PUBLIC SUMMARY DOCUMENT
Product: ROMIPLOSTIM, powder for injection, 100 micrograms, 250 micrograms and 500 micrograms, Nplate®
Sponsor: Amgen Australia Pty Ltd
Date of PBAC Consideration: July 2010

1. Purpose of Application

1) The submission presented the cost-effectiveness of romiplostim using the new TGA recommended minimum extractable volumes instead of the average extractable volumes presented in the March 2010 submission.
2) The submission proposed amendments to the restriction criteria finalised after the March 2010 PBAC meeting to better identify the intended population of adult patients with chronic immune (idiopathic) thrombocytopenia purpura (ITP).

2. Background

At the July 2009 meeting, the PBAC rejected a submission to list romiplostim for the initial and continuing treatment of adult patients with chronic immune (idiopathic) thrombocytopenic purpura (ITP) who meet certain criteria because of the uncertain place in treatment for romiplostim, uncertain clinical benefit and uncertain and unacceptable cost-effectiveness.

At the March 2010 meeting, the PBAC recommended listing romiplostim as a pharmaceutical benefit under section 100 (Highly Specialised Drug) Public and Private Hospital Authority Required for treatment of adult patients with chronic immune (idiopathic) thrombocytopenia purpura (ITP) who meet certain criteria, on the basis of a high but acceptable cost effectiveness ratio, in the context of a high clinical need in a small subgroup of ITP patients.

Full details in the March 2010 Public Summary Document

In March 2010, the TGA notified the sponsor that the labels for romiplostim were to be amended by replacing the actual amount in each vial with the minimum extractable volume (i.e from 375 micrograms to 250 micrograms in 0.5 mL and from 625 micrograms to 500 micrograms in 1 mL). The sponsor then notified the Department of the label change.

Subsequently, the sponsor was requested to reassess the cost-effectiveness of romiplostim using the minimum extractable volumes instead of the average extractable volumes which were used in the March 2010 submission.

3. Registration Status

Romiplostim 375 micrograms and 625 micrograms were TGA registered on 8 August 2008 for the indication:

> For the treatment of thrombocytopaenia in adult patients with chronic immune (idiopathic) thrombocytopaenic purpura (ITP)
> - who are non-splenectomised and have had an inadequate response, or are intolerant, to both corticosteroids and immunoglobulins;
> - who are splenectomised and have had an inadequate response to splenectomy.

4. Listing Requested and PBAC's View

Section 100 listing (Highly Specialised Drug) Public and Private hospital authority required

The submission proposed amendments to the restriction criteria to better identify the intended population.

For PBAC's view, see Recommendation and Reasons.

5. Clinical Trials

No new data were presented in the submission.

Details of trials 212, 105, and 131 have been previously reported in the July 2009 and March 2010 Public Summary Documents.

6. Results of Trials

Trial results have been previously reported in the July 2009 and March 2010 Public Summary Documents.

7. Clinical Claim

In the March 2010 resubmission, it was claimed that romiplostim is superior in terms of comparative effectiveness to placebo, but associated with a higher incidence of mild to moderate drug-related adverse events.

8. Economic Analysis

The submission stated that each vial of romiplostim has an actual amount (ie 375 or 625 micrograms), which once reconstituted then has an average and minimum extractable volume.

The economic evaluations for the July 2009 and March 2010 PBAC submissions used the average extractable volumes which were higher than the minimal extractable volumes.

The re-submission stated that the cost-effectiveness had been reassessed using minimum extractable volumes and the same model as presented in the March 2010 submission and incorporating the IVIg results from study 212 and 105.

The revised economic analyses produced ICERs in the range of $45,000 to $75,000 per QALY in the post-splenectomy population and dominant in the non-splenectomy population. This was higher than in the previous submission.

The submission correctly highlighted an error in the March 2010 Public Summary Document for romiplostim where the ICER range for the post-splenectomy population was incorrectly reported as being between $45,000 and $75,000. The correct ICER for this population should have between $15,000 and $45,000 per QALY.

The submission claimed that romiplostim remains a cost-effective treatment option in the proposed population.

For PBAC's view, see Recommendation and Reasons.

9. Estimated PBS Usage and Financial Implications

The re-submission did not present an estimate of PBS usage and financial implications.

10. Recommendation and Reasons

The PBAC confirmed its previous recommendation to list romiplostim under Section 100 (Highly Specialised Drug) Public and Private Hospital Authority Required for treatment of adult patients with chronic immune (idiopathic) thrombocytopenia purpura (ITP) who meet certain criteria, on the basis of high but acceptable cost-effectiveness ratios.

The PBAC did not agree with the submission's proposed amendments to the restriction and considered that the restriction compiled by the secretariat following its previous recommendation to list romiplostim in March 2010 remained appropriate. However, the Committee agreed to the addition of a NOTE stating that 'romiplostim is not a PBS-subsidised alternative to splenectomy' to help clarify the intent of the restriction. The restriction should be reviewed after 3 years of operation.

The PBAC noted that the cost-effectiveness ratios increased as a result of the use of the minimum extractable volume for pricing purposes. The PBAC accepted that the ICERs for splenectomised and non-splenectomised patients represented acceptable cost effectiveness, in the context of high clinical need. The PBAC considered that the ICERs calculated using the outer 95% CIs were most likely implausible.

Recommendation:
ROMIPLOSTIM, powder for injection, 100 micrograms, 250 micrograms and 500 micrograms, Nplate®

Restriction:

Section 100 listing (Highly Specialised Drug)
Public and Private hospital authority required
Note:
Romiplostim is not a PBS-subsidised alternative to splenectomy.

Any queries concerning the arrangements to prescribe romiplostim may be directed to Medicare Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

Written applications for authority to prescribe romiplostim should be forwarded to:

Medicare Australia
Prior Written Approval of Specialised Drugs
Reply Paid 9826
GPO Box 9826
HOBART TAS 7001

Further prescribing information is on the Medicare Australia website at www.medicareaustralia.gov.au.

Public and Private hospital authority required
Initial (new patients)

Initial treatment of severe thrombocytopenia in an adult patient with severe chronic immune (idiopathic) thrombocytopenic purpura (ITP) who is:

(1) Splenectomised and

(a) has had an inadequate response to, or is intolerant to, corticosteroid therapy post splenectomy; and

(b) has had an inadequate response to, or is intolerant to, immunoglobulin therapy post splenectomy;

OR

(2) Not splenectomised and

(a) has had an inadequate response, or is intolerant to, corticosteroid therapy at a dose equivalent to 0.5-2 mg/kg/day of prednisone for at least 4-6 weeks; and

(b) has had an inadequate response, or is intolerant to, immunoglobulin therapy; and

(c) in whom splenectomy is contraindicated for medical reasons.

The following criteria indicate failure to achieve an adequate response and must be demonstrated in all patients at the time of initial application:

(a) a platelet count of $\leq 20 \times 10^9$/L,

OR

(b) a platelet count of 20-30 x 10^9/L, where the patient is experiencing significant bleeding or has a history of significant bleeding in this platelet range.

The authority application must be made in writing and must include:
(1) a completed authority prescription form,
(2) a signed patient acknowledgement,
(3) a completed Romiplostim PBS Authority Application - Supporting Information Form [may be downloaded from the Medicare Australia website (www.medicareaustralia.gov.au)],
(4) a copy of a full blood count pathology report supporting the diagnosis of ITP, and
(5) where the application is sought on the basis of a medical contraindication to surgery, a signed and dated letter from the clinician making this assessment which includes the date upon which the patient was assessed for surgery and the clinical grounds upon which surgery is contraindicated.

The full blood count must be no more than 1 month old at the time of application.

At the time of the written authority application, medical practitioners should request the appropriate quantity of vials of appropriate strength to provide sufficient drug for a single treatment at a dose of 1 microgram/kg. Up to 1 repeat may be requested with the initial written application.

Subsequently during the initial period of dose titration, authority applications for a single dose and up to 1 repeat may be made by telephone by contacting Medicare Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). The dose (microgram/kg/wk) must be provided at the time of application.

Once a patient's dose has been stable for a period of 4 weeks, authority approvals for sufficient vials of appropriate strength based on the weight of the patient and dose (microgram/kg/wk) for up to 4 weeks of treatment and up to 4 repeats may be granted, as long as the total period of treatment authorised under this restriction does not exceed 24 weeks.

Authority approval will not be given for doses of higher than 10 micrograms/kg/week.

Public and Private Hospital Authority Required

Initial (grandfather patients)

Initial PBS-subsidised treatment of severe thrombocytopenia in an adult patient with severe chronic immune (idiopathic) thrombocytopenic purpura (ITP) who was receiving treatment with romiplostim prior to [listing date] and in whom the criteria for initial treatment can be demonstrated to have been met at the time romiplostim was commenced.

The authority application must be made in writing and must include:
(1) a completed authority prescription form,
(2) a signed patient acknowledgement,
(3) a completed Romiplostin PBS Authority Application - Supporting Information Form [may be downloaded from the Medicare Australia website (www.medicareaustralia.gov.au)], and
(4) where the application is sought on the basis of a medical contraindication to surgery, a signed and dated letter from the clinician making this assessment which includes the date upon which the patient was assessed for surgery and the clinical grounds upon which surgery is contraindicated.

For patients whose dose of romiplostim had been stable for at least 4 weeks at the time of the initial application for PBS-subsidy, the medical practitioner should request sufficient number of vials based on the weight of the patient and dose (microgram/kg/wk) to provide up to 4 weeks of treatment. Up to a maximum of 5 repeats may be authorised.

Where the patient is in the titration phase of treatment with romiplostim, medical practitioners should request the appropriate quantity of vials of appropriate strength to provide sufficient drug for

a single treatment at a dose of 1 microgram/kg. Up to 1 repeat may be requested with the initial written application.

Subsequently during the initial period of dose titration, authority applications for a single dose and up to 1 repeat may be made by telephone by contacting Medicare Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). The dose (microgram/kg/wk) must be provided at the time of application.

Once a patient's dose has been stable for a period of 4 weeks, authority approvals for sufficient vials of appropriate strength based on the weight of the patient and dose (microgram/kg/wk) for up to 4 weeks of treatment and up to 4 repeats may be granted, as long as the total period of treatment authorised under this restriction does not exceed 24 weeks.

For patients whose dose of romiplostim had been stable for at least 4 weeks at the time of the initial application for PBS-subsidy, the medical practitioner should request sufficient number of vials of appropriate strength based on the weight of the patient and dose (microgram/kg/wk) to provide up to 4 weeks of treatment. Up to a maximum of 5 repeats may be authorised.

Authority approval will not be given for doses of higher than 10 micrograms/kg/week.

Public and Private Hospital Authority Required

Continuing therapy or re-initiation after a break in therapy

First period of PBS-subsidised continuing treatment or re-initiation of interrupted PBS-subsidised treatment of severe thrombocytopenia in an adult patient with chronic immune (idiopathic) thrombocytopenic purpura (ITP) who has displayed a sustained platelet response to treatment with romiplostim during the initial period of PBS-subsidised treatment.

For the purposes of this restriction, a sustained platelet response is defined as:

(a) use of rescue medication (corticosteroids or immunoglobulins) on no more than one occasion during the initial period of PBS-subsidised romiplostim,

AND either of the following

(b) a platelet count $\geq 50 \times 10^9$/L on at least four (4) occasions, each at least one week apart;

OR

(c) a platelet count $>30 \times 10^9$/L and which is double the baseline (pre-treatment) platelet count on at least four (4) occasions, each at least one week apart.

Applications for the first period of continuing PBS-subsidised treatment or re-initiation of interrupted treatment must be made in writing and must include:
(1) a completed authority prescription form, and
(2) a completed romiplostim PBS Authority Application - Supporting Information Form [may be downloaded from the Medicare Australia website (www.medicareaustralia.gov.au)],
(3) copies of the platelet count pathology reports (unless previously provided for patients re-initiating therapy).

The most recent platelet count must be no more than one month old at the time of application.

The medical practitioner should request sufficient number of vials of appropriate strength based on the weight of the patient and dose (microgram/kg/wk) to provide 4 weeks of treatment. Up to a maximum of 5 repeats may be authorised.

Where fewer than 5 repeats are initially requested with the authority prescription, authority approvals for sufficient repeats to complete a maximum of 24 weeks of treatment may be made by telephone.

Authority approval will not be given for doses of higher than 10 micrograms/kg/week.

Public and Private Hospital Authority Required
Second and subsequent applications for continuing therapy
Continuing treatment of severe thrombocytopenia in an adult patient with chronic immune (idiopathic) thrombocytopenic purpura (ITP) who has previously received PBS-subsidised therapy with romiplostim and who continues to display a response to treatment with romiplostim.

For the purposes of this restriction, a continuing response to treatment with romiplostim is defined as:

(a) use of rescue medication (corticosteroids or immunoglobulins) on no more than one occasion during the most recent 24 week period of PBS-subsidised treatment with romiplostim,

AND either of the following:

(b) a platelet count $\geq 50 \times 10^9$/L

OR

(c) a platelet count $>30 \times 10^9$/L and which is double the baseline platelet count.

Platelet counts must be no more than 1 month old at the time of application.

Authority applications for second and subsequent periods of continuing therapy may be made by telephone by contacting Medicare Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

The medical practitioner should request sufficient number of vials of appropriate strength based on the weight of the patient and dose (microgram/kg/wk) to provide 4 weeks of treatment. Up to a maximum of 5 repeats may be authorised.

Authority approval will not be given for doses of higher than 10 micrograms/kg/week.

Maximum quantity: 1
Repeats: Nil

13. Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

14. Sponsor's Comment

The sponsor has no comment.