

6.19 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 to extend the current Section 85 (General Schedule), Authority Required listings of subcutaneous (SC) injection presentations of tocilizumab (tocilizumab SC from herein) to include treatment of severe active polyarticular juvenile idiopathic arthritis (JIA).

2 Requested listing

- 2.1 The submission requested to have the same listing for tocilizumab SC as the existing tocilizumab intravenous (IV) injection in severe active JIA, with the removal of the criterion that specifies the medical practitioner must request the appropriate number of vials of appropriate strength to provide sufficient drug, based on the weight of the patient, for two infusions.
- 2.2 The submission also requested different maximum quantities and number of repeats (shown below) for initial and continuing treatment for patients weighing < 30 kg and for patients weighing ≥ 30 kg.
- 2.3 Suggestions and additions proposed by the Secretariat to the requested listing are added in italics and suggested deletions are crossed out with strikethrough. Given the size of the restrictions, only the proposed additions and deletions are shown below.

< 30 kg body weight (dosing Q3W)

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, 4 x 0.9 mL auto-injector	4	4	\$ [REDACTED]	Actemra Roche Products
162 mg/0.9 mL, 4 x 0.9 mL syringe	4	4		

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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, 4 x 0.9 mL auto-injector	4	3	\$ [REDACTED]	Actemra Roche Products
162 mg/0.9 mL, 4 x 0.9 mL syringe	4	3		

≥ 30 kg body weight (dosing Q2W)

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, 4 x 0.9 mL auto-injector	4	0	\$ [REDACTED]	Actemra Roche Products
162 mg/0.9 mL, 4 x 0.9 mL syringe	4	0		

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, 4 x 0.9 mL auto-injector	4	4	\$ [REDACTED]	Actemra Roche Products
162 mg/0.9 mL, 4 x 0.9 mL syringe	4	4		

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, 4 x 0.9 mL auto-injector	1	0	\$ [REDACTED]	Actemra Roche Products
162 mg/0.9 mL, 4 x 0.9 mL syringe	1	0		

Public Summary Document – March 2019 PBAC Meeting

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
Condition:	Severe active juvenile idiopathic arthritis
PBS Indication:	Severe active juvenile idiopathic arthritis
Treatment phase:	Initial treatment - Initial 1 (new patient or patient recommencing treatment after a break of more than 12 months) Initial treatment - Initial 2 (change or recommencement of treatment after break of less than 12 months)
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Clinical criteria:	Patient must not receive more than 16 weeks of treatment under this restriction.
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. <i>At the time of initial authority application, medical practitioners must request the appropriate number of repeats, based on the weight of the patient as follows: for the patients under 30 kg the 162 mg dose every 3 weeks, to provide a sufficient amount for up to 24 weeks of treatment. For the patients of 30 kg or over the 162 mg dose every 2 weeks, to provide sufficient amount for up to 16 weeks of treatment.</i>

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
Condition:	Severe active juvenile idiopathic arthritis
PBS Indication:	Severe active juvenile idiopathic arthritis
Treatment phase:	Continuing treatment Continuing treatment – balance of supply
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined

<p>Prescriber Instructions</p>	<p>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.</p> <p>At the time of continuing authority application, medical practitioners must request the appropriate number of repeats, based on the weight of the patient as follows: for the patients under 30 kg the 162 mg dose every 3 weeks, and for the patients of 30 kg or over the 162 mg dose every 2 weeks to provide a sufficient amount for up to 24 weeks of treatment.</p>
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- 2.4 The pre-PBAC response requested changing the maximum quantity and number of repeats from the Secretariat’s proposed maximum quantity of 1 with 0 repeats to a maximum quantity of 1 with 1 repeat. The pre-PBAC response indicated that this would reduce the number of requests for additional repeats by prescribers.

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

3 Background

- 3.1 Tocilizumab SC was TGA registered on 19 November 2018 for the treatment of polyarticular JIA.
- 3.2 The auto-injector presentation of tocilizumab SC was recommended by the PBAC for the treatment of severe active rheumatoid arthritis in July 2018.
- 3.3 The pre-filled syringe presentation of tocilizumab SC was recommended by the PBAC for the treatment of patients with prior DMARD inadequate response as monotherapy or in combination with methotrexate (MTX), on a cost-minimisation basis with other bDMARDs in March 2016.
- 3.4 The IV presentation of tocilizumab was recommended by the PBAC for the treatment of active polyarticular course JIA as a single agent or in combination with MTX on a cost-minimisation basis compared with etanercept and adalimumab at its November 2013 meeting.

4 Comparator

- 4.1 The minor submission nominated IV tocilizumab as its main comparator. This was appropriate. Etanercept and adalimumab are also appropriate comparators.

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 comments

- 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 117 trial, a phase 1b, single-arm, open-label, multicentre trial designed to investigate the pharmacokinetics, pharmacodynamics and safety of tocilizumab SC in paediatric patients who had an inadequate response to or were intolerant to MTX. The efficacy of tocilizumab SC was an exploratory outcome of the trial. The minor submission concluded the results of the study demonstrated adequate pharmacokinetic exposures and pharmacodynamic responses similar to those achieved with the tocilizumab IV dosing regimens for severe active JIA. The minor submission further noted 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 severe active JIA.
- 5.4 As this was a minor submission, the data was not independently evaluated.

Clinical claim

- 5.5 The minor submission claimed that based on data from the JIGSAW 117 trial, tocilizumab SC is equivalent in efficacy and safety to IV tocilizumab.

Economic analysis

- 5.6 The minor submission presented a cost-minimisation analysis against tocilizumab IV over a 52-week period (Table 1 below).
- 5.7 The minor submission proposed the following equi-effective doses:
- Tocilizumab 162 mg administered as SC injection (Q3W for patients < 30 kg or Q2W for patients ≥ 30 kg)
 - Tocilizumab administered as an IV infusion Q3W (10 mg/kg for patients < 30 kg or 8 mg/kg for patients ≥ 30 kg)

Table 1: Cost-minimisation analysis against IV tocilizumab over 52 weeks (a year)

Tocilizumab SC		Tocilizumab IV	
Cost-minimised AEMP		Effective AEMP	
162 mg (pack of 4): \$ [REDACTED]		80 mg: \$ [REDACTED]	
162 mg (single syringe/pen): \$ [REDACTED]		200 mg: \$ [REDACTED]	
400 mg: \$ [REDACTED]		400 mg: \$ [REDACTED]	
Cost-minimised DPMQ		*Prices above are indication specific	
\$ [REDACTED]			
Mean body weight of patient ^a			
< 30 kg	≥ 30 kg	< 30 kg	≥ 30 kg
21.51 kg	50.02 kg	21.51 kg	50.02 kg
Dose per administration			
< 30 kg	≥ 30 kg	< 30 kg	≥ 30 kg
162 mg	162 mg	215.09 mg	400.16 mg
AEMP per administration			
< 30 kg	≥ 30 kg	< 30 kg	≥ 30 kg
\$ [REDACTED]	\$ [REDACTED]	[REDACTED]	[REDACTED]
Number of administrations over 52 weeks			
< 30 kg	≥ 30 kg	< 30 kg	≥ 30 kg
17.33	26.0	13.0	13.0
AEMP per patient over 52 weeks			
< 30 kg	≥ 30 kg	< 30 kg	≥ 30 kg
\$ [REDACTED]	\$ [REDACTED]	[REDACTED]	[REDACTED]
Weighted AEMP per patient over 52 weeks ^b			
	\$ [REDACTED]		[REDACTED]
AEMP per patient over 52 weeks weighted by public/private hospital usage ^c			
	-		[REDACTED]
Administration costs over 52 weeks ^d			
	-		[REDACTED]
Copayment over 52 weeks			
	\$124.88		[REDACTED]
Average net cost over 52 weeks			
	\$ [REDACTED]		[REDACTED]

Source: Table 3, p16 and Table 4 p17 of the minor submission

Abbreviations: AEMP: approved ex-manufacturer price, IV: intravenous, SC: subcutaneous

Notes: ^a Based on data from the CHERISH trial comparing tocilizumab IV with placebo in patients with polyarticular active course JIA;

^b Weighted AEMP based on weight group proportions from the CHERISH trial; ^c Private/public hospital split of 18.2%/81.8% derived from Medicare statistics (PBS/RPBS items processed between September 2017 to October 2018); ^d Based on MBS item 14245

5.8 The minor submission utilised patient data from the CHERISH trial (which the November 2013 tocilizumab IV submission was based on), a phase III randomised double-blind placebo controlled trial comparing tocilizumab IV with placebo, to inform average body weight and proportion of patients in the < 30 kg and ≥ 30 kg weight groups for the cost-minimisation analysis. The PBAC considered this was appropriate. The minor submission deemed JIGSAW 117 insufficient to inform an economic evaluation as there were less than 50 patients enrolled in the trial.

5.9 The Product Information (PI) specified 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 (including resuscitation equipment, protocols and appropriately trained personnel) in case of the need to initiate management of serious hypersensitivity reactions, including anaphylaxis (tocilizumab PI, p3). A consultation item fee has not been included in the

tocilizumab SC arm of the cost-minimisation analysis. The pre-PBAC response claimed it is standard practice to administer the initial dose of tocilizumab SC at the time of prescribing and that this practice is facilitated by a Sampling Program run by the sponsor that provides the prescriber with free tocilizumab SC that can be administered at the time of prescribing. As such, the pre-PBAC response argued that the consultation fees applicable when prescribing both IV and SC formulations are effectively offset and therefore excluded from the cost-minimisation analysis. The PBAC noted that free samples would not be permitted in all hospitals.

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

- 5.10 The minor submission estimated the cost of treatment over 52 weeks to be \$ [REDACTED], based on the cost-minimised AEMP of \$ [REDACTED] for a pack of 4 syringes/pens.

Estimated PBS usage & financial implications

- 5.11 The minor submission claimed that the listing of tocilizumab for severe active JIA would have no financial impact to the PBS. The minor submission stated that the SC presentation was expected to substitute for the existing IV presentation and not change the number of patients accessing tocilizumab. As such, the sponsor did not expect there to be a financial impact to Government and hence a Section 4 workbook was not completed. While it is true that the SC listing may not result in a net financial impact for Government, there would likely to be an impact to the MBS with a reduction in the number of infusions required and the PBS/RPBS with displacement of IV tocilizumab by tocilizumab SC.
- 5.12 The pre-PBAC response provided estimates of the change in number of MBS services from switching to tocilizumab SC (Table 2) based on an assumed 55% uptake of tocilizumab SC in year 1 of listing increasing to 85% on the basis the adoption rate of SC formulations in the treatment of rheumatoid arthritis has reached approximately 85% in Australia.

Table 2: Estimated number of patients and change in MBS services

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Patients with JIA ^a	■	■	■	■	■	■
Patients with polyarticular JIA ^b	■	■	■	■	■	■
Tocilizumab SC uptake (%)	55%	65%	75%	85%	85%	85%
Tocilizumab SC patients	■	■	■	■	■	■
Volume of MBS services	■	■	■	■	■	■

Source: 6.19 Tocilizumab S pJIA Section 4 workbook.xlsx and p2 of the pre-PBAC response

Abbreviations: JIA, juvenile idiopathic arthritis; SC, subcutaneous

Notes: ^a Projected number of patients based on 10% PBS sample of number of tocilizumab scripts;

^b Based on assumption that 90% of patients with JIA have polyarticular JIA.

The redacted table shows that at Year 6, the estimated number of tocilizumab SC patients would be less than 10,000.

- 5.13 As this was a minor submission, the 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 subcutaneous (SC) presentations of tocilizumab for the treatment of severe active polyarticular juvenile idiopathic arthritis (JIA) on a cost-minimisation basis to IV (intravenous) tocilizumab. The PBAC considered that tocilizumab SC was likely to be equivalent in efficacy and safety to IV tocilizumab.
- 6.2 Based on the evidence presented in the submission, the PBAC considered the equi-effective doses were tocilizumab SC 162 mg Q3W for the patients <30 kg and Q2W for patients ≥ 30 kg and IV tocilizumab 10 mg/kg for patients < 30 kg and 8 mg/kg for patients ≥ 30 kg.
- 6.3 For paediatric patients <30 kg, the PBAC recommended a maximum quantity of one with one repeat for both initial and continuing treatment. For paediatric patients ≥ 30 kg, the PBAC recommended a maximum quantity of one with one repeat for initial treatment and one with two repeats for continuing treatment. For adult patients, the PBAC recommended a maximum quantity of one with three repeats for initial treatment and one with five repeats for continuing treatment. This would provide most patients (except for patients <30 kg) with up to 16 weeks of initial treatment and 24 weeks of continuing treatment consistent with other bDMARD listings in this indication. The PBAC noted that a maximum quantity of one with one repeat for paediatric patients <30 kg would instead provide up to 24 weeks of initial treatment. However, the PBAC considered that, despite this being inconsistent with other bDMARDs in this indication and the recommendation for patients ≥ 30 kg, given the available pack size of 4 and the Q3W dosing regimen for patients <30 kg, a treatment

period of 24 weeks (corresponding to 2 packs) would be required to allow for adequate assessment of treatment response.

- 6.4 The PBAC considered it would be appropriate to write to the Australian Rheumatology Association (ARA) prior to the listing of tocilizumab SC for severe active JIA so that the ARA may notify prescribers of the upcoming listing. The PBAC considered it would be beneficial for prescribers to become familiar with the restrictions prior to the PBS listing date given the differences to the current restrictions for IV tocilizumab for the same indication.
- 6.5 The PBAC noted the cost-minimisation analysis of tocilizumab SC versus IV tocilizumab. The PBAC considered etanercept and adalimumab were also appropriate comparators however noted that tocilizumab IV was the lowest cost comparator.
- 6.6 The PBAC noted the argument presented in the pre-PBAC response that the sponsor facilitates administration of tocilizumab SC at the time of prescribing through a sampling program regarding the exclusion of a consultation item fee from the cost-minimisation analysis for the administration of the first dose of tocilizumab SC (see paragraph 5.9). However, the PBAC considered that the exclusion of the consultation item fee from the cost-minimisation analysis was not appropriate as a significant proportion of hospitals do not permit free samples of medicines.
- 6.7 The PBAC considered that tocilizumab SC would provide an additional treatment option with greater convenience, particularly for patients in rural areas without access to a nearby hospital.
- 6.8 The PBAC recommended that IV tocilizumab and the 162 mg in 0.9 mL SC forms of tocilizumab should not be considered equivalent for the purposes of substitution (i.e., 'a' flagged in the Schedule).
- 6.9 The PBAC advised that tocilizumab SC is not suitable for prescribing by nurse practitioners.
- 6.10 The PBAC recommended that the Early Supply Rule should apply to the continuing treatment phase listings.
- 6.11 The PBAC noted that this submission is not eligible for an Independent review, as it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

7.1 Add new item:

Amendments to the General statement for Treatment of Patients with Severe Active Juvenile Idiopathic Arthritis are shown separately below the tables.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
TOCILIZUMAB			
162 mg/0.9 mL, 4 x 0.9 mL auto-injector	1	1	Actemra Roche Products
162 mg/0.9 mL, 4 x 0.9 mL syringe	1	1	

Initial treatment (patients < 30 kg & ≥ 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
Condition:	Severe active juvenile idiopathic arthritis
PBS Indication:	Severe active juvenile idiopathic arthritis
Treatment phase:	Initial treatment - Initial 1 (new patient or patient recommencing treatment after a break of more than 12 months)
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a paediatric rheumatologist; or Patient must be undergoing treatment under the supervision of a paediatric rheumatology treatment centre.

Public Summary Document – March 2019 PBAC Meeting

Clinical criteria:	Patient must have severe active juvenile idiopathic arthritis; AND Patient must have received no prior PBS-subsidised treatment with a biological disease modifying anti-rheumatic drug (bDMARD) for this condition; or Patient must not have received PBS-subsidised treatment with adalimumab, etanercept or tocilizumab for this condition in the previous 12 months; AND Patient must have demonstrated severe intolerance of, or toxicity due to, methotrexate; or Patient must have demonstrated failure to achieve an adequate response to 1 or more of the following treatment regimens: (i) oral or parenteral methotrexate at a dose of at least 20 mg per square metre weekly, alone or in combination with oral or intra-articular corticosteroids, for a minimum of 3 months; or (ii) oral methotrexate at a dose of at least 10 mg per square metre weekly together with at least 1 other disease modifying anti-rheumatic drug (DMARD), alone or in combination with corticosteroids, for a minimum of 3 months.
Population criteria:	Patient must be under 18 years of age and a parent or authorised guardian must have signed a patient acknowledgement.

Prescriber Instructions	<p>For the purposes of this restriction 'biological disease modifying anti-rheumatic drug' and 'bDMARD' mean adalimumab, etanercept or tocilizumab.</p> <p>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.</p> <p>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.</p> <p>If treatment with methotrexate alone or in combination with another DMARD is contraindicated according to the relevant TGA-approved Product Information, details must be provided at the time of application.</p> <p>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.</p> <p>The following criteria indicate failure to achieve an adequate response and must be demonstrated in all patients at the time of the initial application:</p> <p>(a) an active joint count of at least 20 active (swollen and tender) joints; OR</p> <p>(b) at least 4 active joints from the following list:</p> <p>(i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or</p> <p>(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).</p> <p>The joint count assessment must be performed preferably whilst still on DMARD treatment, but no longer than 4 weeks following cessation of the most recent prior treatment.</p> <p>The authority application must be made in writing and must include:</p> <p>(1) completed authority prescription form(s); and</p> <p>(2) a completed Juvenile Idiopathic Arthritis PBS Authority Application - Supporting Information Form; and</p> <p>(3) an acknowledgement signed by a parent or authorised guardian.</p> <p>Patients under 30 kg may receive up to 24 weeks of treatment under this restriction. Patients 30 kg and over may receive up to 16 weeks of treatment under this restriction.</p> <p>If a patient fails to respond to PBS-subsidised bDMARD treatment 3 times (once with each agent) they will not be eligible to receive further PBS-subsidised bDMARD therapy in this treatment cycle. A patient may re-trial tocilizumab after a minimum of 12 months have elapsed between the date the last PBS-subsidised bDMARD was stopped and the date of the first application under a new treatment cycle.</p>
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Public Summary Document – March 2019 PBAC Meeting

Administrative Advice:	<p>Use of alternative DMARDs in children is dependent on approval by the Therapeutic Goods Administration as age restrictions may apply.</p> <p>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).</p> <p>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</p> <p>Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
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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
Condition:	Severe active juvenile idiopathic arthritis
PBS Indication:	Severe active juvenile idiopathic arthritis
Treatment phase:	Initial treatment - Initial 2 (new patient or patient recommencing treatment after a break of less than 12 months)
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a paediatric rheumatologist; or Patient must be undergoing treatment under the supervision of a paediatric rheumatology treatment centre.
Clinical criteria:	Patient must have a documented history of severe active juvenile idiopathic arthritis; AND Patient must have received prior PBS-subsidised treatment with adalimumab, etanercept or tocilizumab for this condition in this treatment cycle; AND Patient must not have failed PBS-subsidised therapy with tocilizumab for this condition in the current treatment cycle; AND
Population criteria:	Patient must be under 18 years of age

Public Summary Document – March 2019 PBAC Meeting

<p>Prescriber Instructions</p>	<p>For the purposes of this restriction 'biological disease modifying anti-rheumatic drug' and 'bDMARD' mean adalimumab, etanercept or tocilizumab.</p> <p>The authority application must be made in writing and must include:</p> <p>(1) completed authority prescription form(s); and</p> <p>(2) a completed Juvenile Idiopathic Arthritis PBS Authority Application - Supporting Information Form.</p> <p>Patients under 30 kg may receive up to 24 weeks of treatment under this restriction. Patients 30 kg and over may receive up to 16 weeks of treatment under this restriction.</p> <p>Applications for a patient who has received PBS-subsidised treatment with tocilizumab in this treatment cycle and who wishes to recommence therapy with this drug, must be accompanied by evidence of a response to the patient's most recent course of PBS-subsidised tocilizumab treatment, within the timeframes specified below.</p> <p>Where the most recent course of PBS-subsidised tocilizumab treatment was approved under either of the Initial 1 or 2 treatment restrictions, the patient must have been assessed for response following a minimum of 12 weeks of therapy. This assessment must be submitted no later than 4 weeks from the date that course was ceased.</p> <p>Where the most recent course of PBS-subsidised tocilizumab treatment was approved under the continuing treatment criteria, the patient must have been assessed for response, and the assessment must be submitted no later than 4 weeks from the date that course was ceased.</p> <p>Where a response assessment is not undertaken and submitted within these timeframes, the patient will be deemed to have failed to respond to treatment with tocilizumab.</p> <p>If a patient fails to respond to PBS-subsidised biological disease modifying anti-rheumatic drug (bDMARD) treatment 3 times (once with each agent) they will not be eligible to receive further PBS-subsidised bDMARD therapy in this treatment cycle.</p> <p>An adequate response to treatment is defined as:</p> <p>(a) 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</p> <p>(b) a reduction in the number of the following active joints, from at least 4, by at least 50%:</p> <p>(i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or</p> <p>(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).</p>
<p>Administrative Advice:</p>	<p>Use of alternative DMARDs in children is dependent on approval by the Therapeutic Goods Administration as age restrictions may apply.</p> <p>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).</p> <p>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</p> <p>Applications for authority to prescribe should be forwarded to:</p> <p>Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>

Public Summary Document – March 2019 PBAC Meeting

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
Condition:	Severe active juvenile idiopathic arthritis
PBS Indication:	Severe active juvenile idiopathic arthritis
Treatment phase:	Initial Treatment - Initial 1 (new patient or patient recommencing treatment after a break of more than 12 months) or Initial 2 (change or recommencement of treatment after break of less than 12 months) – balance of supply.
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a paediatric rheumatologist; or Patient must be undergoing treatment under the supervision of a paediatric rheumatology treatment centre.
Clinical criteria:	Patient must have received insufficient tocilizumab therapy under the Initial 1 (new patient or patient recommencing treatment after break of more than 12 months) restriction to complete 16 or 24 weeks treatment; or Patient must have received insufficient tocilizumab therapy under the Initial 2 (change or recommencement of treatment after break of less than 12 months) restriction to complete 16 or 24 weeks treatment; AND The treatment must provide no more than the balance of up to 16 weeks treatment available under the above restrictions for patients 30 kg or over; or The treatment must provide no more than the balance of up to 24 weeks treatment available under the above restrictions for patients under 30 kg.
Administrative Advice:	Authority approval for sufficient therapy to complete a maximum of 16 weeks of treatment 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). Written application for authority approval for sufficient therapy to complete a maximum of 16 weeks of treatment should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001

Continuing treatment (paediatric 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
Condition:	Severe active juvenile idiopathic arthritis
PBS Indication:	Severe active juvenile idiopathic arthritis
Treatment phase:	Continuing Treatment
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a paediatric rheumatologist; or Patient must be undergoing treatment under the supervision of a paediatric rheumatology treatment centre.
Clinical criteria:	Patient must have a documented history of severe active juvenile idiopathic arthritis; AND Patient must have demonstrated an adequate response to treatment with tocilizumab; AND Patient must have received tocilizumab as their most recent course of PBS-subsidised biological disease modifying anti-rheumatic drug (bDMARD) treatment in this treatment cycle; AND Patient must be under 30kg AND Patient must not receive more than 24 weeks of treatment per continuing treatment course authorised under this restriction.

Public Summary Document – March 2019 PBAC Meeting

<p>Prescriber Instructions</p>	<p>For the purposes of this restriction 'biological disease modifying anti-rheumatic drug' and 'bDMARD' mean adalimumab, etanercept or tocilizumab.</p> <p>An adequate response to treatment is defined as:</p> <p>(a) 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</p> <p>(b) a reduction in the number of the following active joints, from at least 4, by at least 50%:</p> <p>(i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or</p> <p>(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).</p> <p>Determination of whether a response has been demonstrated to initial and subsequent courses of treatment will be based on the baseline measurement of joint count submitted with the initial treatment application.</p> <p>The authority application must be made in writing and must include:</p> <p>(1) completed authority prescription form(s); and</p> <p>(2) a completed Juvenile Idiopathic Arthritis PBS Authority Application - Supporting Information Form.</p> <p>All applications for continuing treatment with tocilizumab must include a measurement of response to the prior course of therapy. This assessment must be submitted no later than 4 weeks from the cessation of that treatment course. If the application is the first application for continuing treatment with tocilizumab, it must be accompanied by an assessment of response to a minimum of 12 weeks of treatment with an initial treatment course.</p> <p>Where a response assessment is not undertaken and submitted within these timeframes, the patient will be deemed to have failed to respond to treatment with tocilizumab.</p> <p>If a patient fails to respond to PBS-subsidised bDMARD treatment 3 times (once with each agent) they will not be eligible to receive further PBS-subsidised bDMARD therapy in this treatment cycle.</p>
<p>Administrative Advice:</p>	<p>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</p> <p>Applications for authority to prescribe should be forwarded to:</p> <p>Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>

Public Summary Document – March 2019 PBAC Meeting

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
Condition:	Severe active juvenile idiopathic arthritis
PBS Indication:	Severe active juvenile idiopathic arthritis
Treatment phase:	Continuing Treatment – balance of supply
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a paediatric rheumatologist; or Patient must be undergoing treatment under the supervision of a paediatric rheumatology treatment centre.
Clinical criteria:	Patient must have received insufficient tocilizumab therapy 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.
Administrative Advice:	Authority approval for sufficient therapy to complete a maximum of 24 weeks of treatment 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). Written application for authority approval for sufficient therapy to complete a maximum of 24 weeks of treatment should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001

Public Summary Document – March 2019 PBAC Meeting

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
TOCILIZUMAB 162 mg/0.9 mL, 4 x 0.9 mL auto-injector	1	2	Actemra Roche Products
162 mg/0.9 mL, 4 x 0.9 mL syringe	1	2	

Continuing treatment (paediatric 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
Condition:	Severe active juvenile idiopathic arthritis
PBS Indication:	Severe active juvenile idiopathic arthritis
Treatment phase:	Continuing Treatment
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a paediatric rheumatologist; or Patient must be undergoing treatment under the supervision of a paediatric rheumatology treatment centre.
Clinical criteria:	Patient must have a documented history of severe active juvenile idiopathic arthritis; AND Patient must have demonstrated an adequate response to treatment with tocilizumab; AND Patient must have received tocilizumab as their most recent course of PBS-subsidised biological disease modifying anti-rheumatic drug (bDMARD) treatment in this treatment cycle; AND Patient must be 30kg or over AND Patient must not receive more than 24 weeks of treatment per continuing treatment course authorised under this restriction.

Public Summary Document – March 2019 PBAC Meeting

<p>Prescriber Instructions</p>	<p>For the purposes of this restriction 'biological disease modifying anti-rheumatic drug' and 'bDMARD' mean adalimumab, etanercept or tocilizumab.</p> <p>An adequate response to treatment is defined as:</p> <p>(a) 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</p> <p>(b) a reduction in the number of the following active joints, from at least 4, by at least 50%:</p> <p>(i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or</p> <p>(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).</p> <p>Determination of whether a response has been demonstrated to initial and subsequent courses of treatment will be based on the baseline measurement of joint count submitted with the initial treatment application.</p> <p>The authority application must be made in writing and must include:</p> <p>(1) completed authority prescription form(s); and</p> <p>(2) a completed Juvenile Idiopathic Arthritis PBS Authority Application - Supporting Information Form.</p> <p>All applications for continuing treatment with tocilizumab must include a measurement of response to the prior course of therapy. This assessment must be submitted no later than 4 weeks from the cessation of that treatment course. If the application is the first application for continuing treatment with tocilizumab, it must be accompanied by an assessment of response to a minimum of 12 weeks of treatment with an initial treatment course.</p> <p>Where a response assessment is not undertaken and submitted within these timeframes, the patient will be deemed to have failed to respond to treatment with tocilizumab.</p> <p>If a patient fails to respond to PBS-subsidised bDMARD treatment 3 times (once with each agent) they will not be eligible to receive further PBS-subsidised bDMARD therapy in this treatment cycle.</p>
<p>Administrative Advice:</p>	<p>Use of alternative DMARDs in children is dependent on approval by the Therapeutic Goods Administration as age restrictions may apply.</p> <p>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).</p> <p>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</p> <p>Applications for authority to prescribe should be forwarded to:</p> <p>Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>

Public Summary Document – March 2019 PBAC Meeting

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
Condition:	Severe active juvenile idiopathic arthritis
PBS Indication:	Severe active juvenile idiopathic arthritis
Treatment phase:	Continuing Treatment – balance of supply
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a paediatric rheumatologist; or Patient must be undergoing treatment under the supervision of a paediatric rheumatology treatment centre.
Clinical criteria:	Patient must have received insufficient tocilizumab therapy 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.
Administrative Advice:	Authority approval for sufficient therapy to complete a maximum of 24 weeks of treatment 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). Written application for authority approval for sufficient therapy to complete a maximum of 24 weeks of treatment should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001

Public Summary Document – March 2019 PBAC Meeting

Initial treatment (adult patients)

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
TOCILIZUMAB			
162 mg/0.9 mL, 4 x 0.9 mL auto-injector	1	3	Actemra Roche Products
162 mg/0.9 mL, 4 x 0.9 mL syringe	1	3	

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
Condition:	Severe active juvenile idiopathic arthritis
PBS Indication:	Severe active juvenile idiopathic arthritis
Treatment phase:	Initial treatment - Initial 1 (new patient or patient recommencing treatment after a break of more than 24 months)
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a rheumatologist; or Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis

Public Summary Document – March 2019 PBAC Meeting

<p>Clinical criteria:</p>	<p>Patient must have a documented history of severe active juvenile idiopathic arthritis with onset prior to the age of 18 years;</p> <p>AND</p> <p>Patient must have received no PBS-subsidised treatment with a biological disease modifying anti-rheumatic drug (bDMARD) for this condition in the previous 24 months; or</p> <p>Patient must have received no PBS-subsidised bDMARD treatment for at least 5 years if they failed or ceased to respond to PBS-subsidised bDMARD treatment 3 times (once with each agent) in their last treatment cycle;</p> <p>AND</p> <p>Patient must have failed, in the 24 months immediately prior to the date of the application, to achieve an adequate response to a trial of at least 6 months of intensive treatment with disease modifying anti-rheumatic drugs (DMARDs) which must include at least 3 months continuous treatment with each of at least 2 DMARDs, one of which must be methotrexate at a dose of at least 20 mg weekly and one of which must be: (i) hydroxychloroquine at a dose of at least 200 mg daily; or (ii) leflunomide at a dose of at least 10 mg daily; or (iii) sulfasalazine at a dose of at least 2 g daily; or</p> <p>Patient must have failed, in the 24 months immediately prior to the date of the application, to achieve an adequate response to a trial of at least 6 months of intensive treatment with DMARDs which, if methotrexate is contraindicated according to the Therapeutic Goods Administration (TGA)-approved Product Information or cannot be tolerated at a 20 mg weekly dose, must include at least 3 months continuous treatment with each of at least 2 of the following DMARDs: (i) hydroxychloroquine at a dose of at least 200 mg daily; and/or (ii) leflunomide at a dose of at least 10 mg daily; and/or (iii) sulfasalazine at a dose of at least 2 g daily; or</p> <p>Patient must have failed, in the 24 months immediately prior to the date of the application, to achieve an adequate response to a trial of at least 6 months of intensive treatment with DMARDs which, if 3 or more of methotrexate, hydroxychloroquine, leflunomide and sulfasalazine are contraindicated according to the relevant TGA-approved Product Information or cannot be tolerated at the doses specified above, must include at least 3 months continuous treatment with each of at least 2 DMARDs, with one or more of the following DMARDs being used in place of the DMARDs which are contraindicated or not tolerated: (i) azathioprine at a dose of at least 1 mg/kg per day; and/or (ii) cyclosporin at a dose of at least 2 mg/kg/day; and/or (iii) sodium aurothiomalate at a dose of 50 mg weekly;</p> <p>AND</p> <p>Patient must not receive more than 16 weeks of treatment under this restriction.</p>
<p>Population Criteria:</p>	<p>Patient must be aged 18 years or older.</p>

<p>Prescriber Instructions</p>	<p>For the purposes of this restriction 'biological disease modifying anti-rheumatic drug' and 'bDMARD' mean adalimumab, etanercept or tocilizumab.</p> <p>If methotrexate is contraindicated according to the TGA-approved Product Information or cannot be tolerated at a 20 mg weekly dose, the application must include details of the contraindication or intolerance to methotrexate. The maximum tolerated dose of methotrexate must be documented in the application, if applicable.</p> <p>The application must include details of the DMARDs trialled, their doses and duration of treatment, and all relevant contraindications and/or intolerances.</p> <p>The requirement to trial at least 2 DMARDs for periods of at least 3 months each can be met using single agents sequentially or by using one or more combinations of DMARDs.</p> <p>If the requirement to trial 6 months of intensive DMARD therapy with at least 2 DMARDs cannot be met because of contraindications and/or intolerances of a severity necessitating permanent treatment withdrawal to all of the DMARDs specified above, details of the contraindication or intolerance and dose for each DMARD must be provided in the authority application.</p> <p>The following criteria indicate failure to achieve an adequate response and must be demonstrated in all patients at the time of the initial application:</p> <p>an elevated erythrocyte sedimentation rate (ESR) greater than 25 mm per hour or a C-reactive protein (CRP) level greater than 15 mg per L; AND either</p> <p>(a) an active joint count of at least 20 active (swollen and tender) joints; or</p> <p>(b) at least 4 active joints from the following list:</p> <p>(i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or</p> <p>(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).</p> <p>The joint count and ESR and/or CRP must be determined at the completion of the 6 month intensive DMARD trial, but prior to ceasing DMARD therapy. All measures must be no more than one month old at the time of initial application.</p> <p>If the above requirement to demonstrate an elevated ESR or CRP cannot be met, the application must state the reasons why this criterion cannot be satisfied.</p> <p>The authority application must be made in writing and must include:</p> <p>(1) completed authority prescription form(s); and</p> <p>(2) a completed Juvenile Idiopathic Arthritis PBS Authority Application - Supporting Information Form.</p> <p>If a patient fails to respond to PBS-subsidised bDMARD treatment 3 times (once with each agent) they will not be eligible to receive further PBS-subsidised bDMARD therapy in this treatment cycle. A patient may re-trial tocilizumab after a minimum of 5 years have elapsed between the date of the last approval for PBS-subsidised bDMARD therapy in the last treatment cycle and the date of the first application under a new treatment cycle.</p>
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Public Summary Document – March 2019 PBAC Meeting

Administrative Advice:	<p>The Department of Human Services website (www.humanservices.gov.au) has details of the toxicities, including severity, which will be accepted for the following purposes:</p> <p>(a) exempting a patient from the requirement to undertake a minimum 3 month trial of methotrexate at a 20 mg weekly dose;</p> <p>(b) substituting azathioprine, cyclosporin or sodium aurothiomalate for another DMARD as part of the 6 month intensive DMARD trial;</p> <p>(c) exempting a patient from the requirement for a 6 month trial of intensive DMARD therapy.</p> <p>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</p> <p>Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
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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
Condition:	Severe active juvenile idiopathic arthritis
PBS Indication:	Severe active juvenile idiopathic arthritis
Treatment phase:	Initial treatment - Initial 2 (change or recommencement of treatment after break of less than 24 months)
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a rheumatologist; or Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis
Clinical criteria:	Patient must have a documented history of severe active juvenile idiopathic arthritis with onset prior to the age of 18 years; AND Patient must have received prior PBS-subsidised treatment with adalimumab, etanercept or tocilizumab for this condition in this treatment cycle; AND Patient must not have failed PBS-subsidised therapy with tocilizumab for this condition in the current treatment cycle; Patient must not receive more than 16 weeks of treatment under this restriction;
Population Criteria:	Patient must be aged 18 years or older

Public Summary Document – March 2019 PBAC Meeting

<p>Prescriber Instructions</p>	<p>For the purposes of this restriction 'biological disease modifying anti-rheumatic drug' and 'bDMARD' mean adalimumab, etanercept or tocilizumab.</p> <p>The authority application must be made in writing and must include:</p> <p>(1) completed authority prescription form(s); and</p> <p>(2) a completed Juvenile Idiopathic Arthritis PBS Authority Application - Supporting Information Form.</p> <p>Applications for a patient who has received PBS-subsidised treatment with tocilizumab in this treatment cycle and who wishes to recommence therapy with this drug, must be accompanied by evidence of a response to the patient's most recent course of PBS-subsidised tocilizumab treatment, within the timeframes specified below.</p> <p>Where the most recent course of PBS-subsidised tocilizumab treatment was approved under either of the Initial 1 or 2 treatment restrictions, the patient must have been assessed for response following a minimum of 12 weeks of therapy. This assessment must be submitted no later than 4 weeks from the date that course was ceased.</p> <p>Where the most recent course of PBS-subsidised tocilizumab treatment was approved under the continuing treatment criteria, the patient must have been assessed for response, and the assessment must be submitted no later than 4 weeks from the date that course was ceased.</p> <p>Where a response assessment is not undertaken and submitted within these timeframes, the patient will be deemed to have failed to respond to treatment with tocilizumab.</p> <p>If a patient fails to respond to PBS-subsidised biological disease modifying anti-rheumatic drug (bDMARD) treatment 3 times (once with each agent) they will not be eligible to receive further PBS-subsidised bDMARD therapy in this treatment cycle.</p> <p>An adequate response to treatment is defined as:</p> <p>an ESR no greater than 25 mm per hour or a CRP level no greater than 15 mg per L or either marker reduced by at least 20% from baseline;</p> <p>AND either of the following:</p> <p>(a) an active joint count of fewer than 10 active (swollen and tender) joints; or</p> <p>(b) a reduction in the active (swollen and tender) joint count by at least 50% from baseline; or</p> <p>(c) a reduction in the number of the following active joints, from at least 4, by at least 50%:</p> <p>(i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or</p> <p>(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).</p>
<p>Administrative Advice:</p>	<p>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).</p> <p>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</p> <p>Applications for authority to prescribe should be forwarded to:</p> <p>Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
<p>Category / Program</p>	<p>GENERAL – General Schedule (Code GE)</p>

Public Summary Document – March 2019 PBAC Meeting

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
Condition:	Severe active juvenile idiopathic arthritis
PBS Indication:	Severe active juvenile idiopathic arthritis
Treatment phase:	Initial Treatment - Initial 1 (new patient or patient recommencing treatment after a break of more than 24 months) or Initial 2 (change or recommencement of treatment after break of less than 24 months) – balance of supply.
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a paediatric rheumatologist; or Patient must be undergoing treatment under the supervision of a paediatric rheumatology treatment centre.
Clinical criteria:	Patient must have received insufficient tocilizumab therapy under the Initial 1 (new patient or patient recommencing treatment after break of more than 12 months) restriction to complete 16 weeks treatment; or Patient must have received insufficient tocilizumab therapy under the Initial 2 (change or recommencement of treatment after break of less 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.
Administrative Advice:	Authority approval for sufficient therapy to complete a maximum of 16 weeks of treatment 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). Written application for authority approval for sufficient therapy to complete a maximum of 16 weeks of treatment should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001

Public Summary Document – March 2019 PBAC Meeting

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
TOCILIZUMAB 162 mg/0.9 mL, 4 x 0.9 mL auto-injector	1	5	Actemra Roche Products
162 mg/0.9 mL, 4 x 0.9 mL syringe	1	5	

Continuing treatment (adult patients)

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
Condition:	Severe active juvenile idiopathic arthritis
PBS Indication:	Severe active juvenile idiopathic arthritis
Treatment phase:	Continuing Treatment
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a rheumatologist; or Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Clinical criteria:	Patient must have a documented history of severe active juvenile idiopathic arthritis with onset prior to the age of 18 years; AND Patient must have demonstrated an adequate response to treatment with tocilizumab; AND Patient must have received tocilizumab as their most recent course of PBS-subsidised biological disease modifying anti-rheumatic drug (bDMARD) treatment in this treatment cycle; AND Patient must not receive more than 24 weeks of treatment per continuing treatment course authorised under this restriction.
Population Criteria:	Patient must be aged 18 years or older

Public Summary Document – March 2019 PBAC Meeting

<p>Prescriber Instructions</p>	<p>For the purposes of this restriction 'biological disease modifying anti-rheumatic drug' and 'bDMARD' mean adalimumab, etanercept or tocilizumab.</p> <p>An adequate response to treatment is defined as: an ESR no greater than 25 mm per hour or a CRP level no greater than 15 mg per L or either marker reduced by at least 20% from baseline; AND either of the following: (a) an active joint count of fewer than 10 active (swollen and tender) joints; or (b) a reduction in the active (swollen and tender) joint count by at least 50% from baseline; or (c) a reduction in the number of the following active joints, from at least 4, by at least 50%: (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).</p> <p>Where the baseline active joint count is based on total active joints (i.e. more than 20 active joints), response will be determined according to the reduction in the total number of active joints. Where the baseline is determined on total number of major joints, the response must be demonstrated on the total number of major joints. If only an ESR or CRP level is provided with the initial application, the same marker will be used to determine response.</p> <p>The authority application must be made in writing and must include: (1) completed authority prescription form(s); and (2) a completed Juvenile Idiopathic Arthritis PBS Authority Application - Supporting Information Form.</p> <p>All applications for continuing treatment with tocilizumab must include a measurement of response to the prior course of therapy. This assessment must be submitted no later than 4 weeks from the cessation of that treatment course. If the application is the first application for continuing treatment with tocilizumab, it must be accompanied by an assessment of response to a minimum of 12 weeks of treatment with an initial treatment course.</p> <p>Where a response assessment is not undertaken and submitted within these timeframes, the patient will be deemed to have failed to respond to treatment with tocilizumab.</p> <p>If a patient fails to respond to PBS-subsidised bDMARD treatment 3 times (once with each agent) they will not be eligible to receive further PBS-subsidised bDMARD therapy in this treatment cycle.</p>
<p>Administrative Advice:</p>	<p>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</p> <p>Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>

Public Summary Document – March 2019 PBAC Meeting

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
Condition:	Severe active juvenile idiopathic arthritis
PBS Indication:	Severe active juvenile idiopathic arthritis
Treatment phase:	Continuing Treatment – balance of supply
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a paediatric rheumatologist; or Patient must be undergoing treatment under the supervision of a paediatric rheumatology treatment centre.
Clinical criteria:	Patient must have received insufficient tocilizumab therapy 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.
Administrative Advice:	Authority approval for sufficient therapy to complete a maximum of 24 weeks of treatment 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). Written application for authority approval for sufficient therapy to complete a maximum of 24 weeks of treatment should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001

TREATMENT OF PATIENTS WITH SEVERE ACTIVE JUVENILE IDIOPATHIC ARTHRITIS

The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of adalimumab, etanercept and tocilizumab for a patient who has severe active juvenile idiopathic arthritis. Where the term bDMARD appears in notes and restrictions, it refers to adalimumab, etanercept and tocilizumab only.

A patient is eligible for PBS-subsidised treatment with only 1 of the 3 bDMARDs at any one time.

From 1 April 2014, a patient receiving PBS-subsidised bDMARD therapy is considered to be in a treatment cycle where they may swap to an alternate bDMARD without having to experience a disease flare. Under these interchangeability arrangements, within a single treatment cycle, a patient may:

- (i) continue to receive long-term treatment with a PBS-subsidised bDMARD while they continue to show a response to therapy; and
- (ii) fail to respond or to sustain a response to each PBS-subsidised bDMARD once only.

Once a patient has either failed or ceased to respond to PBS-subsidised bDMARD treatment 3 times, they are deemed to have completed a single treatment cycle and they must have, at a minimum, a 12 month break in PBS-subsidised biological therapy before they are eligible to receive further PBS-subsidised bDMARD therapy. The length of a treatment break is

Public Summary Document – March 2019 PBAC Meeting

measured from the date the most recent treatment with PBS-subsidised bDMARD treatment was stopped to the date of the first application for initial treatment with a bDMARD under the new treatment cycle.

A patient who was receiving PBS-subsidised bDMARD treatment immediately prior to 1 April 2014 is considered to be in their first cycle as of 1 April 2014. A patient who has had a break in bDMARD treatment of at least 12 months immediately prior to making a new application, on or after 1 April 2014, will commence a new treatment cycle.

A patient who has failed fewer than 3 trials of a bDMARD in a treatment cycle and who has a break in therapy of less than 12 months may commence a further course of treatment within the same treatment cycle.

A patient who has failed fewer than 3 trials of a bDMARD in a treatment cycle and who has a break in therapy of more than 12 months must commence a new treatment cycle.

There is no limit to the number of treatment cycles a patient may undertake.

(1) How to prescribe PBS-subsidised bDMARD therapy after 1 April 2014.

(a) Initial treatment.

Applications for initial treatment should be made where:

- (i) a patient has received no prior PBS-subsidised bDMARD treatment in this treatment cycle and wishes to commence such therapy (Initial 1); or
- (ii) a patient wishes to re-commence treatment with a bDMARD following a break in PBS-subsidised therapy of more than 12 months (Initial 1); or
- (iii) a patient has received prior PBS-subsidised (initial or continuing) bDMARD therapy and wishes to trial an alternate agent (Initial 2) [further details are under 'Swapping therapy' below]; or
- (iv) a patient wishes to re-commence treatment with a specific bDMARD following a break of less than 12 months in PBS-subsidised therapy with that agent (Initial 2).

Initial treatment authorisations will be limited to provide for a maximum of 16 weeks of therapy, *or 24 weeks of therapy for patients under 30kg receiving subcutaneous tocilizumab.*

A patient must be assessed for response to any course of initial PBS-subsidised treatment following a minimum of 12 weeks of therapy, and this assessment must be submitted to the Department of Human Services no later than 4 weeks from the date that course was ceased.

Where a response assessment is not submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with that bDMARD.

For second and subsequent courses of PBS-subsidised bDMARD, it is recommended that a patient is reviewed in the 4 weeks prior to completing their current course of treatment and that an application is posted to the Department of Human Services no later than 2 weeks prior to the patient completing their current treatment course.

(b) Continuing treatment.

Following the completion of an initial treatment course with a specific bDMARD, a patient may qualify to receive up to 24 weeks of continuing treatment with that drug providing they have demonstrated an adequate response to treatment. The patient remains eligible to receive continuing bDMARD treatment with the same drug in courses of up to 24 weeks providing they continue to sustain the response.

It is recommended that a patient be reviewed in the month prior to completing their current course of treatment to ensure uninterrupted bDMARD supply.

Assessments of response to a course of PBS-subsidised therapy must be submitted to the Department of Human Services no later than 4 weeks from the date that course was ceased.

Where a response assessment is not submitted to the Department of Human Services within these timeframes, the patient will be deemed to have failed to respond to treatment with that bDMARD.

(2) Swapping therapy.

Public Summary Document – March 2019 PBAC Meeting

Once initial treatment with the first PBS-subsidised bDMARD is approved, a patient may swap to an alternate bDMARD without having to requalify with respect to the indices of disease severity (joint count) or the prior non-bDMARD therapy requirements, except if the patient has had a break in therapy of more than 12 months.

A patient may trial an alternate bDMARD at any time, regardless of whether they are receiving therapy (initial or continuing) with a bDMARD at the time of the application. However, they cannot swap to a particular bDMARD if they have failed to respond to prior treatment with that drug within the current treatment cycle.

To ensure a patient receives the maximum treatment opportunities allowed under the interchangeability arrangements, it is important that they are assessed for response to every course of treatment approved, within the timeframes specified in the relevant restriction.

To avoid confusion, an application for a patient who wishes to swap to an alternate bDMARD should be accompanied by the approved authority prescription or remaining repeats for the bDMARD the patient is ceasing.

(3) Baseline measurements to determine response.

The Department of Human Services will determine whether a response to treatment has been demonstrated based on the baseline measurements of the joint count submitted with the first authority application for a bDMARD. However, prescribers may provide a new baseline measurement any time that an initial treatment authority application is submitted within a treatment cycle and the Department of Human Services will assess response according to the revised baseline measurement.

(4) Re-commencement of treatment after a 12 month break in PBS-subsidised therapy.

A patient who wishes to start a second or subsequent treatment cycle following a break in PBS-subsidised bDMARD therapy of at least 12 months, must requalify for treatment under the Initial 1 treatment restriction.

(5) Withdrawal of treatment after sustained remission.

Withdrawal of treatment with bDMARDs should be considered in a patient who has achieved and sustained complete remission of disease for 12 months. A demonstration of response to the current treatment should be submitted to the Department of Human Services at the time treatment is ceased.

8 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.

9 Sponsor's Comment

The sponsor had no comment.