CONSULTATION

PHARMAC
Pharmaceutical Management Agency

13 September 2013

Proposal to widen hospital funding restrictions for rituximab

PHARMAC is seeking feedback on a proposal to amend the funding restrictions for rituximab in hospitals to include the following indications:

- Cold haemagglutinin disease;
- Warm autoimmune haemolytic anaemia;
- Immune thrombocytopenic purpura;
- Thrombotic thrombocytopenic purpura;
- Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis;
- Systemic lupus erythematosus;
- Antibody-mediated renal transplant rejection; and
- ABO-incompatible renal transplant.

We do not have a proposed implementation date because it would be dependent on the consultation responses received. We may have to seek further clinical advice following consultation. We will notify all relevant parties when a decision is made on any aspect of this proposal.

Details of the proposals are provided on the following pages.

Feedback sought

PHARMAC welcomes feedback on this proposal. To provide feedback, please submit it in writing by **Monday, 30 September 2013** to:

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All feedback received before the closing date will be considered by PHARMAC's Board (or its delegate) prior to making a decision on this proposal.

Feedback we receive is subject to the Official Information Act 1982 (OIA) and we will consider any request to have information withheld in accordance with our obligations under the OIA. Anyone providing feedback, whether on their own account or on behalf of an organisation, and whether in a personal or professional capacity, should be aware that the content of their feedback and their identity may need to be disclosed in response to an OIA request.

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We are not able to treat any part of your feedback as confidential unless you specifically request that we do, and then only to the extent permissible under the OIA and other relevant laws and requirements. If you would like us to withhold any commercially sensitive, confidential proprietary, or personal information included in your submission, please clearly state this in your submission and identify the relevant sections of your submission that you would like it withheld. PHARMAC will give due consideration to any such request

Details of the proposal

- The restrictions applying to rituximab in Part II of Section H of the Pharmaceutical Schedule would be widened to include a number of new indications as follows:

  Cold haemagglutinin disease (CHAD)

  Initiation – severe cold haemagglutinin disease - haematologist
  Limited to 4 weeks' treatment

  Both:

  1. Patient has cold haemagglutinin disease; and
  2. Patient has severe disease which is characterized by symptomatic anaemia, transfusion dependence or disabling circulatory symptoms.

  Continuation – severe cold haemagglutinin disease - haematologist
  Limited to 4 weeks' treatment

  Either:

  1. Previous treatment with lower doses of rituximab (100 mg weekly for 4 weeks) have proven ineffective and treatment with higher doses (375 mg/m^2 weekly for 4 weeks) is now planned; or
  2. All of the following:
     2.1 Patient was previously treated with rituximab for severe cold haemagglutinin disease; and
     2.2 An initial response lasting at least 12 months was demonstrated; and
     2.3 Patient now requires repeat treatment.

  Warm autoimmune haemolytic anaemia (warm AIHA)

  Initiation – warm autoimmune haemolytic anaemia - haematologist
  Limited to 4 weeks' treatment

  Both:

  1. Patient has warm autoimmune haemolytic anaemia; and
  2. One of the following treatments has been ineffective: steroids (including if patient requires ongoing steroids at doses equivalent to >5 mg daily), cytotoxic agents (e.g. cyclophosphamide monotherapy or in combination), intravenous immunoglobulin.

  Continuation – warm autoimmune haemolytic anaemia - haematologist

  Limited to 4 weeks' treatment

  Either:

1. Previous treatment with lower doses of rituximab (100 mg weekly for 4 weeks) have proven ineffective and treatment with higher doses (375 mg/m^2 weekly for 4 weeks) is now planned; or
2. All of the following:
   2.1 Patient was previously treated with rituximab for warm autoimmune haemolytic anaemia; and
   2.2 An initial response lasting at least 12 months was demonstrated; and
   2.3 Patient now requires repeat treatment.

Immune thrombocytopenic purpura (ITP)

Initiation – immune thrombocytopenic purpura - haematologist
Limited to 4 weeks' treatment

Both:

1. Patient has immune thrombocytopenic purpura with a platelet count of < 20x10^9/L; and
2. Any of the following:
   2.1. Treatment with steroids and splenectomy have been ineffective; or
   2.2. Treatment with steroids has been ineffective and splenectomy is an absolute contraindication; or
   2.3. Other treatments including steroids have been ineffective and patient is being prepared for elective surgery (e.g. splenectomy).

Continuation – immune thrombocytopenic purpura - haematologist
Limited to 4 weeks' treatment

Either:

1. Previous treatment with lower doses of rituximab (100 mg weekly for 4 weeks) have proven ineffective and treatment with higher doses (375 mg/m^2 weekly for 4 weeks) is now planned; or
2. All of the following:
   2.1 Patient was previously treated with rituximab for immune thrombocytopenic purpura; and
   2.2 An initial response lasting at least 12 months was demonstrated; and
   2.3 Patient now requires repeat treatment.

Thrombotic thrombocytopenic purpura (TTP)

Initiation – thrombotic thrombocytopenic purpura - haematologist

Both:

1. Patient has thrombotic thrombocytopenic purpura; and
2. Clinical response to plasma exchange was suboptimal or plasma exchange is contraindicated.

Continuation – thrombotic thrombocytopenic purpura - haematologist

All of the following:

1. Patient was previously treated with rituximab for thrombotic thrombocytopenic purpura; and
2. An initial response lasting at least 12 months was demonstrated; and
3. Patient now requires repeat treatment.

ANCA associated vasculitis

Initiation - ANCA associated vasculitis – rheumatologist or nephrologist
Limited to 4 weeks' treatment

All of the following:

1. Patient has been diagnosed with ANCA associated vasculitis; and
2. Either:
    2.1. Patient does not have MPO-ANCA positive vasculitis; or
    2.2. Mycophenolate mofetil has not been effective in those patients who have MPO-ANCA positive vasculitis; and
3. The rituximab dose would not exceed 375 mg/m^2 of body-surface area per week for a total of 4 weeks; and
4. Any of the following:
    4.1. Induction therapy with daily oral or pulse intravenous cyclophosphamide has failed to achieve complete absence of disease after 3 months; or
    4.2. Patient has previously had a cumulative dose of cyclophosphamide >15g or a further repeat 3 month induction course of cyclophosphamide would result in a cumulative dose >15g; or
    4.3. Cyclophosphamide and methotrexate are contraindicated; or
    4.4. Patient is a woman of childbearing age; or
    4.5. Patient has a previous history of haemorrhagic cystitis, urological malignancy or haematological malignancy.

Continuation - ANCA associated vasculitis - rheumatologist or nephrologist
Limited to 4 weeks' treatment

All of the following:

1. Patient has been diagnosed with ANCA associated vasculitis; and
2. Patient has previously responded to treatment with rituximab but is now experiencing an acute flare of vasculitis; and
3. The rituximab dose would not exceed 375 mg/m^2 of body-surface area per week for a total of 4 weeks.

Systemic lupus erythematosus (SLE)

Initiation – treatment refractory systemic lupus erythematosus (SLE) – rheumatologist or nephrologist

All of the following:

1. The patient has severe, immediately life- or organ-threatening SLE; and
2. The disease has proved refractory to treatment with steroids at a dose of at least 1 mg/kg; and
3. The disease has relapsed following prior treatment for at least 6 months with maximal tolerated doses of azathioprine, mycophenolate and high dose cyclophosphamide, or cyclophosphamide is contraindicated; and
4. Maximum of four 1000 mg infusions of rituximab.

Continuation – treatment refractory systemic lupus erythematosus (SLE) – rheumatologist or nephrologist

All of the following:

1. Patient's SLE achieved at least a partial response to the previous round of prior rituximab treatment; and
2. The disease has subsequently relapsed; and
3. Maximum of two 1000 mg infusions of rituximab.

Antibody-mediated renal transplant rejection

Antibody-mediated renal transplant rejection – nephrologist

Patient has been diagnosed with antibody-mediated renal transplant rejection.

ABO-incompatible renal transplant

ABO-incompatible renal transplant – nephrologist

Patient is to undergo an ABO-incompatible renal transplant.

We would make a decision on this proposal as soon as practicable, but until a decision is made, clinicians will need to continue to submit NPPA (Named Patient Pharmaceutical Assessment) applications for rituximab in these indications which would be assessed on a case by case basis.

Background

Rituximab is currently included in the Part II of Section H of the Pharmaceutical Schedule (the Hospital Medicines List - HML) for use in rheumatoid arthritis and haemophilia, as well as for use as a Pharmaceutical Cancer Treatment. The use of rituximab for treatment of the proposed indications was recommended during the process to establish the HML; however, we were not previously in a position to make a final decision on these uses.

We note that rituximab is not registered by Medsafe for these indications (i.e these are off-label indications). Although not all DHBs currently administer rituximab in all of the indications set out in this consultation, we understand that it has become standard treatment for some of them in some hospitals.

CHAD, warm AIHA and ITP

At its meeting in August 2012, the Haematology Subcommittee of PTAC recommended that rituximab be included in the HML for the treatment of CHAD, warm AIHA and ITP. The Subcommittee considered that it would be appropriate to restrict rituximab prescribing in

these settings to haematologists. Although the Subcommittee considered that it was unable to recommend the lower dose of rituximab (100mg weekly for four weeks versus 375mg/m2 weekly for four weeks) as the standard of care when it reviewed rituximab in ITP, it noted that the lower dose was used in Wellington hospital currently.

PTAC (February 2013) agreed with the recommendations of the Haematology Subcommittee in relation to the use of rituximab in these settings, but considered that it would be necessary for access criteria for these indications to be carefully defined. The criteria proposed above have been put together following further discussions with the Haematology Subcommittee and various haematologists in New Zealand.

TTP

When consulting with haematologists in New Zealand, including with the National Haematology Work Group, PHARMAC received feedback that rituximab was currently being used to treat TTP and therefore should be allowed to be used in that setting in hospitals. The feedback we have received indicate that it is a rare and serious disorder and rituximab should only be available to those who have failed plasma therapy or in whom plasma therapy is contraindicated. The Haematology Subcommittee advised that rituximab should be available for use in this setting.

ANCA associated vasculitis

Following a submission from the New Zealand Rheumatology Association (NZRA), PTAC (May 2013) recommended that rituximab should be available for use in patients with ANCA associated vasculitis subject to the prescribing restrictions detailed in this consultation. PTAC remains open to reviewing its recommendation for rituximab use prior to mycophenolate mofetil in patients with MPO-ANCA vasculitis if additional evidence is provided to support the benefit of rituximab over mycophenolate mofetil in this setting.

SLE

PTAC reviewed a funding application from the NZRA for rituximab use in treatment-refractory SLE in November 2012. PTAC recommended that rituximab is available for use in hospitals for patients with this indication subject to the prescribing restrictions detailed in this consultation.

Antibody-mediated renal transplant rejection and ABO-incompatible renal transplant

PHARMAC received clinical feedback in response to our consultation on the HML that rituximab is currently being used to treat antibody-mediated renal transplant rejection and is on the treatment protocol for ABO incompatible renal transplantation. After reviewing this feedback, PTAC (February 2013) considered that PHARMAC should discuss this issue further with paediatric renal physicians. We have sought the advice of adult and paediatric renal physicians who have advised the proposed restriction criteria are acceptable to them.

The advice we have received indicate that there are no treatment alternatives in these settings.