subcommittee noted that dextrose with sodium citrate and citric acid (acid citric dextrose A) was used in a number of niche indications including as an anticoagulant in stem cell harvest, and recommended that it be included in a national PML.

12.10 The Subcommittee noted that the Hospital Pharmaceuticals Subcommittee has sought advice on the presentations of intravenous heparin infusions that should be included in a national PML. The Subcommittee recommended that only the 100 iu per ml, 250 ml presentation be included for safety reasons.

12.11 The Subcommittee noted that the Hospital Pharmaceuticals Subcommittee has sought advice on the presentations of heparinised saline that should be included in a national PML. The Subcommittee recommended that all three presentations that are currently in use be included.

12.12 The Subcommittee recommended that filgrastim be subject to recommendation by haematologists and oncologists. Members noted that while others, such as renal physicians, do prescribe filgrastim, it is usual and appropriate for them to seek advice from haematologists or oncologists before prescribing.

12.13 The Subcommittee noted that the Hospital Pharmaceuticals Subcommittee had recommended including pegfilgrastim in a national PML. The Subcommittee noted that the benefits of pegfilgrastim relate to convenience rather than clinical superiority over filgrastim. The Subcommittee noted that most people however, are able to self-administer filgrastim.

12.14 The Subcommittee considered that, if pegfilgrastim was listed in a national PML, prescribing restrictions would be required, due to the cost difference between it and filgrastim. The Subcommittee considered that defining criteria would be difficult, as they would need to relate to a patient's ability to self-administer filgrastim, and would likely be difficult to enforce.

12.15 The Subcommittee recommended that pegfilgrastim not be included in a national PML. The Subcommittee noted that individual patients would be able to have pegfilgrastim funded under NPPA, and considered that this would be appropriate.

12.16 The Subcommittee noted that plerixafor had been used in some DHBs. The Subcommittee considered that this should undergo a formal review by PTAC and the Subcommittee, and recommended that PHARMAC seek a funding application for it.

12.17 The Subcommittee agreed with the Hospital Pharmaceuticals Subcommittee that an oral magnesium preparation also be included in a national PML and considered that the selection of salt is not important.

12.18 The Subcommittee noted and agreed with the recommendation from the Hospital Pharmaceuticals Subcommittee that the prescribing of rasburicase be subject to recommendation by haematologists.

12.19 The Subcommittee noted that there has been some use of imatinib in the treatment of hypereosinophilic syndrome. The Subcommittee noted that this is a rare condition, and considered that it was appropriate for this to be managed through NPPA.

12.20 The Subcommittee noted that the Hospital Pharmaceuticals Subcommittee had recommended that the 150 mcg dose form of desmopressin nasal spray not be listed in a national PML. The Subcommittee noted that this form is not widely used, with desmopressin injection being the predominant formulation used in haematology.

12.21 The Subcommittee noted also that defibrotide is currently being used by major transplant centres for venous occlusive disease prophylaxis in stem cell transplant recipients. The Subcommittee considered that the patient numbers are small (<10 per year). The Subcommittee recommended that defibrotide is included in a national PML and access criteria can be guided by hospital guidelines which are currently being used.

13 Treatments for HIT

Application

13.1 The Subcommittee reviewed a memorandum from PHARMAC staff regarding the inpatient treatments for heparin-induced thrombocytopenia (HIT) including bivalirudin, danaparoid, lepirudin, fondaparinux and argatroban.

Recommendation

13.2 The Subcommittee recommended that bivalirudin, danaparoid and fondaparinux are included on the national Preferred Medicines List for the management of heparin-induced thrombocytopenia.

Discussion

13.3 The Subcommittee considered that heparin-induced thrombocytopenia (HIT) was strongly associated with venous thromboembolism (VTE) and arterial thromboembolism as well as an increased risk of warfarin-related tissue necrosis. The Subcommittee considered that haemorrhagic complications are rare even with severe thrombocytopenia (platelets <15 x 109/L) which occurs in 5% of patients. The Subcommittee considered that overall the incidence of HIT is variable depending on the specific patient population and it also depends on the type of heparin used (a greater incidence in bovine versus porcine heparin) and the duration of heparin treatment. The Subcommittee considered that HIT occurs in approximately 2.5% of medical cardiac patients. The Subcommittee also considered that at most 10% of patients with suspected HIT are finally diagnosed with it.

13.4 The Subcommittee noted that thrombotic complications can occur at any time prior/during/after the onset of thrombocytopenia despite the cessation of heparin treatment. The Subcommittee considered that the thrombosis risk is approximately 5-10% per day for the first 1-2 days and the 30-day cumulative risk was about 50%. The Subcommittee also noted that the rate of thrombosis was similar even if heparin was replaced with warfarin. The Subcommittee considered that an alternative anticoagulant was therefore required.

13.5 The Subcommittee noted that the possible alternative anticoagulants include lepirudin, desirudin, bivalirudin, argatroban, danaparoid and fondaparinux. The Subcommittee noted that there is no published evidence with direct head-to-head comparisons of any of these agents. The Subcommittee noted that the PREVENT-HIT study comparing argatroban and desirudin was terminated before full recruitment. The Subcommittee considered that indirect comparison suggests that these treatments are effective.

13.6 The Subcommittee noted that the pivotal studies for argatroban that led to its approval were non-randomised single arm open label studies with untreated historical controls for comparison and serologic confirmation was not required for study inclusion (Lewis et al. Arch Intern Med 2003 Aug 11-25; 163(15): 1849-56 and Lewis et al. Circulation 2001 Apr 10; 103(14): 1838-43). The Subcommittee noted that 36% of those enrolled were antibody negative on post-hoc tests and a subset of patients had a remote history of HIT but no acute disease. The Subcommittee noted that the study results were in favour of argatroban for the primary end point (composite all-cause death, all-cause amputation or new thrombosis in 37 days) with an odds ratio (OR) of 0.61; 95% CI 0.39-0.98; p=0.04. The Subcommittee noted that there was no

significant difference in bleeding between argatroban and controls in those trials. The Subcommittee noted that argatroban is metabolised in the liver and therefore caution is required in patients with liver failure. The Subcommittee noted that the American College of Chest Physicians (ACCP) guidelines favour argatroban in patients with renal failure. The Subcommittee noted also that argatroban is not registered in Australia or New Zealand.

13.7 The Subcommittee noted that lepirudin is registered in New Zealand and the evidence for its use in HIT is based on single arm studies with untreated historical controls for comparison however serologic confirmation of diagnosis was required prior to study enrolment. The Subcommittee noted that the study results favoured lepirudin with a reduction in new thromboses (11.9% vs. 32.1%, P = 0.0008)(Lubenow et al. J Thromb Haemost. 2005 Nov;3(11):2428-36) but there was a higher rate of bleeding (29.4% vs. 9.1%, P = 0.0148) which was dose-dependent. The Subcommittee also noted that lepirudin is renally cleared. The Subcommittee noted that approximately half of the patients developed anti-lepirudin antibodies but this is usually not problematic. The Subcommittee however noted that the supplier has discontinued supply of this treatment worldwide since April 2012.

13.8 The Subcommittee noted that bivalirudin is indicated and used mainly in percutaneous intravascular procedures in New Zealand. The Subcommittee noted that the evidence for its use in HIT is mainly from open label single arm studies. The Subcommittee noted that it is currently being used to treat HIT in the cardiac ICU setting in Auckland Hospital. The Subcommittee noted that the ACCP guidelines recommend the use of bivalirudin (Level 2C evidence) in the setting of acute or subacute HIT associated with cardiac surgery.

13.9 The Subcommittee considered that treatment with intravenous danaparoid showed benefit when compared to Dextran 70 (Chong et al. Thromb Haemost 2001 Nov; 86(5): 1170-5). The Subcommittee noted that the ACCP guidelines recommended that danaparoid is used in patients with HIT or HIT with thrombosis who have normal renal function (Level 2C evidence). The Subcommittee noted that it was previously used in Auckland Hospital but there were was an interruption of supply. The Subcommittee noted that the supply issues are being resolved by the supplier.

13.10 The Subcommittee noted that fondaparinux is given as a subcutaneous injection and it is not registered for use in the treatment of HIT or systematically studied in this indication. The Subcommittee noted that there are several case series. The Subcommittee noted that a pooled analysis of 71 patients showed that none of the patients treated with fondaparinux developed new thrombotic events, major haemorrhage occurred in 4 patients but 3 of these patients had a creatinine clearance level of <30ml/min (Warkentin TE. Expert Review of Haematology 2010; 3(5): 567-581). The Subcommittee noted that there have been a few cases reported where fondaparinux potentially cause HIT but attribution remains uncertain. The Subcommittee noted that given its ease of administration with subcutaneous and once-daily administration, it is increasingly being used in stable patients.

13.11 The Subcommittee considered that the choice of treatment for HIT would be largely dependent on what treatments are actually available and taking into account the different clinical settings. The Subcommittee considered that it would be appropriate to include bivalirudin, fondaparinux and danaparoid on the national Preferred Medicines List for the treatment of HIT.

13.12 The Subcommittee noted that the newer oral anticoagulants like dabigatran and rivaroxaban could be efficacious in HIT but there is currently no evidence for their use in this setting.

14 Rituximab for ITP and autoimmune haemolytic anaemia

Application

14.1 The Subcommittee reviewed a memorandum from PHARMAC staff regarding rituximab for the treatment of autoimmune haemolytic anaemia and idiopathic thrombocytopenic purpura.

Recommendation

14.2 The Subcommittee recommended that rituximab is included in the national Preferred Medicines List for the treatment of cold haemagglutinin disease (CHD) with high priority and warm autoimmune haemolytic anaemia with medium priority.

14.3 The Subcommittee also recommended that rituximab is included in the hospital Preferred Medicines List for the treatment of refractory idiopathic thrombocytopenic purpura (ITP) (platelet count <20,000 per µL) where there is evidence of clinically significant bleeding.

14.4 The Subcommittee recommended that for these indications, it would be appropriate to restrict rituximab prescribing in hospitals to haematologists.

Discussion

14.5 The Subcommittee considered that cold haemagglutinin disease (CHD) is rare, very difficult to treat and there are no other effective treatment options. The Subcommittee noted that currently first-line treatments include steroids and immunosuppressants. Splenectomy and IVIG are additional options and then rituximab. The Subcommittee considered that rituximab may be considered prior to other immunosuppressants in younger patients. The Subcommittee considered that the limited data available indicates that the response rate to rituximab can be up to 70% and it is also reduces the need for steroids.

14.6 The Subcommittee noted that warm haemagglutinin disease is the most common form of autoimmune haemolytic anaemia and can occur spontaneously or in association with certain disorders including systemic lupus erythematosus (SLE), lymphoma and CLL. The Subcommittee noted that 10-20% of patients with CLL develop haemolytic anaemia and therefore it is not a rare condition. The Subcommittee considered that the evidence for rituximab in haemolytic anaemia associated with CLL is fair. The Subcommittee considered that rituximab is now funded in Section B of the Pharmaceutical Schedule for CLL but not in the context of haemolytic anaemia associated with the disease.

14.7 The Subcommittee considered that <20 patients would access rituximab for cold haemagglutinin disease and warm autoimmune haemolytic anaemia per year as the proportion of patients with severe disease is rare and they are already accessing rituximab in these settings currently. The Subcommittee considered that the dosage for rituximab in these indications would be either 375mg/m2 weekly for four weeks or 100mg weekly for four weeks. The Subcommittee considered there would be some patients would require re-treatment with rituximab in these indications.

14.8 The Subcommittee considered that there are,effective treatment options and clear treatment guidelines for ITP as discussed during the review of eltrombopag in this indication above. The Subcommittee considered that first-line treatments in New Zealand are corticosteroids and intravenous immunoglobulin (IVIG). The Subcommittee considered that if patients failed on these treatments, splenectomy would be the next option followed by immunosuppressant therapies like danazol, azathioprine, cyclosporin and rituximab or if available, eltrombopag. The Subcommittee considered that there is no good quality evidence for the efficacy of rituximab in ITP, only case series. The Subcommittee considered that there is also inconclusive evidence about the appropriate dose for rituximab (375mg/m2 weekly for four weeks versus 100mg weekly for four weeks). The Subcommittee noted the Barcellini et al study (Blood 2012; 119(16): 3691-3697) showed that the lower dose of rituximab resulted in an 82% response rate. The Subcommittee noted however that this was a small study involving only 23 patients with a median follow up of 15 months. For the reasons above, the Subcommittee was unable to recommend the lower dose as the standard of care. The Subcommittee noted that the lower dose is used in Wellington Hospital currently. The Subcommittee however noted that unlike eltrombopag, rituximab is not an ongoing long term treatment.

14.9 Although rituximab could be used to avoid a splenectomy, the Subcommittee noted that only 30% respond and the response is not durable, varying from 12 to 24 months. Therefore, the Subcommittee considered that patients most likely to benefit from rituximab would be patients who have refractory ITP despite a splenectomy and have significant problems with bleeding. The Subcommittee considered that the response rate in this patient group is about 30-40%.

15 Rituximab for haemophilia with inhibitors

Application

15.1 The Subcommittee reviewed a memorandum from PHARMAC staff regarding rituximab for the treatment of haemophilia with inhibitors.

Recommendation

15.2 The Subcommittee recommended that rituximab is included on the national Preferred Medicines List for the treatment of:

15.2.1 Mild congenital haemophilia, complicated by inhibitors with high priority;

15.2.2 Severe congenital haemophilia in patients who have failed immune tolerance therapy with medium priority; and

15.2.3 Acquired haemophilia with low priority.

15.3 The Subcommittee recommended that for these indications, it would be appropriate to restrict rituximab prescribing in hospitals to haematologists.

Discussion

15.4 The Subcommittee considered that the development of alloantibodies or inhibitors in congenital haemophilia is a very significant problem. The Subcommittee considered that it is associated with increased morbidity, poor quality of life and a significant cost where a bleeding event needs to be treated with bypassing agents. These patients

are not on prophylactic treatment and therefore have progressive arthropathies which have long term effect.

15.5 The Subcommittee noted that immune tolerance can be achieved in up to 70% of patients who have severe haemophilia complicated by inhibitors, with immune tolerance therapy (ITT) for which a guideline exists in New Zealand. The Subcommittee considered that the evidence for rituximab in this indication is mainly from case reports and case series. The Subcommittee considered that the most relevant paper in severe haemophilia is the systematic review by Collins et al (J Thromb Haemost 2009; May; 7(5): 787-94) where 40% of 15 patients achieved a negative inhibitor titer and 47% achieved a significant clinical benefit. The Subcommittee noted that 5 patients eventually relapsed. The Subcommittee noted that although this study only involved a small number of patients, it indicated that concomitant treatment with Factor VIII was important for the success of rituximab therapy in severe haemophilia with inhibitors.. The Subcommittee considered that rituximab is currently used in patients who are refractory to ITI and the response rates are about 50% and response tends to be transient.

15.6 The Subcommittee noted that inhibitors are an uncommon complication of mild haemophilia (1% incidence in mild haemophilia A) (Dunkley et al. Haemophilia 2006; 12: 663–667) and patients normally present later in life. The Subcommittee considered that mild haemophilia with inhibitors is a severe disease and these patients have a haemorrhagic tendency. The Subcommittee considered that the evidence available indicates that these patients respond less well to ITI. The Subcommittee noted that observation is a common treatment approach in asymptomatic patients because spontaneous remission is quite common (60%)(Dunkley et al. Haemophilia 2006; 12: 663–667). The Subcommittee noted that Dunkley et al reported successful treatment of mild haemophilia with inhibitors with rituximab in 3 patients.

15.7 The Subcommittee noted that acquired haemophilia was a rare condition, approximately 1 to 4 patients per million per year but when it does occur; it is associated with significant morbidity and mortality. There is a peak in incidence during the postpartum period and in the elderly. The Subcommittee noted that it is idiopathic in 50% of cases. The Subcommittee noted that there are currently no standard protocols for treatment. Current treatment involved treating bleeds and eradicating inhibitors with immune suppression (steroids +/- cyclophosphamide). The Subcommittee however noted that there are significant side-effects with cyclophosphamide. The Subcommittee noted a systematic review involving 65 patients (Franchini M. Crit Rev Oncol Hematol. 2007 Jul;63(1):47-52) showed that the response rate with rituximab treatment in acquired haemophilia was approximately 90% with concomitant immunosuppression.

15.8 The Subcommittee considered that overall, the evidence suggests that rituximab is effective for the treatment of haemophilia with inhibitors and it is relatively safe although longer term data is lacking. The Subcommittee considered however that it is still unknown what the optimal dosing schedule is.

16 Recent PTAC and Subcommittee recommendations

16.1 The Subcommittee noted a verbal report on the recommendations of the Haematology Subcommittee at its August 2012 meeting regarding the listing of listing of various pharmaceuticals on the Hospital Preferred Medicines List (PML). Members noted that it was to also review some of the pharmaceuticals discussed later *[relevant minutes are contained in the Oncology Agents and Immunosuppressants minutes document]*.

16.2 In particular members noted, and disagreed with, the Haematology Subcommittee's recommendation not to list pegfilgrastim on the PML.

16.3 The Subcommittee considered that medical oncologists often initiated pegfilgrastim treatment in hospitals and therefore it was important to consider their view. Members considered that whilst there was not a real health need for pegfilgrastim over filgrastim, it was more convenient and that its use may result in a decrease In community supportive care costs as there may be fewer calls on services to assist with daily injections.

16.4 Members also considered that some medical oncologists felt, pegfilgrastim offered better certainty of appropriate dosing.

16.5 The Subcommittee recommended that pegfilgrastim should be listed on the PML only if cost neutral to filgrastim. Members considered that cost neutrality should take into account the relative current and future costs of the two pharmaceuticals, including dosing equivalence, potential further future price drops on filgrastim, potential market expansion and patent considerations on pegfilgrastim.

Hospital Pharmaceuticals Subcommittee – 11 December 2012

17 Review of Blood and Blood Forming Organs Recommendations

17.1 The Subcommittee reviewed its previous recommendations in relation to products in the Blood and Blood Forming Organs group, feedback from other organisations, and recommendations from the Haematology, Cardiovascular and Reproductive and Sexual Health Subcommittees.

Antianaemics

17.2 The Subcommittee noted that it had previously recommended that a parenteral form of folic acid be included in a national PML. Members noted that a 5 mg per ml, 10 ml form of folic acid is currently being used in DHB hospitals.

Antithrombotics

17.3 The Subcommittee noted that it had deferred making a recommendation in relation to the listing of low molecular weight heparins in a national PML. Members noted that the Cardiovascular Subcommittee, Haematology Subcommittee and the Reproductive and Sexual Health Subcommittee had all considered that there was only a need for enoxaparin to be made available. The Subcommittee noted that PHARMAC had recently made a decision to subsidise dalteparin in the community, and recommended that enoxaparin and dalteparin be listed in a national PML, and that tinzaparin not be listed.

17.4 The Subcommittee noted the recommendations from the Haematology Subcommittee in relation to treatments for heparin-induced thrombocytopaenia. Members noted that some DHBs had recently considered using argatroban for this purpose, but that the Haematology Subcommittee had not recommended that it be listed. The Subcommittee recommended that argatroban not be included in a national PML.

17.5 The Subcommittee noted, and agreed with the recommendation from the Haematology Subcommittee, to list the 100 iu per ml, 250 ml form of heparin sodium injection in a national PML, and to exclude the 50 iu per ml, 500 ml form. Members noted that several DHBs have already started to standardise usage to the 250 ml presentation.

17.6 The Subcommittee noted that it had previously deferred making a recommendation on the formulations of heparinised saline that should be included in a national PML. The Subcommittee recommended including all three forms that are currently in use: 10 iu per ml, 5 ml; 100 iu per ml, 2 ml; and 100 iu per ml, 5 ml.

17.7 The Subcommittee agreed with the recommendation of the Haematology Subcommittee to include dextrose with sodium citrate and citric acid in a national PML.

17.8 The Subcommittee noted feedback recommending that a 75 mg form of aspirin be included in a national PML. The Subcommittee noted that this is not subsidised in the community, and considered that it should only be included in a national PML if it becomes subsidised in the community.

Fluids and Electrolytes

17.9 The Subcommittee noted that it had previously deferred making a recommendation in relation to glucose 50% syringes and sodium bicarbonate 8.4% syringes. The Subcommittee considered that there was not a need for prefilled glucose syringes to be available in DHB hospitals, and recommended that these not be included in a national PML. Members noted that other presentations of these pharmaceuticals would still be available.

17.10 The Subcommittee noted feedback suggesting that hydroxyethyl starch 200/0.5 be excluded from a national PML. The Subcommittee recommended that it not be included.

17.11 The Subcommittee noted one respondent had requested that potassium acetate 4 mmol per ml, 20 ml and sodium hydrogen phosphate 3 mmol per ml, 5 ml be included in a national PML. The Subcommittee noted that these are likely to be used in the preparation of parenteral nutrition.

17.12 The Subcommittee noted feedback suggesting that glucose 10% with potassium chloride 10 mmol and sodium chloride 15 mmol in 500 ml was in use in DHB hospitals, and recommended that this be included in a national PML.

Pharmacology and Therapeutics Advisory Committee – 14 & 15 February 2013

18 Hospital Pharmaceuticals Review

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

18.2 The Committee noted that the Cardiovascular Subcommittee had recommended that, due to the faster onset of action of prasugrel over clopidogrel, that prasugrel be available for use in hospital for short-term use in patients who have experienced STEMI, with patients switching to clopidogrel upon discharge.

18.3 The Committee noted that there were no prospective studies considering such a protocol, but noted that the pharmacokinetic data for prasugrel indicated that such an approach may be reasonable. Members noted that, as ticagrelor also has a fast onset of action, listing prasugrel for this indication would not be necessary if ticagrelor became funded for STEMI patients.

18.4 The Committee noted that feedback from anaesthetists was that 4% dextrose with 0.18% sodium chloride should be withdrawn from DHB hospitals. Members noted that use of this has a risk of hyponatraemia, and considered that there was not a need for it to remain available. The Committee recommended that this be excluded from a national PML.

18.5 The Committee agreed with the recommendations by the Haematology Subcommittee in relation to the use of rituximab for idiopathic thrombocytopenic purpura, cold haemagglutinin disease and haemophilia. Members considered however that it would be necessary for access criteria for these indications to be carefully defined, and considered that the advice of the Haematology Subcommittee should be sought.