Hospital Pharmaceuticals Review

PTAC, Hospital Pharmaceutical Subcommittee and Rheumatology Subcommittee minutes for web publishing

Musculoskeletal System therapeutic group

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This document contains minutes relevant to the consultation document of 3 August 2012 relating to products in the Musculoskeletal System 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 the consultation document are contained here.

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Hospital Pharmaceuticals Subcommittee – 3 May 2011

1 Anticholinesterases

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

- Edrophonium chloride
  - Inj 10 mg per ml, 1 ml
- Neostigmine
  - Inj 2.5 mg per ml, 1 ml
- Pyridostigmine bromide
  - Tab 60 mg

1.3 The Subcommittee recommended that use of edrophonium be limited to neurologists, or on the recommendation of neurologists, for myasthenia gravis.

1.4 Members noted that a 180 mg modified-release tablet of pyridostigmine has previously been available under section 29 of the Medicines Act 1981 and recommended seeking feedback from neurologists on the need for this presentation.

1.5 The Subcommittee noted that there may be other uses for edrophonium and suggested that PHARMAC consult with gastroenterologists and cardiologists on this matter.

2 Antirheumatoid Agents

2.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Antirheumatoid 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:

- Azathioprine
  - Inj 50 mg
  - Tab 50 mg
- Ciclosporin
  - Cap 25 mg
  - Cap 50 mg
  - Cap 100 mg
  - Oral liq 100 mg per ml
  - Inf 50 mg per ml, 5 ml
- Leflunomide
  - Tab 10 mg
  - Tab 20 mg
  - Tab 100 mg

- Methotrexate
  - Tab 2.5 mg
  - Tab 10 mg
- Penicillimine
  - Tab 125 mg
  - Tab 250 mg
- Sodium aurothiomalate
  - Inj 10 mg per 0.5 ml
  - Inj 20 mg per 0.5 ml
  - Inj 50 mg per 0.5 ml
- Sulphasalazine
  - Tab 500 mg
  - Tab EC 500 mg
- Hydroxychloroquine
  - Tab 200 mg
- Rituximab
  - Inj 100 mg per 10 ml vial
  - Inj 500 mg per 10 ml vial
- Adalimumab
  - Inj 40 mg per 0.8 ml pen
  - Inj 40 mg per 0.8 ml syringe
- Etanercept
  - Inj 25 mg
  - Inj 50 mg autoinjector
  - Inj 50 mg syringe

2.3 The Subcommittee noted that auranofin tab 3 mg is rarely used within hospitals, and while it is subsidised in the Pharmaceutical Schedule its use is low and declining. The Subcommittee considered that its use in hospitals would only be for continuation of care, not initiation of treatment, and recommended that it not be included in a national PML.

2.4 Members noted that ciclosporin is currently included on the Discretionary Community Supply (DCS) list. The Subcommittee recommended that, as it no longer has a Special Authority restriction in the Pharmaceutical Schedule, the DCS listing is no longer required and recommended that it be removed.

2.5 The Subcommittee considered that further advice was required before a recommendation could be made on the listing of hyaluronic acid in a national PML. The Subcommittee recommended that PHARMAC seek input from orthopaedic surgeons, rheumatologists, ENT specialists and plastic surgeons. The Subcommittee noted that it could have significant cost implications depending on the indications, for example if it was used in osteoarthritis which is a very common condition. Members noted that studies suggested that the efficacy of hyaluronic acid is preparation dependent so it could be important to specify brand as well as formulation if it was added to the PML.

2.6 Members noted that use of leflunomide 100 mg tab is low, and that many hospital pharmacies might not stock it due to potential confusion between this and the 10 mg presentation. The Subcommittee recommended that the view of the Ad-hoc Rheumatology Subcommittee be sought to determine if this presentation is needed in the hospital setting.

2.7 The Subcommittee deferring making a recommendation on the inclusion of methotrexate injections until the review of oncology treatments. Members noted that methotrexate is now typically used as prefilled syringes, and that while these were currently obtained by hospitals from compounding manufacturers such as Baxter and Biomed, it would be preferable for prefilled syringes to be available on the Pharmaceutical Schedule as there was a significant cost involved in the compounding.

2.8 The Subcommittee noted that trientine and zinc are used for the treatment of Wilson's disease where penicillamine is not tolerated, with trientine being the preferred agent.

2.9 Members noted that non-rheumatology indications for TNF-α inhibitors and other biologic agents would be considered at subsequent meetings.

2.10 The Subcommittee noted that rituximab is used for rheumatoid arthritis (RA) in the majority of DHBs, generally as a second-line agent following failure of a TNF-α inhibitor, and considered that it should be included in a national PML for RA subject to nationally consistent access criteria. However, members noted that as rituximab is not used in all DHBs for RA and, as the access criteria varies significantly between those that do use it, inclusion of rituximab for RA in a national PML with nationally-consistent access criteria would likely have a significant financial impact on those DHBs that do not currently use it.

2.11 The Subcommittee considered that specialist input would be required when determining the access criteria for rituximab for RA, and recommended that the Ad-hoc Rheumatology Subcommittee be asked to provide recommendations on appropriate restrictions, giving particular consideration to the issues around ongoing safety monitoring (in particular hepatitis B) and clear stopping rules.

2.12 The Subcommittee noted that one of the key issues with regard to the cost of rituximab compared with other available biologic treatments is the frequency of re-treatment. In response to questions from PHARMAC staff, the Subcommittee considered that it was likely that some clinicians would re-treat patients according to the timing of their rheumatology clinics and would not necessarily wait until disease flare. Members noted that if a patient's disease flared between clinic visits they could be seen quickly and treated. Members suggested that information on re-treatment frequency may be able to be available from the British Society of Rheumatology Biologics Register. Members also suggested that DHB hospital pharmacies may be able to provide information on current re-treatment times in New Zealand.

2.13 Members noted that there did not appear to be any data supporting the use of other biologic treatments after rituximab failure, which might have a bearing on its placement in the treatment paradigm. Further, members noted that PTAC had only considered data for 2 doses of rituximab for RA, and recommended that the Ad-hoc Rheumatology Subcommittee review any data regarding the safety and efficacy of more than two doses.

2.14 The Subcommittee noted that tocilizumab was used for RA in a small number of DHBs, and that it was typically being used following failure of TNF-α inhibitors and rituximab despite, as noted above, the apparent lack of evidence to support the use of any biologic agents for RA where rituximab treatment has failed. The Subcommittee considered that further advice was required before a recommendation could be made on the inclusion of tocilizumab in a national PML. The Subcommittee suggested that a funding application be requested from the supplier and that those DHBs that currently provide it be invited to provide information on their own

assessments. The Subcommittee recommended that this be considered by PTAC and the Ad-hoc Rheumatology Subcommittee.

2.15 The Subcommittee recommended that the listing of adalimumab and etanercept 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.

2.16 The Subcommittee noted that the use of infliximab for rheumatology indications has declined significantly since adalimumab and etanercept became subsidised in the Pharmaceutical Schedule for these uses. Members were uncertain of the need for infliximab to be available for rheumatology indications in a national PML. The Subcommittee considered that further advice was required before making a recommendation on the inclusion of infliximab in a national PML for rheumatology indications, and requested that the advice of the Ad-hoc Rheumatology Subcommittee be sought.

2.17 The Subcommittee noted that abatacept, anakinra and golimumab were not currently formulary items in any DHB, and that they were not subsidised in the Pharmaceutical Schedule. The Subcommittee recommended that they not be included in a national PML. The Subcommittee noted that PHARMAC had not reviewed a funding application for anakinra and recommended that the Ad-hoc Rheumatology Subcommittee review the data for anakinra in rheumatology indications.

2.18 Members noted that chloroquine phosphate is also used in rheumatology, and recommended that PHARMAC staff seek the view of rheumatologists on the need for this in a national PML.

3 Enzymes

3.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to hyaluronidase.

3.2 The Subcommittee noted that most DHBs currently used hyaluronidase, although access criteria differed between DHBs.

3.3 The Subcommittee considered that further advice was needed before making a recommendation on the inclusion of hyaluronidase in a national PML, and recommended that PHARMAC seek the opinion of ophthalmologists, anaesthetists and oncologists.

3.4 Members noted that there could be a financial risk associated with the use of hyaluronidase in subcutaneous rehydration.

4 Hyperuricaemia and Antigout

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

- Allopurinol

- Tab 100 mg
- Tab 300 mg

- Colchicine
  - Tab 500 µg
- Probenecid
  - Tab 500 mg
- Rasburicase
  - Inf 1.5 mg

4.3 The Subcommittee noted that benzbromarone is used in some DHBs, but that it was generally only for small numbers of patients through Hospital Exceptional Circumstances. Members noted that it was not subsidised in the Pharmaceutical Schedule, and considered that it did not have a niche use within hospitals. The Subcommittee recommended that benzbromarone only be included in a national PML if it was to be listed in the Pharmaceutical Schedule, in which case it should be subject to restrictions in line with any restrictions in the Pharmaceutical Schedule.

4.4 The Subcommittee recommended that use of rasburicase be limited to haematology, noting that up to 4% of patients have serious reactions to rasburicase injections.

5 Muscle Relaxants

5.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Muscle Relaxants 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:

- Baclofen
  - Inj 0.05 mg per ml, 1 ml
  - Inj 2 mg per ml, 5 ml
  - Tab 10 mg
- Dantrolene
  - Cap 25 mg
  - Cap 50 mg
  - Inj 1 mg per ml, 20 ml
- Orphenadrine citrate
  - Tab 100 mg
- Quinine sulphate
  - Tab 300 mg

5.3 The Subcommittee suggested that the Analgesic Subcommittee be consulted on the need for orphenadrine citrate injection (30 mg per ml, 2 ml) to be included in a national PML.

5.4 The Subcommittee noted that while baclofen oral liquid (5 mg per 5 ml) was not widely used, it was an important to have an oral liquid option for this product and so should be include in a national PML.

5.5 Members noted that quinine sulphate 200 mg tablets were being discontinued, and considered that this was not an essential presentation. Members noted that this

presentation was typically used for leg cramps, which was no longer a registered indication for quinine.

6 Non-Steroidal Anti-Inflammatory Drugs

6.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Non-Steroidal Anti-Inflammatory Drugs 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:

- Diclofenac sodium
  - Tab EC 25 mg
  - Tab EC 50 mg
  - Tab 50 mg dispersible
  - Tab long-acting 75 mg
  - Tab long-acting 100 mg
  - Suppos 12.5 mg
  - Suppos 25 mg
  - Suppos 50 mg
  - Suppos 100 mg
  - Inj 25 mg per ml, 3 ml
- Ibuprofen
  - Inj 5 mg per ml, 2 ml
  - Oral liq 100 mg per 5 ml
  - Tab 200 mg
  - Tab long-acting 800 mg
- Indomethacin
  - Cap 25 mg
  - Cap 50 mg
  - Cap long-acting 75 mg
  - Inj 1 mg
  - Suppos 100 mg
- Meloxicam
  - Tab 7.5 mg
- Naproxen
  - Tab 250 mg
  - Tab 500 mg
  - Tab long-acting 750 mg
  - Tab long-acting 1 g
- Parecoxib
  - Inj 40 mg
- Tenoxicam
  - Inj 10 mg per ml, 2 ml
  - Tab 20 mg

6.3 The Subcommittee noted that celecoxib and etoricoxib are used in some DHBs, and that this usage is relatively low. The Subcommittee considered that as they were not funded in the Pharmaceutical Schedule, and as they do not have a unique use within hospitals, they should not be included in a national PML. Members noted that there is

some use of etoricoxib in surgery, and recommended consulting with anaesthetists on its exclusion.

6.4 The Subcommittee noted that diclofenac potassium tablets (12.5 mg and 25 mg) are used in some DHBs. The Subcommittee considered that, as they were not subsidised in the Pharmaceutical Schedule, as they did not have a unique use within hospitals, and as alternative diclofenac presentations are available, they should not be included in a national PML.

6.5 Members noted that diclofenac sodium dispersible 50 mg tablets are not fully subsidised in the Pharmaceutical Schedule, but considered that as they have a particular use in paediatrics and in patients fed through nasogastric tube or PEG feeding tube, they should be included in a national PML.

6.6 The Subcommittee noted that ibuprofen injection (5 mg per ml, 2 ml) was not a registered medicine in New Zealand, and that it was often used in hospitals for patent ductus arteriosus (PDA) when indomethacin injection was not available. Members considered that it was important to have an alternative option for this indication, and noted that this formulation of ibuprofen was registered overseas for PDA.

6.7 The Subcommittee noted that ibuprofen lysine injection (400 mg per ml, 3 ml) was used in one DHB only. The Subcommittee recommended that it not be included in a national PML.

6.8 Members noted that most presentations of indomethacin had been discontinued in New Zealand, with the suppositories due to be discontinued in the near future. Members considered that indomethacin was an important treatment option, including for some rare neurological conditions, and considered that it should be included in a national PML.

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

6.10 Members noted that naproxen sodium and piroxicam had recently been discontinued in New Zealand, and recommended that they not be included in a national PML.

6.11 The Subcommittee considered that, as the following pharmaceuticals were not fully 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:

- Ibuprofen
  - Tab 400 mg
  - Tab 600 mg
- Mefenamic acid
  - Cap 250 mg
- Sulindac
  - Tab 100 mg
  - Tab 200 mg

6.12 The Subcommittee noted that PHARMAC was currently consulting on fully funding ketoprofen (cap long-acting 100 mg and cap long-acting 200 mg) and tiaprofenic acid (tab 300 mg) in the Pharmaceutical Schedule, and recommended that they be included in a national PML if they do become fully funded. Members recommended

that if these do not become fully funded, then they should be available for continuation of care only, not for initiation of therapy.

6.13 Members noted that the use of tenoxicam injection had been replaced by parecoxib when the previous brand of tenoxicam was discontinued in 2008, and that although a new brand of tenoxicam was now available, anaesthetists were unlikely to be willing to shift back.

7 Rubefactants and Other Topical Antirheumatics

7.1 The Subcommittee reviewed the information from DHB hospitals and PHARMAC in relation to products under the Rubefactants and Other Topical Antirheumatics heading.

7.2 The Subcommittee noted that arnica cream was not used widely in DHB hospitals, and that it is not subsidised in the Pharmaceutical Schedule. Members considered that there was limited evidence of benefit from arnica, and that it should not be included in a national PML.

7.3 The Subcommittee noted that capsaicin 0.025% cream was in use in a majority of DHBs, but that it was not subsidised in the Pharmaceutical Schedule. Members noted that PTAC had previously considered this formulation, and had recommended against its funding. The Subcommittee recommended that it not be included in a national PML.

7.4 Members noted that the funded formulation of capsaicin cream (0.075%), which is indicated for post-herpetic neuralgia, would be considered at a later time alongside analgesic agents.

7.5 Members noted that diclofenac gel 1% was used in a majority of DHBs, but that it was not subsidised on the Pharmaceutical Schedule. The Subcommittee considered that further advice was needed before a recommendation could be made, and requested that Ad-hoc Rheumatology Subcommittee review the evidence for the use of topical NSAIDs.

7.6 The Subcommittee noted that methyl salicylate with menthol creams were in use in around half of all DHBs. Members considered that there was limited evidence of benefit for these products, and that they not be included in a national PML.

Rheumatology Subcommittee – 14 October 2011

8 Access criteria for rituximab for rheumatoid arthritis in DHB hospitals

8.1 The Subcommittee noted that the Hospital Pharmaceuticals Subcommittee of PTAC had recommended that rituximab be included in a national preferred medicines list (PML) for use in DHB hospitals for the treatment of rheumatoid arthritis (RA) and that the Ad-hoc Rheumatology Subcommittee should be asked to provide recommendations on appropriate access criteria in this setting.

Initial treatment with rituximab

8.2 The Subcommittee considered that given the resource implications for DHB hospitals and the availability of community funded tumour necrosis factor (TNF) inhibitors for RA (i.e. adalimumab and etanercept), it would be reasonable to restrict the use of rituximab to patients who had received inadequate benefit or significant adverse effects from a TNF inhibitor or in whom TNF inhibitors are contraindicated. The Subcommittee considered that this was also supported by the available evidence which suggests that American College of Rheumatology (ACR) 20 response rates are higher in patients treated with a TNF inhibitor as their first-line biologic treatment than in those treated with rituximab as the first-line biologic.

8.3 The Subcommittee considered that, on the basis of the available evidence (e.g. Rendas-Baum et al, Arthritis Res Ther 2011;13(1):R25), patients who receive inadequate benefit from their first TNF inhibitor would receive similar benefit from either a second TNF inhibitor or rituximab, and that from a clinical perspective the choice of agent would be based on other factors such as safety and patient preference.

8.4 The Subcommittee noted that rituximab was only indicated for the treatment of RA in combination with methotrexate; however, members considered that any access criteria should permit rituximab to be used in combination with leflunomide instead of methotrexate, based on results from Chatzidionysiou et al (Ann Rheum Dis 2011;Oct 4) and Narvaez et al (Semin Arthritis Rheum 2011;Aug 20).

8.5 Assuming that the pricing of rituximab and the TNF inhibitors was similar, and that there were no significant resource/capacity implications for DHB hospitals in relation to rituximab administration, the Subcommittee recommended the following access criteria be applied to rituximab for RA on a PML:

Initial application - (rheumatoid arthritis – patients with prior Special Authority approvals for adalimumab and/or etanercept) only from a rheumatologist or medical practitioner on the recommendation of a rheumatologist. Approvals valid for 3 months for applications meeting the following criteria:
All of the following:

1 Both:
- 1.1 The patient has had an initial community Special Authority approval for at least one of etanercept and/or adalimumab for rheumatoid arthritis; and
- 1.2 Either:
  - 1.2.1 The patient has experienced intolerable side effects from a reasonable trial of adalimumab and/or etanercept; or
  - 1.2.2 Following at least a four month trial of adalimumab and/or etanercept, the patient did not meet the renewal criteria for adalimumab and/or etanercept for rheumatoid arthritis; and

2 Rituximab to be used as an adjunct to methotrexate or leflunomide therapy; and

3 Approval covers a maximum of two 1,000 mg infusions of rituximab given two weeks apart.

Initial application - (rheumatoid arthritis – patients in whom Tumour Necrosis Factor alpha inhibitors are contraindicated) only from a rheumatologist or medical practitioner on the recommendation of a rheumatologist. Approvals valid for 3 months for applications meeting the following criteria:
All of the following:

1 Treatment with a Tumour Necrosis Factor alpha inhibitor is contraindicated; and
2 Patient has had severe and active erosive rheumatoid arthritis for six months duration or longer; and
3 Patient has tried and not responded to at least three months of oral or parenteral methotrexate at a dose of at least 20 mg weekly or a maximum tolerated dose; and
4 Patient has tried and not responded to at least three months of oral or parenteral methotrexate in combination with sulphasalazine and hydroxychloroquine sulphate (at maximum tolerated doses); and
5 Any of the following:
    5.1 Patient has tried and not responded to at least three months of oral or parenteral methotrexate in combination with the maximum tolerated dose of ciclosporin; or
    5.2 Patient has tried and not responded to at least three months of oral or parenteral methotrexate in combination with intramuscular gold; or
    5.3 Patient has tried and not responded to at least three months of therapy at the maximum tolerated dose of leflunomide alone or in combination with oral or parenteral methotrexate; and
6 Either:
    6.1 Patient has persistent symptoms of poorly controlled and active disease in at least 20 swollen, tender joints; or
    6.2 Patient has persistent symptoms of poorly controlled and active disease in at least four joints from the following: wrist, elbow, knee, ankle, and either shoulder or hip; and
7 Either:
    7.1 Patient has a C-reactive protein level greater than 15 mg/L measured no more than one month prior to the date of this application; or
    7.2 C-reactive protein levels not measured as patient is currently receiving prednisone therapy at a dose of greater than 5 mg per day and has done so for more than three months; and
8 Rituximab to be used as an adjunct to methotrexate or leflunomide therapy; and
9 Approval covers a maximum of two 1,000 mg infusions of rituximab given two weeks apart.

8.6 The Subcommittee considered that the available data suggests that it is safe to commence other biologic agents following rituximab (Buch et al, Ann Rheum Dis 2011;70:909-920), so use of rituximab as a second-line biologic would not necessarily preclude a trial of a second TNF inhibitor if patients do not respond adequately to rituximab.

8.7 The Subcommittee considered that the available evidence suggests that rituximab is more efficacious in rheumatoid factor-positive (seropositive) patients than it is in seronegative patients (Buch et al, Ann Rheum Dis 2011;70:909-920), so members considered it may be preferable to use a second TNF inhibitor rather than rituximab as a second-line biologic agent in seronegative patients.

Rituximab re-treatment

8.8 The Subcommittee considered that following the first course of rituximab there would be three groups of patients to consider for rituximab re-treatment: 'responders,' 'partial-responders' and 'non-responders.'

8.9 The Subcommittee considered that it would be reasonable to define a rituximab 'responder' according to the same criteria as those required to access further treatment with community-funded TNF inhibitor treatments (i.e. a 50% decrease in active joint count from baseline following the first course of rituximab and at least a continuing 30% improvement in active joint count from baseline following the second and subsequent courses of rituximab).

8.10 The Subcommittee considered that a rituximab 'partial responder' should be defined as between a 30% and 50% decrease in active joint count from baseline.

8.11 The Subcommittee considered that, for rituximab responders, it would not be clinically appropriate to wait until a patient's disease has flared, or otherwise deteriorated significantly, before re-treating with rituximab; on the other hand, a fixed-interval dosing regimen could result in patients being treated unnecessarily frequently. The Subcommittee considered that the decision as to when to re-treat an initial responder should be left up to the treating clinician. However, the Subcommittee considered that it would be reasonable to require at least a 6 month gap between courses of treatment, and considered that, in practice, rituximab re-treatment in responding patients would likely occur on average every 11–13 months.

8.12 The Subcommittee considered that the evidence for re-treatment in 'non-responders' to initial treatment with rituximab was conflicting (e.g. Bastian et al, J Rheumatol 2010;37:1069-71; Thurlings et al, Arthritis Rheum 2008;58:3657-3664; Vital et al, Arthritis Rheum 2010:62:1273-1279). Members were not aware of any trials comparing a second course of rituximab with an alternative treatment in rituximab first-course non-responders.

8.13 The Subcommittee considered that it would be reasonable to allow a second course of rituximab to be given at 6 months following the first course in initial 'partial responders.' The Subcommittee considered that first-course 'partial responders' who did not meet the re-treatment criteria for first-course 'responders' at 4 months following their second course should not be eligible to receive any further funded rituximab treatment.

8.14 Taking all these factors into consideration, the Subcommittee recommended the following re-treatment criteria for rituximab in RA:

Renewal - (rheumatoid arthritis re-treatment in 'responders' to initial rituximab treatment) only from a rheumatologist or medical practitioner on the recommendation of a rheumatologist. Approvals valid for 6 months for applications meeting the following criteria:
All of the following:

1 Either:
  1.1 At 4 months following the initial course of rituximab infusions the patient had at least a 50% decrease in active joint count from baseline and a clinically significant response to treatment in the opinion of the physician; or
  1.2 At 4 months following the second and subsequent courses of rituximab infusions, the patient demonstrates at least a continuing 30% improvement in active joint count from baseline and a clinically significant response to treatment in the opinion of the physician; and
2 Rituximab re-treatment not to be given within 6 months of the previous course of

treatment; and
3 Rituximab is to be used as an adjunct to methotrexate or leflunomide therapy; and
4 Approval covers a maximum of two 1,000 mg infusions of rituximab given two weeks apart.

Renewal - (rheumatoid arthritis re-treatment in 'partial responders' to initial rituximab treatment) only from a rheumatologist or medical practitioner on the recommendation of a rheumatologist. Approvals valid for 6 months for applications meeting the following criteria: All of the following:
1 Either:
1.1 At 4 months following the initial course of rituximab infusions the patient had between a 30% and 50% decrease in active joint count from baseline and a clinically significant response to treatment in the opinion of the physician; or
1.2 At 4 months following the second course of rituximab infusions the patient had at least a 50% decrease in active joint count from baseline and a clinically significant response to treatment in the opinion of the physician; or
1.3 At 4 months following the third and subsequent courses of rituximab infusions, the patient demonstrates at least a continuing 30% improvement in active joint count from baseline and a clinically significant response to treatment in the opinion of the physician; and
2 Rituximab re-treatment not to be given within 6 months of the previous course of treatment; and
3 Rituximab is to be used as an adjunct to methotrexate or leflunomide therapy; and
4 Approval covers a maximum of two 1,000 mg infusions of rituximab given two weeks apart.

8.15 The Subcommittee considered that it was difficult to estimate the number of patients who would be treated with rituximab if it was included on a PML for RA subject to the recommended criteria; however, based on current usage in the Wellington region (approximately 32 patients from a total pool of 500,000 people) the total number of patients accessing funded treatment nationally could be in the region of 300 patients per year.

9 Review of topical products for joint and muscular pain

Rubefacients

9.1 The Subcommittee agreed with the view of PHARMAC staff that evidence in support of the use of topical rubefacients in the relief of acute and chronic musculoskeletal pain appears to be lacking. The Subcommittee considered that there was no compelling reason for PHARMAC staff to further investigate this class of agents at this time.

Topical NSAIDs

9.2 The Subcommittee noted that many guidelines (e.g. the European League Against Rheumatism [EULAR], Osteoarthritis Research International [OARSI] and BPACNZ) recommended the use of topical NSAIDs as an option in the management of symptoms in patients with knee or hand osteoarthritis. However, the Subcommittee considered that the evidence for efficacy of topical NSAIDs in hand or knee osteoarthritis is poor, including the evidence cited in the guidelines.

9.3 The Subcommittee noted that a meta-analysis of controlled trials of topical NSAIDs in the treatment of osteoarthritis showed that topical NSAIDs were superior to placebo only in the first two weeks of treatment, after which there was no evidence of any efficacy benefit over placebo (Lin J et al, BMJ 2004;329(7461):324). Members noted that the meta-analysis also found that topical NSAIDs were inferior to oral NSAIDs in

the first week of treatment and were associated with more local side effects such as rashes, itching or burning.

9.4 The Subcommittee considered that there may be some short-term benefit of topical NSAIDs in patients with osteoarthritis who could not tolerate oral treatment options (including paracetamol, non-topical NSAID preparations and intra-articular corticosteroids). The Subcommittee considered that these would primarily be elderly patients or those with renal impairment. However, the Subcommittee considered that this was not a high unmet clinical need and there was uncertainty, given the evidence, as to whether topical NSAIDs would adequately meet this need anyway.

9.5 The Subcommittee considered that there would be a significant financial risk associated with funding topical NSAIDs without restrictions as it was likely that they would be used extensively for numerous common conditions for which alternative funded treatments are available, for example in people with sports injuries. In addition, the Subcommittee considered that if topical NSAIDs were funded without restriction, they would be used primarily as add-on/supplementary treatment and would not replace the use of any other funded treatment to any significant degree.

9.6 The Subcommittee considered that, taking into account the financial considerations, the lack of good evidence for topical NSAIDs in osteoarthritis did not warrant further investigation of funding this class of agents by PHARMAC staff at this time.

Capsaicin 0.025% cream

9.7 The Subcommittee noted that in November 2002 PTAC considered an application to fund capsaicin 0.025% cream (Zostrix) for the symptomatic relief of pain associated with osteoarthritis and that, following a recommendation from PTAC to decline the application, it was declined by PHARMAC in March 2005. The Subcommittee noted that capsaicin 0.075% cream is currently funded only for post-herpetic neuralgia or diabetic peripheral neuropathy.

9.8 The Subcommittee noted that, like topical NSAIDs, capsaicin was frequently recommended in international guidelines as a treatment option for symptom management in patients with osteoarthritis.

9.9 The Subcommittee considered that evidence from 5 randomised controlled trials, one of which used a higher strength preparation (0.075%), suggested that capsaicin cream was more efficacious than placebo in reducing tenderness and pain in osteoarthritis (Deal et al, Clin Ther 1991;13:383-95; McCarthy and McCarty, J Rheumatol 1992;19:604-7; Altman et al, Semin Arthritis Rheum 1994;23(6 Suppl 3):25-33; Gemmell et al, J Manipulative Physiol Ther 2003;26:315-23; McCleane G. Eur J Pain 2000;4:355-60). Of note, in a 12-week study patients with osteoarthritis treated four times daily with capsaicin cream 0.025% reported a 53% reduction in pain compared with 27% of placebo-treated patients at week 12 (Altman et al, 1994); in another study patients with rheumatoid arthritis and osteoarthritis treated with capsaicin cream 0.025% or placebo four times daily demonstrated mean reductions in pain of 57% and 33%, respectively, at four weeks (Deal et al, 1991). The Subcommittee considered that the quality of the evidence was moderate, noting that it is difficult to conduct a placebo controlled trial with an agent such as topical capsaicin. The Subcommittee noted that PTAC appeared to have reviewed only two of these studies in 2002 (Altman et al, 1994 and Deal et al, 1991).

9.10 The Subcommittee noted that the mechanism of action of capsaicin (primarily related to depletion of substance P at the application site) is different from other funded

agents so there is a possibility that topical capsaicin could have an additive effect on the efficacy of other currently funded options such as NSAIDs and paracetamol. However, the Subcommittee noted that there appeared to be no evidence to support this, nor were members aware of any studies comparing topical capsaicin with other treatment options such as NSAIDs and paracetamol.

9.11 The Subcommittee considered that if it was funded, capsaicin 0.025% cream would be used mainly as an add-on/supplementary treatment and would not replace the use of any currently funded treatment to any significant degree.

9.12 The Subcommittee considered that the patient population that would benefit the most from capsaicin 0.025% cream would be patients with osteoarthritis who could not tolerate oral treatment options (including paracetamol, non-topical NSAID preparations and intra-articular corticosteroids) although, as noted previously, the Subcommittee considered that this was not a high unmet clinical need.

9.13 The Subcommittee considered that any restrictions placed on the use of capsaicin 0.025% cream would be for financial rather than clinical reasons, noting that if it was funded without restrictions it would likely be used in a wide range of indications, potentially including neuropathic pain and sports injuries.

9.14 The Subcommittee considered that the need to apply capsaicin 0.025% cream four times daily may limit compliance. Members also noted that capsaicin causes irritation to mucous membranes (e.g. in eyes and mouth) which could cause problems if patients were not careful about washing their hands after applying the cream.

9.15 Overall, the Subcommittee considered that the level of evidence in support of funding capsaicin 0.025% cream warranted further investigation and recommended that PHARMAC staff take the application back to PTAC for an updated review.

10 Other pharmaceuticals

10.1 The Subcommittee reviewed a series of recommendations by the Hospital Pharmaceuticals Subcommittee in regards to which pharmaceuticals relevant to rheumatology should be included on a national PML. The Subcommittee also reviewed the responses and comments on the draft recommendations that PHARMAC had received from relevant colleges and professional societies.

Antirheumatoid agents

10.2 The Subcommittee considered that there was no need for leflunomide 100 mg tablets to be funded in hospitals.

10.3 The Subcommittee considered that there was no major unmet need for hyaluronic acid (sodium hyaluronate) injection in the area of rheumatology, noting that this was a relatively expensive product that produces only moderate benefit for about 6 months. The Subcommittee considered that there would be a financial risk from making it available for osteoarthritis. The Subcommittee suggested that further advice on this agent be sought from orthopaedic surgeons.

10.4 The Subcommittee considered that there was no need for chloroquine phosphate 250 mg tablets to be funded in hospitals for rheumatology-related uses, noting that hydroxychloroquine was preferred in this setting. The Subcommittee suggested that further advice on chloroquine phosphate be sought from dermatologists around its

potential use in treating SLE-related dermatological problems, and from infectious disease physicians.

10.5 The Subcommittee considered that sodium aurothiomalate (inj 10 mg, 20 mg and 50 mg per 0.5 ml) should be included on a national PML, noting that these presentations are fully funded in Section B of the Pharmaceutical Schedule and that intramuscular gold is one of the prior treatment options in the Special Authority criteria for adalimumab and etanercept for rheumatoid arthritis.

Hyperuricaemia and antigout

10.6 The Subcommittee noted that the Hospital Pharmaceuticals Subcommittee had recommended including rasburicase 1.5 mg infusion on a national PML, limited to use in haematology. The Subcommittee considered that there was a role for rasburicase in tophaceous gout; however, there could be a significant financial impact from its use in this indication as it could be used for up to 2 years, unlike haematology uses which would likely be short-term, e.g. in the management of tumor lysis syndrome. The Subcommittee considered that nephrologists may also need access to rasburicase as they may be involved in the management of tumor lysis syndrome.

Muscle relaxants

10.7 The Subcommittee had no comments in relation to the recommendations of the Hospital Pharmaceuticals Subcommittee for this subheading.

Non-steroidal anti-inflammatory drugs

10.8 In relation to celecoxib and etoricoxib, the Subcommittee considered that there could be problems relating to continuance treatment for patients entering hospital on these agents if they were not included on a national PML.

Topical products for joint and muscular pain

10.9 The Subcommittee had no comments in relation to the recommendations of the Hospital Pharmaceuticals Subcommittee for this subheading.

Hospital Pharmaceuticals Subcommittee – 6 March 2012

11 Review of Musculoskeletal System Recommendations

11.1 The Subcommittee reviewed its previous recommendations in relation to products in the Musculoskeletal System group, feedback from other organisations such as the Rheumatology Association and the Paediatric Society, and recommendations from the Rheumatology Subcommittee.

Anticholinesterases

11.2 Members noted that feedback had not yet been received from neurologists in relation to a 180 mg modified-release form of pyridostigmine, and noted that the Neurological Subcommittee would be asked for comment on this.

Antirheumatoid Agents

11.3 The Subcommittee noted that the Rheumatology Subcommittee considered that the 100 mg tablet form of leflunomide could be excluded from a national PML. The Subcommittee considered that this should remain available in hospitals while it is funded in the community.

11.4 The Subcommittee noted the access criteria for rituximab for use in rheumatoid arthritis that were recommended by the Rheumatology Subcommittee. Members noted that the access criteria as proposed would likely result in a widening of access to this treatment in all DHBs.

11.5 The Subcommittee noted that the proposed criteria for rituximab would result in rituximab becoming a second-line biologic agent for rheumatoid arthritis, after one TNF inhibitor.

11.6 Members noted that the proposed criteria for rituximab did not include reference to disease activity scores (DAS), which are a feature of the current criteria at Hutt Valley DHB. The Subcommittee noted that the continuation criteria included the phrase “a clinically significant response to treatment in the opinion of the physician” which members considered could be open to wide interpretation. However, members noted that the same wording is currently used in the community funding criteria for adalimumab and etanercept.

11.7 The Subcommittee noted that some feedback had been received in relation to hyaluronic acid in rheumatology, but that no responses were received from other specialities. The Subcommittee continued to defer a recommendation in relation to this product.

11.8 The Subcommittee noted the information from the Rheumatology Subcommittee in relation to the use of infliximab within rheumatology, and noted that the Rheumatology Association would be asked to provide a submission to PTAC in relation to a number of off-label uses.

11.9 The Subcommittee noted that a funding application for tocilizumab was provided to the Rheumatology Subcommittee, and that this application had also been considered by PTAC.

11.10 The Subcommittee noted responses in relation to anakinra, and recommended that this not be included in a national PML.

11.11 The Subcommittee noted the feedback from rheumatologists that chloroquine is not widely used in rheumatology, but noted that there may be some use in dermatology for SLE-related issues. The Subcommittee recommended that an opinion on this be sought from dermatologists.

11.12 The Subcommittee noted and agreed with the recommendation of the Rheumatology Subcommittee that sodium aurothiomalate be included in a national PML.

Enzymes

11.13 The Subcommittee noted that feedback had not yet been received in relation to hyaluronidase. Members noted that hyaluronidase is used for extravasation, and recommended that it be included in a national PML.

Hypercuriacemia and Antigout

11.14 The Subcommittee noted the comments from the Rheumatology Subcommittee in relation to access criteria for rasburicase. The Subcommittee reaffirmed its previous recommendation that prescribing of rasburicase be subject to recommendation by haematologists.

Muscle Relaxants

11.15 The Subcommittee noted that the Analgesic Subcommittee will be considering orphenadrine at its next meeting.

Rubefacients and Other Topical Antirheumatics

11.16 The Subcommittee noted the review of topical NSAIDs by the Rheumatology Subcommittee, and recommended that these not be included in a national PML.

11.17 The Subcommittee noted that the Rheumatology Subcommittee considered that PTAC should re-review capsaicin 0.025% cream, and noted that this would be going to the next PTAC meeting.

Pharmacology and Therapeutics Advisory Committee – 10 & 11 May 2012

12 Hospital Pharmaceuticals Review

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

12.2 The Committee noted that the Hospital Pharmaceuticals Subcommittee had recommended that edrophonium chloride injection be limited to prescribing by, or under the recommendation of, neurologists for the diagnosis of myasthenia gravis. Members requested that the advice of the Neurology Subcommittee be sought on this matter as it could be used by general physicians in small hospitals without easy access to neurology.

12.3 The Committee noted and accepted the proposed PML access criteria for rituximab from the Rheumatology Subcommittee.

12.4 The Committee noted that it had considered an application in relation to tocilizumab, and reaffirmed its previous recommendation in relation to this product. Members noted that this would be considered by PHARMAC under its usual processes for new investments.

12.5 The Committee noted that the Hospital Pharmaceuticals Subcommittee had recommended that rasburicase be limited to prescribing by, or under the recommendation of, haematologists. Members considered that rasburicase was a high cost pharmaceutical and several specialities may wish to use rasburicase; members also considered that for safety reasons there should be tight guidelines around the use of rasburicase and requested that the advice of the Haematology Subcommittee be sought on these matters.

12.6 The Committee noted that indomethacin capsules and suppositories had been discontinued and were currently unavailable.

12.7 The Committee noted that the Hospital Pharmaceuticals Subcommittee had deferred making a recommendation in relation to orphenadrine, and that the Analgesic Subcommittee had considered that it was not necessary to have this product available.