

6.14 TOCILIZUMAB

Injection 162 mg in 0.9 mL single use pre-filled pen, Injection 162 mg in 0.9 mL single use pre-filled syringe, Actemra[®], Roche Products Pty Ltd

1 Purpose of Application

- 1.1 The minor submission requested an extension to the current Authority Required listings of subcutaneous (SC) injection presentations (syringes and pen devices) of tocilizumab (tocilizumab SC from herein) to include treatment of systemic juvenile idiopathic arthritis (sJIA).

2 Background

- 2.1 At the time of PBAC consideration, tocilizumab SC was under review by the TGA for an extended indication of:
- treatment of active systemic juvenile idiopathic arthritis in patients 1 year of age and older.
- 2.2 The TGA Delegate's summary and request for ACM advice was provided with the submission. The Delegate raised concerns regarding the safety and efficacy of SC tocilizumab in the 1-2 year old age group, and therefore sought the advice of ACM.
- 2.3 The TGA ACM advice was provided on 25 February 2020. The ACM was generally supportive of the application. Regarding the safety and efficacy of tocilizumab SC in the 1-2 year old age group, the ACM was of the view that "the safety of SC tocilizumab was comparable to the IV formulation, but acknowledged that this is based on very limited data."
- 2.4 Tocilizumab SC is currently PBS listed for the treatment of rheumatoid arthritis, severe active juvenile idiopathic arthritis and giant cell arteritis.

For more detail on PBAC's view, see section 6 PBAC outcome.

3 Requested listing

- 3.1 Tocilizumab intravenous (IV) is currently PBS listed under the Section 100 Highly Specialised Drugs Program for treatment of sJIA. The submission requested the same restriction for tocilizumab SC as that of tocilizumab IV for sJIA.
- 3.2 Suggested additions are in italics and deletions are in strikethrough. Given the size of the restrictions, only the proposed additions and deletions are shown below.

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< 30 kg body weight (dosing every 2 weeks)

Initial treatment

| Name, Restriction, Manner of administration and form | Max. Qty | No. of Rpts | Dispensed Price for Max. Qty | Proprietary Name and Manufacturer |
|---|-------------|----------------|---------------------------------|--------------------------------------|
| TOCILIZUMAB | | | | |
| 162 mg/0.9 mL injection, 4 x 0.9 mL syringes | 1 | 1 | ⋄ [REDACTED] | Actemra Roche Products |
| 162 mg/0.9 mL injection, 4 x 0.9 mL pen devices | 1 | 1 | ⋄ [REDACTED] | Actemra |

Continuing treatment

| Name, Restriction, Manner of administration and form | Max. Qty | No. of Rpts | Dispensed Price for Max. Qty | Proprietary Name and Manufacturer |
|---|-------------|----------------|---------------------------------|--------------------------------------|
| TOCILIZUMAB | | | | |
| 162 mg/0.9 mL injection, 4 x 0.9 mL syringes | 1 | 2 | ⋄ [REDACTED] | Actemra Roche Products |
| 162 mg/0.9 mL injection, 4 x 0.9 mL pen devices | 1 | 2 | ⋄ [REDACTED] | Actemra |

≥ 30 kg body weight (dosing once weekly)

Initial treatment

| Name, Restriction, Manner of administration and form | Max. Qty | No. of Rpts | Dispensed Price for Max. Qty | Proprietary Name and Manufacturer |
|---|-------------|----------------|---------------------------------|--------------------------------------|
| TOCILIZUMAB | | | | |
| 162 mg/0.9 mL injection, 4 x 0.9 mL syringes | 1 | 3 | ⋄ [REDACTED] | Actemra Roche Products |
| 162 mg/0.9 mL injection, 4 x 0.9 mL pen devices | 1 | 3 | ⋄ [REDACTED] | Actemra |

Continuing treatment

| Name, Restriction, Manner of administration and form | Max. Qty | No. of Rpts | Dispensed Price for Max. Qty | Proprietary Name and Manufacturer |
|---|-------------|----------------|---------------------------------|--------------------------------------|
| TOCILIZUMAB | | | | |
| 162 mg/0.9 mL injection, 4 x 0.9 mL syringes | 1 | 5 | ⋄ [REDACTED] | Actemra Roche Products |
| 162 mg/0.9 mL injection, 4 x 0.9 mL pen devices | 1 | 5 | ⋄ [REDACTED] | Actemra |

| | |
|------------------------------------|--|
| Category / Program | GENERAL – General Schedule (Code GE) |
| Prescriber type: | <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives |
| PBS Indication: | Systemic juvenile idiopathic arthritis |
| Treatment phase: | Initial treatment - Initial 1 (new patient) Initial treatment - Initial 2 (retial or recommencement of treatment after a break of less than 12 months) |
| Restriction Level / Method: | <input checked="" type="checkbox"/> Authority Required - In Writing Only |
| Prescriber Instructions | At the time of authority application, medical practitioners must request the appropriate number of vials of appropriate strength to provide sufficient drug, based on the weight of the patient, for one infusion. A separate authority prescription form must be completed for each strength requested. Up to a maximum of 3 repeats will be authorised |

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| | |
|-----------------------------|--|
| Category / Program | GENERAL – General Schedule (Code GE) |
| Prescriber type: | <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives |
| PBS Indication: | Systemic juvenile idiopathic arthritis |
| Treatment phase: | Continuing treatment |
| Restriction Level / Method: | <input checked="" type="checkbox"/> Authority Required - In Writing Only |
| Prescriber Instructions | At the time of authority application, medical practitioners must request the appropriate number of vials of appropriate strength to provide sufficient drug, based on the weight of the patient, for one infusion. A separate authority prescription form must be completed for each strength requested. Up to a maximum of 3 repeats will be authorised. |

For more detail on PBAC's view, see section 6 PBAC outcome.

4 Comparator

- 4.1 The minor submission nominated tocilizumab IV as the comparator. This was consistent with the approach taken for other indications for tocilizumab SC.

For more detail on PBAC's view, see section 6 PBAC outcome.

5 Consideration of the evidence

Sponsor hearing

- 5.1 There was no hearing for this item as it was a minor submission.

Consumer hearing

- 5.2 The PBAC noted that no consumer comments were received for this item.

Clinical trials

- 5.3 The minor submission presented data from the JIGSAW 118 trial, a phase 1b, single-arm, open-label, multicentre study designed to investigate the pharmacokinetics, pharmacodynamics and safety of tocilizumab SC; and to determine the appropriate dosing regimen across a range of body weights in paediatric patients who had an inadequate response to or were intolerant to non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids. The efficacy of tocilizumab SC was an exploratory outcome of the study.
- 5.4 The minor submission claimed the results of the study demonstrated adequate pharmacokinetic exposures and pharmacodynamic responses similar to those achieved with the tocilizumab IV dosing regimens for SJIA.
- 5.5 The minor submission further claimed that both tocilizumab regimens were well tolerated and that the types of adverse events observed were consistent with the known safety profile for tocilizumab IV in SJIA.
- 5.6 As this was a minor submission, the data was not independently evaluated.

Economic analysis

- 5.7 The minor submission presented a cost-minimisation analysis against tocilizumab IV over a 52-week period (Table 1 below).
- 5.8 The minor submission proposed the following equi-effective doses:
- tocilizumab 162 mg administered as SC injection (every 2 weeks for patients < 30 kg or every week for patients \geq 30 kg) and
 - tocilizumab administered as an IV infusion every 2 weeks (12 mg/kg for patients < 30 kg or 8 mg/kg for patients \geq 30 kg).
- 5.9 The draft Product Information (PI) specifies that at least the first injection of tocilizumab SC must be performed under the supervision of a qualified healthcare professional, in a healthcare facility with the necessary medical treatment available (tocilizumab PI, p3).
- 5.10 The submission did not include this administration cost in the cost-minimisation analysis. In its consideration of tocilizumab SC for pJIA, the PBAC considered that the exclusion of the consultation item fee from the cost-minimisation analysis was not appropriate (paragraph 6.6, tocilizumab PSD, March 2019 PBAC Meeting).
- 5.11 The Pre-PBAC response provided a revised cost minimisation analysis, which included a consultation item fee of \$132.20 (MBS item 110) in the calculations. Table 1 was updated accordingly.

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Table 1: Cost-minimisation analysis against tocilizumab IV over 52 weeks

| Tocilizumab SC | | Tocilizumab IV | |
|--|------------|--|------------|
| Cost-minimised AEMP | | Indication-specific AEMP (sJIA) | |
| 162 mg (pack of 4): ██████████ | | 80 mg: \$ ██████ | |
| 162 mg (single syringe/pen): ██████████ | | 200 mg: \$ ██████ | |
| 400 mg: \$ ██████ | | | |
| Cost-minimised DPMQ | | | |
| ██████████ | | | |
| Mean body weight of patient ^a | | | |
| < 30 kg | ≥ 30 kg | < 30 kg | ≥ 30 kg |
| 20.20 | 48.94 kg | 20.20 kg | 48.94 kg |
| Dose per administration | | | |
| < 30 kg | ≥ 30 kg | < 30 kg | ≥ 30 kg |
| 162mg | 162mg | 242.44mg | 391.50mg |
| AEMP per administration | | | |
| < 30 kg | ≥ 30 kg | < 30 kg | ≥ 30 kg |
| ██████████ | ██████████ | ██████████ | ██████████ |
| Number of administrations over 52 weeks | | | |
| < 30 kg | ≥ 30 kg | < 30 kg | ≥ 30 kg |
| 26.0 | 52.00 | 26.0 | 26.0 |
| AEMP per patient over 52 weeks | | | |
| < 30 kg | ≥ 30 kg | < 30 kg | ≥ 30 kg |
| ██████████ | ██████████ | ██████████ | ██████████ |
| Weighted AEMP per patient over 52 weeks ^b | | | |
| ██████████ | ██████████ | ██████████ | ██████████ |
| DPMQ per patient over 52 | | | |
| ██████████ | ██████████ | ██████████ | ██████████ |
| Administration costs over 52 weeks | | | |
| \$0 \$132.20 ^d | | \$2,587.00 ^e | |
| Copayment over 52 weeks | | | |
| \$237.52 \$259.95 | | \$645.57 \$706.53 | |
| Average net cost over 52 weeks | | | |
| ██████████ | | ██████████ | |

Source: pre-PBAC response worksheet

Abbreviations: AEMP: approved ex-manufacturer price, DPMQ: dispense price for maximum quantity, IV: intravenous, SC: subcutaneous

^a Based on data from the JIGSAW 118 study: phase 1b, single-arm, open label, multicentre PK/PD bridging study,

^b Weighted DPMQ based on weight group proportions from the TENDER trial,

^c Weighted by private/public hospital split of 22.3%/77.7% derived from Medicare statistics (PBS/RPBS items processed between October 2018 to September 2019),

^d Based on MBS item 110 ^e Based on MBS item 14245

Strikethrough represents figures presented in the submission that were subsequently amended in the pre-PBAC response.

5.12 The minor submission utilised patient data from the TENDER trial (which the November 2011 tocilizumab IV submission was based on), a phase III randomised, double-blind, placebo-controlled trial to inform average body weight and proportion of patients in the < 30 kg and ≥ 30 kg weight groups for the cost-minimisation analysis. This was appropriate and consistent with the methodology used for consideration of tocilizumab SC for severe active polyarticular juvenile idiopathic arthritis (pJIA) (paragraph 6.6, tocilizumab PSD, March 2019 PBAC Meeting).

Drug cost/patient/year (52 weeks): \$ [REDACTED]

5.13 The estimated weighted cost of treatment over 52 weeks is \$ [REDACTED], based on the cost-minimised DPMQ of \$ [REDACTED] for a pack of four syringes/pens (see Table 1).

5.14 The average net cost of treatment over 52 weeks, including the administration costs, remains the same as tocilizumab IV, based on an AEMP of \$ [REDACTED] for a pack of four syringes/pens.

Estimated PBS usage & financial implications

5.15 The sponsor proposed that tocilizumab SC would substitute for the existing tocilizumab IV and therefore there would not be an increase in usage. The weighted DPMQ per patient over 52 weeks is \$ [REDACTED] for the tocilizumab SC compared to \$ [REDACTED] for tocilizumab IV (weighted by public/private hospital usage).

5.16 The pre-PBAC response provided estimates of the number of patients expected to switch from tocilizumab IV to tocilizumab SC and the resulting financial impact to the PBS/RPBS (Table 2).

Table 2: Estimated use and financial implications

| | Year 1 | Year 2 | Year 3 | Year 4 | Year 5 | Year 6 |
|---|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| Estimated extent of use of tocilizumab SC in sJIA | | | | | | |
| Patients treated with tocilizumab IV | 15 | 17 | 19 | 22 | 24 | 28 |
| Patients electing treatment with tocilizumab SC (%) | 65% | 75% | 85% | 85% | 85% | 85% |
| Number of patients treated with tocilizumab SC | 10 | 13 | 16 | 18 | 21 | 23 |
| Number of scripts dispensed PBS/RPBS | 93 | 122 | 156 | 176 | 199 | 225 |
| Estimated financial implications of tocilizumab SC in sJIA | | | | | | |
| Cost to PBS/RPBS for tocilizumab SC (co-payments removed) | \$ [REDACTED] | \$ [REDACTED] | \$ [REDACTED] | \$ [REDACTED] | \$ [REDACTED] | \$ [REDACTED] |
| Cost to PBS/RPBS for displaced tocilizumab IV (co-payments removed) | \$ [REDACTED] | \$ [REDACTED] | \$ [REDACTED] | \$ [REDACTED] | \$ [REDACTED] | \$ [REDACTED] |
| Net cost to PBS/RPBS (co-payments removed) | \$ [REDACTED] | \$ [REDACTED] | \$ [REDACTED] | \$ [REDACTED] | \$ [REDACTED] | \$ [REDACTED] |
| Net cost to MBS ^a | -\$23,913 | -\$31,186 | -\$39,948 | -\$45,152 | -\$51,034 | -\$57,682 |
| Net cost to Government | \$0 | \$0 | \$0 | \$0 | \$0 | \$0 |

^a MBS costs based on MBS items 110 (tocilizumab SC) and MBS item 14245 (tocilizumab IV)

Source: pre-PBAC response

5.17 At year 6, the estimated number of patients was 23 and the net cost to the PBS would be \$ [REDACTED]. As a minor submission, the financial estimates have not been independently evaluated.

For more detail on PBAC’s view, see section 6 PBAC outcome.

6 PBAC Outcome

- 6.1 The PBAC recommended the Authority Required listing of tocilizumab SC (syringes and pen devices) for the treatment of sJIA on a cost-minimisation basis to tocilizumab IV.
- 6.2 The PBAC considered that tocilizumab SC was likely to be equivalent in efficacy and safety to tocilizumab IV.
- 6.3 The PBAC considered the cost-minimisation analysis of tocilizumab SC versus tocilizumab IV was appropriate.
- 6.4 Based on the evidence presented in the submission, the PBAC considered the equi-effective doses were:
- for patients <30 kg tocilizumab SC 162 mg every two weeks and tocilizumab IV 12 mg/kg every two weeks;
 - for patients \geq 30 kg tocilizumab SC 162 mg every week and tocilizumab IV 8 mg/kg every two weeks.
- 6.5 For patients weighing less than 30 kg, the PBAC recommended a maximum quantity of one with one repeat for initial treatment and a maximum quantity of one with two repeats for continuing treatment. For patients weighing more than 30 kg, the PBAC recommended a maximum quantity of one with three repeats for initial treatment and a maximum quantity of one with five repeats for continuing treatment.
- 6.6 The PBAC noted the pre-PBAC response provided a revised financial spreadsheet. The PBAC considered that the inclusion of a consultation item fee from the cost-minimisation analysis was appropriate given the first dose of tocilizumab SC needs to be administered under the supervision of a qualified healthcare professional, in a healthcare facility with the necessary medical treatment available.
- 6.7 The PBAC noted that there would be limited budget impact due to the small size of the treated population and the cost-minimisation to tocilizumab IV.
- 6.8 The PBAC advised that the restriction should be based on that of tocilizumab IV, with the removal of the prescriber instructions referencing IV administration. The PBAC noted that tocilizumab pen should not be used to treat children and adolescents less than 12 years of age due to risk of inadvertent intramuscular injection, and that this should be reflected in an administrative note in the PBS restriction for the pen device formulation only.
- 6.9 The PBAC advised that balance of supply restrictions for initial and continuing treatment phases was appropriate.
- 6.10 The PBAC advised that tocilizumab should not be treated as interchangeable on an individual patient basis with any other drug.
- 6.11 The PBAC advised that tocilizumab SC is not suitable for prescribing by nurse practitioners.

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6.12 The PBAC recommended that the Early Supply Rule should not apply to tocilizumab SC.

Outcome:

Recommended

7 Recommended listing

7.1 Add new items:

| Name, Restriction, Manner of administration and form | PBS item code | Max. qty packs | Max. qty units | No. of Rpts | Proprietary Name and Manufacturer | |
|--|---------------|----------------|----------------|-------------|-----------------------------------|----------------|
| TOCILIZUMAB | | | | | | |
| 162 mg/0.9 mL injection, 4 x 0.9 mL pen devices | NEW | 1 | 4 | 1 | Actemra | Roche Products |
| 162 mg/0.9 mL injection, 4 x 0.9 mL syringes | NEW | 1 | 4 | 1 | Actemra | |

Initial treatment: patients < 30 kg

| |
|---|
| Category / Program: GENERAL – General Schedule (Code GE) |
| Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives |
| Restriction Level / Method: <input checked="" type="checkbox"/> Authority Required – In Writing Only |
| Indication: Systemic juvenile idiopathic arthritis |
| Treatment Phase: Initial treatment - Initial 1 (new patient) - Initial treatment in a patient weighing less than 30 kg Initial treatment - Initial 2 (retrial or recommencement of treatment after a break of less than 12 months) - Initial treatment in a patient weighing less than 30 kg Initial treatment – Initial 3 (recommencement of treatment after a break of more than 12 months) - Initial treatment in a patient weighing less than 30 kg |
| Clinical criteria: <ul style="list-style-type: none"> ▪ Patient must not have received PBS-subsidised treatment with a biological medicine for this condition. <p>AND</p> <ul style="list-style-type: none"> ▪ Patient must have polyarticular course disease which has failed to respond adequately to oral or parenteral methotrexate at a dose of at least 15 mg per square metre weekly, alone or in combination with oral or intra-articular corticosteroids, for a minimum of 3 months; OR ▪ Patient must have polyarticular course disease and have demonstrated severe intolerance of, or toxicity due to, methotrexate; OR ▪ Patient must have refractory systemic symptoms, demonstrated by an inability to decrease and maintain the dose of prednisolone (or equivalent) below 0.5 mg per kg per day following a minimum of 2 months of therapy. <p>AND</p> <ul style="list-style-type: none"> ▪ Patient must not receive more than 16 weeks of treatment under this restriction. |
| Treatment criteria: <ul style="list-style-type: none"> ▪ Must be treated by a rheumatologist; OR ▪ Patient must be undergoing treatment under the supervision of a paediatric rheumatology treatment centre. |
| Population criteria: <ul style="list-style-type: none"> ▪ Patient must be under 18 years of age. |
| Prescribing Instructions: The following criteria indicate failure to achieve an adequate response to prior methotrexate therapy in a patient with polyarticular course disease and must be demonstrated in the patient at the time of the initial application: (a) an active joint count of at least 20 active (swollen and tender) joints; or (b) at least 4 active joints from the following list of major joints: (i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or |

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(ii) shoulder, cervical spine and/or hip (assessed as pain in passive movement and restriction of passive movement, where pain and limitation of movement are due to active disease and not irreversible damage such as joint destruction or bony overgrowth).

The following criteria indicate failure to achieve an adequate response to prior therapy in a patient with refractory systemic symptoms and must be demonstrated in the patient at the time of the initial application:

- (a) an active joint count of at least 2 active joints; and
- (b) persistent fever greater than 38 degrees Celsius for at least 5 out of 14 consecutive days; and/or
- (c) a C-reactive protein (CRP) level and platelet count above the upper limits of normal (ULN).

The baseline measurements of joint count, fever and/or CRP level and platelet count must be performed preferably whilst on treatment, but no longer than 4 weeks following cessation of the most recent prior treatment.

The same indices of disease severity used to establish baseline at the commencement of treatment with each initial treatment application must be used to determine response for all subsequent continuing treatments.

Severe intolerance to methotrexate is defined as intractable nausea and vomiting and general malaise unresponsive to manoeuvres, including reducing or omitting concomitant non-steroidal anti-inflammatory drugs (NSAIDs) on the day of methotrexate administration, use of folic acid supplementation, or administering the dose of methotrexate in 2 divided doses over 24 hours.

Toxicity due to methotrexate is defined as evidence of hepatotoxicity with repeated elevations of transaminases, bone marrow suppression temporally related to methotrexate use, pneumonitis, or serious sepsis.

If treatment with methotrexate alone or in combination with other treatments is contraindicated according to the relevant TGA-approved Product Information, details must be provided at the time of application.

If intolerance to treatment develops during the relevant period of use, which is of a severity necessitating permanent treatment withdrawal, details of this toxicity must be provided at the time of application.

The authority application must be made in writing and must include:

- (1) completed authority prescription form(s); and
- (2) a completed Systemic Juvenile Idiopathic Arthritis PBS Authority Application - Supporting Information Form which includes the following:
 - (i) the date of assessment of severe active systemic juvenile idiopathic arthritis;
 - (ii) details of prior treatment including dose and duration of treatment;
 - (iii) pathology reports detailing CRP and platelet count where appropriate.

An assessment of a patient's response to an initial course of treatment must be conducted following a minimum of 12 weeks of therapy. An application for the continuing treatment must be accompanied with the assessment of response and submitted to the Department of Human Services no later than 4 weeks from the date of completion of the most recent course of treatment. This will enable ongoing treatment for those who meet the continuing restriction for PBS-subsidised treatment.

Where the response assessment is not submitted within this timeframe, the patient will be deemed to have failed to respond to treatment with this drug.

If a patient fails to demonstrate a response to treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition. Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.

Caution: [APPLIES TO PEN DEVICE ONLY]

Inadvertent muscular injection in patients aged less than 12 years may occur with the pen device.

Administrative Advice:

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

Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au

Applications for authority to prescribe should be forwarded to:

Department of Human Services
Complex Drugs

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Reply Paid 9826
HOBART TAS 7001

7.2 Add new items:

| Name, Restriction, Manner of administration and form | PBS item code | Max. qty packs | Max. qty units | No. of Rpts | Proprietary Name and Manufacturer | |
|--|---------------|----------------|----------------|-------------|-----------------------------------|----------------|
| TOCILIZUMAB | | | | | | |
| 162 mg/0.9 mL injection, 4 x 0.9 mL pen devices | NEW | 1 | 4 | 2 | Actemra | Roche Products |
| 162 mg/0.9 mL injection, 4 x 0.9 mL syringes | NEW | 1 | 4 | 2 | Actemra | |

Continuing treatment: patients < 30 kg

Category / Program: GENERAL – General Schedule (Code GE)

Prescriber type: Dental Medical Practitioners Nurse practitioners Optometrists Midwives

Restriction Level / Method: Authority Required – In Writing Only

Indication: Systemic juvenile idiopathic arthritis

Treatment Phase: Continuing treatment - Continuing treatment in a patient weighing less than 30 kg

Clinical criteria:

- Patient must have previously received PBS-subsidised treatment with this drug for this condition.

AND

- Patient must have demonstrated an adequate response to treatment with this drug.

AND

- Patient must not receive more than 24 weeks of treatment under this restriction.

Treatment criteria:

- Must be treated by a rheumatologist; OR
- Patient must be undergoing treatment under the supervision of a paediatric rheumatology treatment centre.

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Prescribing Instructions:

An adequate response to treatment is defined as:

(a) in a patient with polyarticular course disease:

(i) a reduction in the total active (swollen and tender) joint count by at least 50% from baseline, where baseline is at least 20 active joints; or

(ii) a reduction in the number of the following major active joints, from at least 4, by at least 50%:

- elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or

- shoulder, cervical spine and/or hip (assessed as pain in passive movement and restriction of passive movement, where pain and limitation of movement are due to active disease and not irreversible damage such as joint destruction or bony overgrowth).

(b) in a patient with refractory systemic symptoms:

(i) absence of fever greater than 38 degrees Celsius in the preceding seven days; and/or

(ii) a reduction in the C-reactive protein (CRP) level and platelet count by at least 30% from baseline; and/or

(iii) a reduction in the dose of corticosteroid by at least 30% from baseline.

Determination of whether a response has been demonstrated to initial and subsequent courses of treatment will be based on the baseline measurements of disease severity submitted with the initial treatment application.

The authority application must be made in writing and must include:

(1) completed authority prescription form(s); and

(2) a completed Systemic Juvenile Idiopathic Arthritis PBS Authority Application - Supporting Information Form which includes baseline and current pathology reports detailing CRP and platelet count where appropriate.

The most recent systemic juvenile idiopathic arthritis assessment must be no more than 1 month old at the time of application.

Where the most recent course of PBS-subsidised treatment with this drug was approved under either Initial 1, Initial 2, or Initial 3 treatment restrictions, an assessment of a patient's response must have been conducted following a minimum of 12 weeks of therapy and submitted to the Department of Human Services no later than 4 weeks from the date of completion of treatment.

An application for the continuing treatment must be accompanied with the assessment of response following a minimum of 12 weeks of therapy with this drug and submitted to the Department of Human Services no later than 4 weeks from the date of completion of treatment. This will enable ongoing treatment for those who meet the continuing restriction for PBS-subsidised treatment.

Where the response assessment is not submitted within this timeframe, the patient will be deemed to have failed to respond to treatment with this drug.

If a patient fails to demonstrate a response to 2 courses of treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition. Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.

A patient may re-trial this drug after a minimum of 12 months have elapsed between the date the last prescription for a PBS-subsidised biological medicine was approved in this cycle and the date of the first application under a new cycle under the Initial 3 treatment restriction.

Caution: [APPLIES TO PEN DEVICE ONLY]

Inadvertent muscular injection in patients aged less than 12 years may occur with the pen device.

Administrative Advice:

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

Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au

Applications for authority to prescribe should be forwarded to:

Department of Human Services

Complex Drugs

Reply Paid 9826

HOBART TAS 7001

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7.3 Add new item:

| Name, Restriction, Manner of administration and form | PBS item code | Max. qty packs | Max. qty units | No. of Rpts | Proprietary Name and Manufacturer | |
|--|---------------|----------------|----------------|-------------|-----------------------------------|----------------|
| TOCILIZUMAB | | | | | | |
| 162 mg/0.9 mL injection, 4 x 0.9 mL pen devices | NEW | 1 | 4 | 3 | Actemra | Roche Products |
| 162 mg/0.9 mL injection, 4 x 0.9 mL syringes | NEW | 1 | 4 | 3 | Actemra | |

Initial treatment: patients ≥ 30 kg

Category / Program: GENERAL – General Schedule (Code GE)

Prescriber type: Dental Medical Practitioners Nurse practitioners Optometrists Midwives

Restriction Level / Method: Authority Required – In Writing Only

Indication: Systemic juvenile idiopathic arthritis

Treatment Phase:

Initial treatment - Initial 1 (new patient) - Initial treatment in a patient weighing more than 30 kg

Initial treatment - Initial 2 (retrial or recommencement of treatment after a break of less than 12 months) - Initial treatment in a patient weighing more than 30 kg

Initial treatment – Initial 3 (recommencement of treatment after a break of more than 12 months) - Initial treatment in a patient weighing more than 30 kg

Clinical criteria:

- Patient must not have received PBS-subsidised treatment with a biological medicine for this condition.

AND

- Patient must have polyarticular course disease which has failed to respond adequately to oral or parenteral methotrexate at a dose of at least 15 mg per square metre weekly, alone or in combination with oral or intra-articular corticosteroids, for a minimum of 3 months; OR
- Patient must have polyarticular course disease and have demonstrated severe intolerance of, or toxicity due to, methotrexate; OR
- Patient must have refractory systemic symptoms, demonstrated by an inability to decrease and maintain the dose of prednisolone (or equivalent) below 0.5 mg per kg per day following a minimum of 2 months of therapy.

AND

- Patient must not receive more than 16 weeks of treatment under this restriction.

Treatment criteria:

- Must be treated by a rheumatologist; OR
- Patient must be undergoing treatment under the supervision of a paediatric rheumatology treatment centre.

Population criteria:

- Patient must be under 18 years of age.

Prescribing Instructions:

The following criteria indicate failure to achieve an adequate response to prior methotrexate therapy in a patient with polyarticular course disease and must be demonstrated in the patient at the time of the initial application:

(a) an active joint count of at least 20 active (swollen and tender) joints; or

(b) at least 4 active joints from the following list of major joints:

(i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or

(ii) shoulder, cervical spine and/or hip (assessed as pain in passive movement and restriction of passive movement, where pain and limitation of movement are due to active disease and not irreversible damage such as joint destruction or bony overgrowth).

The following criteria indicate failure to achieve an adequate response to prior therapy in a patient with refractory systemic symptoms and must be demonstrated in the patient at the time of the initial application:

(a) an active joint count of at least 2 active joints; and

(b) persistent fever greater than 38 degrees Celsius for at least 5 out of 14 consecutive days; and/or

(c) a C-reactive protein (CRP) level and platelet count above the upper limits of normal (ULN).

The baseline measurements of joint count, fever and/or CRP level and platelet count must be performed preferably whilst on treatment, but no longer than 4 weeks following cessation of the most recent prior treatment.

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The same indices of disease severity used to establish baseline at the commencement of treatment with each initial treatment application must be used to determine response for all subsequent continuing treatments.

Severe intolerance to methotrexate is defined as intractable nausea and vomiting and general malaise unresponsive to manoeuvres, including reducing or omitting concomitant non-steroidal anti-inflammatory drugs (NSAIDs) on the day of methotrexate administration, use of folic acid supplementation, or administering the dose of methotrexate in 2 divided doses over 24 hours.

Toxicity due to methotrexate is defined as evidence of hepatotoxicity with repeated elevations of transaminases, bone marrow suppression temporally related to methotrexate use, pneumonitis, or serious sepsis.

If treatment with methotrexate alone or in combination with other treatments is contraindicated according to the relevant TGA-approved Product Information, details must be provided at the time of application.

If intolerance to treatment develops during the relevant period of use, which is of a severity necessitating permanent treatment withdrawal, details of this toxicity must be provided at the time of application.

The authority application must be made in writing and must include:

- (1) completed authority prescription form(s); and
- (2) a completed Systemic Juvenile Idiopathic Arthritis PBS Authority Application - Supporting Information Form which includes the following:
 - (i) the date of assessment of severe active systemic juvenile idiopathic arthritis;
 - (ii) details of prior treatment including dose and duration of treatment;
 - (iii) pathology reports detailing CRP and platelet count where appropriate.

An assessment of a patient's response to an initial course of treatment must be conducted following a minimum of 12 weeks of therapy. An application for the continuing treatment must be accompanied with the assessment of response and submitted to the Department of Human Services no later than 4 weeks from the date of completion of the most recent course of treatment. This will enable ongoing treatment for those who meet the continuing restriction for PBS-subsidised treatment.

Where the response assessment is not submitted within this timeframe, the patient will be deemed to have failed to respond to treatment with this drug.

If a patient fails to demonstrate a response to treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition. Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.

Caution: [APPLIES TO PEN DEVICE ONLY]

Inadvertent muscular injection in patients aged less than 12 may occur with the pen device.

Administrative Advice:

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

Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au

Applications for authority to prescribe should be forwarded to:
Department of Human Services
Complex Drugs
Reply Paid 9826
HOBART TAS 7001

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7.4 Add new item:

| Name, Restriction, Manner of administration and form | PBS item code | Max. qty packs | Max. qty units | No. of Rpts | Proprietary Name and Manufacturer | |
|--|---------------|----------------|----------------|-------------|-----------------------------------|----------------|
| TOCILIZUMAB | | | | | | |
| 162 mg/0.9 mL injection, 4 x 0.9 mL pen devices | NEW | 1 | 4 | 5 | Actemra | Roche Products |
| 162 mg/0.9 mL injection, 4 x 0.9 mL syringes | NEW | 1 | 4 | 5 | Actemra | |

Continuing treatment: patients ≥ 30 kg

Category / Program: GENERAL – General Schedule (Code GE)

Prescriber type: Dental Medical Practitioners Nurse practitioners Optometrists Midwives

Restriction Level / Method: Authority Required – In Writing Only

Indication: Systemic juvenile idiopathic arthritis

Treatment Phase: Continuing treatment - Continuing treatment in a patient weighing more than 30 kg

Clinical criteria:

- Patient must have previously received PBS-subsidised treatment with this drug for this condition
- AND**
- Patient must have demonstrated an adequate response to treatment with this drug
- AND**
- Patient must not receive more than 24 weeks of treatment under this restriction

Treatment criteria:

- Must be treated by a rheumatologist; OR
- Patient must be undergoing treatment under the supervision of a paediatric rheumatology treatment centre

Prescribing Instructions:

An adequate response to treatment is defined as:

(a) in a patient with polyarticular course disease:

(i) a reduction in the total active (swollen and tender) joint count by at least 50% from baseline, where baseline is at least 20 active joints; or

(ii) a reduction in the number of the following major active joints, from at least 4, by at least 50%:

- elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or

- shoulder, cervical spine and/or hip (assessed as pain in passive movement and restriction of passive movement, where pain and limitation of movement are due to active disease and not irreversible damage such as joint destruction or bony overgrowth).

(b) in a patient with refractory systemic symptoms:

(i) absence of fever greater than 38 degrees Celsius in the preceding seven days; and/or

(ii) a reduction in the C-reactive protein (CRP) level and platelet count by at least 30% from baseline; and/or

(iii) a reduction in the dose of corticosteroid by at least 30% from baseline.

Determination of whether a response has been demonstrated to initial and subsequent courses of treatment will be based on the baseline measurements of disease severity submitted with the initial treatment application.

The authority application must be made in writing and must include:

(1) completed authority prescription form(s); and

(2) a completed Systemic Juvenile Idiopathic Arthritis PBS Authority Application - Supporting Information Form which includes baseline and current pathology reports detailing CRP and platelet count where appropriate.

The most recent systemic juvenile idiopathic arthritis assessment must be no more than 1 month old at the time of application.

Where the most recent course of PBS-subsidised treatment with this drug was approved under either Initial 1, Initial 2, or Initial 3 treatment restrictions, an assessment of a patient's response must have been conducted following a minimum of 12 weeks of therapy and submitted to the Department of Human Services no later than 4 weeks from the date of completion of treatment.

An application for the continuing treatment must be accompanied with the assessment of response following a minimum of 12 weeks of therapy with this drug and submitted to the Department of Human Services no later than 4 weeks from the date of completion of treatment. This will enable ongoing treatment for those who meet the continuing restriction for PBS-subsidised treatment.

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Where the response assessment is not submitted within this timeframe, the patient will be deemed to have failed to respond to treatment with this drug.

If a patient fails to demonstrate a response to 2 courses of treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition. Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.

A patient may re-trial this drug after a minimum of 12 months have elapsed between the date the last prescription for a PBS-subsidised biological medicine was approved in this cycle and the date of the first application under a new cycle under the Initial 3 treatment restriction.

Caution: [APPLIES TO PEN DEVICE ONLY]

Inadvertent muscular injection in patients aged less than 12 may occur with the pen device.

Administrative Advice:

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

Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au

Applications for authority to prescribe should be forwarded to:
 Department of Human Services
 Complex Drugs
 Reply Paid 9826
 HOBART TAS 7001

7.5 Add new item:

| Name, Restriction, Manner of administration and form | PBS item code | Max. qty packs | Max. qty units | No. of Rpts | Proprietary Name and Manufacturer | |
|--|---------------|----------------|----------------|-------------|-----------------------------------|----------------|
| TOCILIZUMAB | | | | | | |
| 162 mg/0.9 mL injection, 4 x 0.9 mL pen devices | NEW | 1 | 4 | 0 | Actemra | Roche Products |
| 162 mg/0.9 mL injection, 4 x 0.9 mL syringes | NEW | 1 | 4 | 0 | Actemra | |

Balance of supply: initial treatment

Category / Program: GENERAL – General Schedule (Code GE)

Prescriber type: Dental Medical Practitioners Nurse practitioners Optometrists Midwives

Restriction Level / Method: Authority Required – Telephone/Electronic/Emergency

Indication: Systemic juvenile idiopathic arthritis

Treatment Phase:

Initial treatment - Initial 1 (new patient) or Initial 2 (retrial or recommencement of treatment after a break of less than 12 months) or Initial 3 (recommencement of treatment after a break of more than 12 months) - balance of supply

Clinical criteria:

- Patient must have received insufficient therapy with this drug for this condition under the Initial 1 (new patient) restriction to complete 16 weeks treatment; OR
- Patient must have received insufficient therapy with this drug for this condition under the Initial 2 (retrial or recommencement of treatment after a break of less than 12 months) restriction to complete 16 weeks treatment; OR
- Patient must have received insufficient therapy with this drug for this condition under Initial 3 (recommencement of treatment after a break of more than 12 months) restriction to complete 16 weeks treatment

AND

- The treatment must provide no more than the balance of up to 16 weeks treatment available under the above restrictions

Treatment criteria:

- Must be treated by a rheumatologist; OR
- Patient must be undergoing treatment under the supervision of a paediatric rheumatology treatment centre

Caution: [APPLIES TO PEN DEVICE ONLY]

Inadvertent muscular injection in patients aged less than 12 may occur with the pen device.

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Administrative Advice:

Authority approval for sufficient therapy to complete the balance of supply may be requested by telephone by contacting the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

Balance of supply: continuing treatment

Indication: Systemic juvenile idiopathic arthritis

Treatment Phase: Continuing treatment - balance of supply

Clinical criteria:

- Patient must have received insufficient therapy with this drug for this condition under the continuing treatment restriction to complete 24 weeks treatment.

AND

- The treatment must provide no more than the balance of up to 24 weeks treatment available under the above restriction.

Treatment criteria:

- Must be treated by a rheumatologist; OR
- Patient must be undergoing treatment under the supervision of a paediatric rheumatology treatment centre.

Caution: [APPLIES TO PEN DEVICE ONLY]

Inadvertent muscular injection in patients aged less than 12 may occur with the pen device.

Administrative Advice:

Authority approval for sufficient therapy to complete the balance of supply may be requested by telephone by contacting the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

‘The Department of Human Services’ to be updated to Services Australia where it appears.

This restriction may be subject to further review. Should there be any changes made to the restriction the Sponsor will be informed.

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor’s Comment

The sponsor had no comment.