

## 6.14 INFLIXIMAB,

**Solution for injection 120 mg in 1 mL pre-filled pen;  
Solution for injection 120 mg in 1 mL pre-filled  
syringe,  
Remsima® SC,  
Celltrion Healthcare Australia Pty Ltd**

### 1 Purpose of Submission

- 1.1 The Category 3 submission requested a new Authority Required listing that provides loading doses for infliximab (Remsima® SC) for the treatment of severe active rheumatoid arthritis (RA) whereby 120 mg is given subcutaneously at weeks 0, 1, 2, 3 and 4 (herein referred to as IFX SC loading doses), and then every 2 weeks thereafter for maintenance.

### 2 Background

- 2.1 At its November 2020 meeting, the PBAC recommended the listing of IFX SC for RA whereby patients required 2 intravenous induction doses (3 mg/kg) given at weeks 0 and 2 (herein referred to as IFX IV induction).
- 2.2 In July 2022, the TGA approved a new dose schedule for RA which allows for loading doses with IFX SC (at weeks 0, 1, 2, 3 and 4) rather than the induction doses with IFX IV.
- 2.3 The current dosage schedule listed on the PBS and proposed dosage schedule is summarised in Table 1.

Table 1: Current and proposed dosage schedule for IFX SC for RA

	Current (with IFX IV induction doses)	Proposed (with IFX SC loading doses)
Dose schedules for rheumatoid arthritis	IFX IV at week 0 and 2 followed by IFX SC at week 6 and then every 2 weeks	IFX SC at week 0, 1, 2, 3 and 4 then every 2 weeks

IFX infliximab; IV intravenous; SC subcutaneous

### 3 Requested listing

New PBS Items Numbers	Name, Restriction, Manner of administration and form	Max Qty (pack)	Max Qty (Injections)	No. of Rpts	DPMQ (s.85)	Name and Manufacturer
TBD	For Initiation: Infliximab SC, 120mg/ml injection, 1 mL pre-filled syringe	1	5	0	\$■	Remsima SC – Celltrion Healthcare Australia Pty Ltd.

New PBS Items Numbers	Name, Restriction, Manner of administration and form	Max Qty (pack)	Max Qty (Injections)	No. of Rpts	DPMQ (s.85)	Name and Manufacturer
TBD	<b>For Initiation:</b> Infliximab SC, 120mg/ml, 1 mL pen device vial/pen	1	5	0	\$■	Remsima SC – Celltrion Healthcare Australia Pty Ltd.

3.1 The submission proposed a new initial listing with a maximum quantity of 5 and no repeats to provide doses for weeks 0, 1, 2, 3 and 4. The submission proposed that the new dosing schedule restrictions should align with the current initial treatment – Initial 1 (new patient) with the removal of the following clinical criterion:

Patient must have undergone two loading dose intravenous infusions of infliximab 3 mg/kg given 2 weeks apart.

3.2 The Secretariat proposed that the new dosing schedule align with the Initial 1, Initial 2, and Initial 3 listings for the IV induction doses of infliximab and include a listing for grandfathering. The PBAC advised this was appropriate.

3.3 The Secretariat proposed that the new IFX SC listing (to provide the loading doses) have a maximum quantity of 3 with 3 repeats. This will provide patients with 20 weeks of treatment<sup>1</sup>, sufficient to demonstrate a response and enough time for the prescriber to seek authority for continuing treatment (similar to 22 weeks with IV). The PBAC advised this was appropriate.

3.4 The Pre-PBAC response accepted the proposed restrictions though noted that patients will have a limited window to fill their next script for weeks 3, 4 and 6 (the start of maintenance) and advised that the 21-day rule would need to be waived.

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

## 4 Comparator

4.1 The submission nominated infliximab IV induction as the main comparator. Whilst infliximab IV induction may be an appropriate comparator, without the requirement of IFX IV induction doses, there are other alternative therapies.

4.2 At its November 2020 meeting, the PBAC considered that while there were alternative biologic disease-modifying drugs (bDMDs) which may be less costly, a switch from those alternative agents to IFX SC for maintenance treatment was less likely, in particular where an assessment of response makes it inappropriate and/or when re-induction with IFX IV would be required. The PBAC further considered that IFX IV followed by IFX SC was likely to deliver improved outcomes, for some patients, compared with a switch to an alternative agent (para 7.12, infliximab Public Summary

---

<sup>1</sup> Script one provides for injections at weeks 0, 1 and 2; script two provides for injections at 3, 4 and 6; script three provides for injections at week 8, 10 and 12 and script four provides for injections at week 14, 16 and 18.

Document (PSD), Nov 2020). With the removal of the requirement for the IFX IV induction doses, IFX SC may replace any of the currently listed bDMDs.

- 4.3 The PBAC could only recommend listing infliximab SC (with loading doses) at a higher price than alternative therapies if it is satisfied that it provides, for some patients, a significant improvement in efficacy or reduction of toxicity over the alternative therapy or therapies (*National Health Act 1953, Section 101(3B)*). Alternative therapies include abatacept, adalimumab, baricitinib, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, tocilizumab, tofacitinib and upadacitinib.

*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.

### ***Consumer comments***

- 5.2 The PBAC noted and welcomed the input from an organisation (1) via the Consumer Comments facility on the PBS website. The National Paediatric Medicines Forum (NPMF) requested the PBAC consider that no age restriction apply to the listing of infliximab for the treatment of severe active rheumatoid arthritis. The NPMF advised that paediatric hospitals have a significant number of adolescent patients with rheumatological conditions that are not able to access PBS funded treatment due to prescribing restrictions. It commented that a subcutaneous pre-filled syringe and pen would improve the quality of life for juvenile patients by enabling administration within the home environment, and that the cost savings to public hospitals for their day stay procedures would be immense as paediatric hospitals have cohorts of hundreds of patients that require regular infusions six-eight weekly.
- 5.3 The PBAC acknowledged that access to appropriate medicines for patients with childhood rheumatic diseases continues to be an important issue.

### ***Clinical trials***

- 5.4 The submission stated there are no clinical trials with IFX SC 120 mg given subcutaneously without intravenous loading doses of infliximab in patients with RA (i.e., using IFX SC in weeks 0, 1, 2, 3, 4 followed by SC administration every two weeks). The submission stated there was one simulation study included in the TGA submission to support registration of IVX SC loading doses (see Table 2).
- 5.5 As a Category 3 submission, no evaluation of the clinical evidence was undertaken.

**Table 2: Trials and associated reports presented in the submission**

Study identifier (ID)	Key data source: PK Study Report	Additional publications
Pharmacokinetic (PK) Study	CERTARA 2021. PK simulations of ct-p13 in rheumatoid arthritis Patients in support of response to EMA: Reference treatment regimen 1. CSC Reference Number: CELL-PMX-CTP13-2581. (Certara 2021)	TGA 2021. Therapeutic Goods Administration. Clinical Evaluation Report, Infliximab, Remsima. Submission number: PM-2021-03776. (TGA 2021)
		EUROPEAN MEDICINES AGENCY 2021. Type II variation assessment report: Infliximab (Remsima). European Medicines Agency. (European Medicines Agency 2021)
		CELLTRION 2022. Population PK and PK-PD Modelling and Simulation (PowerPoint). Celltrion. (Celltrion 2022)

Source: Table 2-5, p27 of the submission

- 5.6 The TGA Clinical Evaluator (TGA Clinical Evaluation Report) noted that although no clinical studies have been conducted with the proposed SC only dosing regimen, population pharmacokinetic simulations indicate that this new posology most closely mimics infliximab exposure over the first 14 weeks following the previously TGA approved dosing regimen combining IV loading doses (3 mg/kg) with SC maintenance dosing. In consideration of the evidence, the TGA Clinical Evaluator recommended that IFX SC be approved to be administered without IV induction by SC injection at a dose of 120 mg at Weeks 0, 1, 2, 3, 4 and every two weeks thereafter.

### ***Clinical claim***

- 5.7 The submission claimed non-inferior comparative effectiveness and safety of IFX SC loading doses compared with IFX IV induction doses.
- 5.8 The PBAC noted no clinical data was presented; however considered that, overall, the claim of non-inferior comparative effectiveness and safety was likely to be reasonable.

### ***Economic analysis***

- 5.9 As a Category 3 submission, the economic analysis has not been independently evaluated.
- 5.10 The submission presented a cost-minimisation approach of IFX SC loading doses compared with IFX IV induction doses over the first 6 weeks of treatment. The equi-effective doses were estimated as IFX SC 120 mg at weeks 0, 1, 2, 3, and 4, and IFX IV 3 mg/kg at weeks 0 and 2.

**Table 3: IFX SC loading doses cost-minimised to IFX IV induction doses for RA**

	IFX SC	IFX IV
Dose	120 mg SC injection	3 mg/ kg IV infusion
Dose regimen	0, 1, 2, 3, 4 weeks (providing 6 weeks of treatment)	0, 2 weeks (providing 6 weeks of treatment)
Number of doses	5	2
Average number of vials per dose	-	3.38 <sup>1</sup> , submission rounded to 4
EMP	\$ [REDACTED] per syringe	\$320.71 per 100 mg vial <sup>2</sup>
% Public hospital use	-	65%
Total drug cost (net of patient copayment at DPMQ level)	\$ [REDACTED]	\$1,268.43
Total admin cost	\$6.38	\$163.04 <sup>3</sup>
Total cost	\$ [REDACTED]	\$2,699.90

Source: Tables 3-3 and 3-4 of the submission.

DPMQ dispensed price for maximum quantity; EMP ex-manufacturer price; IFX infliximab; IV intravenous; SC subcutaneous

<sup>1</sup> Based on a Prospection Analysis. This would be an appropriate dose for a patient weighing 112 kg.

<sup>2</sup> The Secretariat noted the price of IFX IV price reduced on the 1 October to \$253.52 per 100 mg vial

<sup>3</sup> Cost of administration \$81.52 per infusion

- 5.11 The sponsor noted that the calculated ex-manufacturer price (EMP) per injection (\$) is higher than the current EMP of \$332.80 per SC injection.
- 5.12 The sponsor noted that with a change to a maximum quantity of 5 for the loading doses (as proposed in the submission) and using the current EMP per injection (\$332.80), the DPMQ for continuing scripts reduced by \$29.82 to \$728.70 due to a change in supply chain marks-ups (Table ).

**Table 4: DPMQ with different maximum quantities**

IFX SC	Current	Proposed with current price		Proposed with revised price	
	Initial and cont	Initial	Cont	Initial	Cont
Max. quantity	2	5	2	5	2
EMP per dose	\$332.80	\$332.80	\$332.80	\$ [REDACTED]	\$ [REDACTED]
DPMQ	\$758.58	\$1,811.13	\$728.70	\$ [REDACTED]	\$ [REDACTED]

Source: Table 3-5 of the submission

Cont continuing; DPMQ dispensed price for maximum quantity; EMP ex-manufacturer price; IFX infliximab; SC subcutaneous

- 5.13 The sponsor proposed a price increase to an EMP of \$ [REDACTED] per syringe to account for the savings which are generated by the reduction in supply chain costs (from introducing a listing with a larger maximum quantity). The Secretariat noted that changes to costs in the supply chain due to a change in PBS maximum quantity is inadequate justification for an increase to the existing IFX SC EMP.

### **Estimated PBS utilisation and financial implications**

- 5.14 The submission used a market share approach to estimate the financial implications of the proposed listing and Table 5 summarises the key inputs.

**Table 5: Key inputs into financial estimates**

Input	Value	Source/ comment
IFX initiating script market growth	-█%	Based on observed decrease in IFX IV use over last 3 calendar years. With the listing of IFX SC without the requirement of IFX IV loading doses, IFX SC may substitute for other listed treatments for RA.
Script substitution rate	0.5	2 scripts for IFX IV induction doses will be displaced by 1 script for 5 syringe/pens of IFX SC.
Uptake of IFX SC loading doses	█% in Yr 1 increasing to █% in Yr 6	Sponsor assumption
Cost, DPMQ, IFX SC	\$█	For a maximum quantity of 5 injections
IFX vials per script (for cost offset calculation)	3.38, rounded to 4	Analysis of PBS data
Cost DPMQ, IFX IV	\$█	65% public use

Source: Table 4-3 of submission;  
DPMQ dispensed price for maximum quantity; IFX infliximab; IV intravenous; SC subcutaneous

5.15 Table summarises the estimated net financial implications for the proposed listing of IFX SC loading doses on the PBS/RPBS.

**Table 6: Estimated use and financial implications**

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
<b>Estimated extent of use, scripts dispensed</b>						
SC loading dose	█ <sup>1</sup>	█ <sup>1</sup>	█ <sup>1</sup>	█ <sup>1</sup>	█ <sup>1</sup>	█ <sup>1</sup>
IV induction dose	-█ <sup>1</sup>	-█ <sup>1</sup>	-█ <sup>1</sup>	-█ <sup>1</sup>	-█ <sup>1</sup>	-█ <sup>1</sup>
<b>Estimated financial implications, cost to PBS/ RPBS less copayments</b>						
SC loading dose (\$)	█ <sup>2</sup>	█ <sup>2</sup>	█ <sup>2</sup>	█ <sup>2</sup>	█ <sup>2</sup>	█ <sup>2</sup>
IV induction dose (\$)	-█ <sup>3</sup>	-█ <sup>3</sup>	-█ <sup>3</sup>	-█ <sup>3</sup>	-█ <sup>3</sup>	-█ <sup>3</sup>
<b>Net financial implications</b>						
Net cost to PBS/RPBS (\$)	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>
Net cost to MBS (\$)	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>
Net cost to health budget (\$)	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>	█ <sup>3</sup>

The redacted values correspond to the following ranges:

<sup>1</sup> < 500

<sup>2</sup> \$0 to < \$10 million

<sup>3</sup> net cost saving

5.16 The submission estimated the listing of IFX SC loading doses on the PBS/ RPBS would be cost saving. This assumes only substitution of IFX IV induction doses.

5.17 The submission also provided an estimate of the financial consequences of all IFX SC use in maintenance (across all indications) being dispensed using different supply chain costs which flow from the proposed change to the EMP to reflect the supply chain cost savings. The Secretariat noted the net cost of this was zero as the DPMQ for continuing scripts remained unchanged (\$758.58, see Table ).

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

## 6 PBAC Outcome

6.1 The PBAC recommended a new Authority Required listing that provides loading doses for infliximab (Remsima® SC) for the treatment of severe active rheumatoid arthritis

- (RA) whereby 120 mg is given subcutaneously at weeks 0, 1, 2, 3 and 4 (herein referred to as IFX SC loading doses), and then every 2 weeks thereafter.
- 6.2 The PBAC accepted infliximab IV induction as the main comparator, though noted that without the requirement of IFX IV induction doses, IFX SC may replace any of the currently listed alternative therapies (as outlined in paragraph 4.3).
  - 6.3 The PBAC noted the TGA approval to administer IFX SC without IFX IV induction for RA based on similar infliximab exposures over 14 weeks and considered that the claim of non-inferior comparative effectiveness and safety was likely to be reasonable. The PBAC noted no clinical data was provided to support IFX SC providing a significant improvement in efficacy or reduction in toxicity over any of the alternative therapies.
  - 6.4 The PBAC recommended listing on a cost minimisation basis with the lowest cost alternative treatment, calculated over 2 years at the ex-manufacturer price (consistent with the established approach for bDMDs). The PBAC considered the equi-effective doses of IFX SC and the alternative therapies could be derived with reference to the therapeutic relativity sheets and relevant Product Information documents.
  - 6.5 The PBAC recommended listing with a maximum quantity of 3 with 3 repeats, which will provide 20 weeks of initial treatment.
  - 6.6 The PBAC noted that, with a recommendation to list on the basis of cost minimisation to the lowest cost alternative, the listing of IFX SC loading doses would likely be cost neutral to the PBS or result in a modest net save as it will predominantly replace therapies that are either of equivalent cost or more expensive.
  - 6.7 The PBAC recommended flow-ons to the existing infliximab SC balance of supply listing to ensure patients initiating via the SC loading doses are eligible.
  - 6.8 The PBAC recommended that infliximab subcutaneous listings with maximum quantity of 3 with 3 repeats for rheumatoid arthritis should be exempt from the Early Supply Rule because the proposed maximum quantity is not sufficient for one months' treatment.
  - 6.9 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because infliximab SC (with loading doses) is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over the alternative therapies, or not expected to address a high and urgent unmet clinical need given the presence of alternative therapies, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met.
  - 6.10 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:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
INFLIXIMAB					
infliximab 120 mg/mL injection, 1 mL syringe	NEW	3	3	3	Remsima SC
infliximab 120 mg/mL injection, 1 mL pen device	NEW	3	3	3	Remsima SC
<b>Restriction Summary [new] / Treatment of Concept: [new]</b>					
<b>Concept ID</b> (for internal Dept. use)	<b>Category / Program:</b> GENERAL – General Schedule (Code GE)				
	<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners				
	<b>Restriction type:</b> <input checked="" type="checkbox"/> Authority Required (in writing only via post/HPOS upload):				
	<b>Administrative Advice:</b> PBS AUTHORITY APPLICATIONS FOR SEVERE ACTIVE RHEUMATOID ARTHRITIS...				
	<b>Administrative Advice:</b> <i>The patient will require two supplies to complete their loading doses. The first supply will provide for the loading doses at weeks 0, 1 and 2, and the second supply will provide for the remaining loading doses at weeks 3 and 4, as well as the first fortnightly dose at week 6.</i>				
	<b>Administrative Advice:</b> The application should indicate which formulation e.g. pre-filled pen or pre-filled syringe to ensure appropriate item is approved.				
	<b>Administrative Advice:</b> No increase in the maximum quantity or number of units may be authorised.				
	<b>Administrative Advice:</b> No increase in the maximum number of repeats may be authorised.				
	<b>Administrative Advice:</b> The Services Australia website ( <a href="http://www.servicesaustralia.gov.au">www.servicesaustralia.gov.au</a> ) has details of the toxicities, including severity, which will be accepted where one is claimed.				
	<b>Administrative Advice:</b> Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at <a href="http://www.servicesaustralia.gov.au">www.servicesaustralia.gov.au</a> Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at <a href="http://www.servicesaustralia.gov.au/hpos">www.servicesaustralia.gov.au/hpos</a> Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001				
	<b>Indication:</b> Severe active rheumatoid arthritis				
	<b>Treatment Phase:</b> <i>Initial treatment with the subcutaneous form – Initial 1 (new patient)</i>				
	<b>Treatment criteria:</b>				
	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– November 2022 PBAC Meeting

	<b>Clinical criteria:</b>
	Patient must not have received PBS-subsidised treatment with a biological medicine for this condition
	<b>AND</b>
	<b>Clinical criteria:</b>
	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
	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
	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 3 months of continuous treatment with a DMARD where 2 of: (i) hydroxychloroquine, (ii) leflunomide, (iii) sulfasalazine, are either contraindicated according to the relevant TGA-approved Product Information or cannot be tolerated at the doses specified above in addition to having a contraindication or intolerance to methotrexate: the remaining tolerated DMARD must be trialled at a minimum dose as mentioned above; or
	Patient must have a contraindication/severe intolerance to each of: (i) methotrexate, (ii) hydroxychloroquine, (iii) leflunomide, (iv) sulfasalazine; in such cases, provide details for each of the contraindications/severe intolerances claimed in the authority application
	<b>AND</b>
	<b>Clinical criteria:</b>
	The treatment must be given concomitantly with methotrexate at a dose of at least 7.5 mg weekly
	<b>Population criteria:</b>
	Patient must be at least 18 years of age
	<b>Prescribing Instructions:</b> 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 including severity to methotrexate. The maximum tolerated dose of methotrexate must be documented in the application, if applicable. The application must include details of the DMARDs trialled, their doses and duration of treatment, and all relevant contraindications and/or intolerances including severity. 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. 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 including severity and dose for each DMARD must be provided in the authority application.
	<b>Prescribing Instructions:</b> The following criteria indicate failure to achieve an adequate response and must be demonstrated in all patients at the time of the initial application: 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 (a) a total 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:

Public Summary Document– November 2022 PBAC Meeting

	(i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or (ii) shoulder 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>Prescribing Instructions:</b> 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.
	<b>Prescribing Instructions:</b> If the requirement to demonstrate an elevated ESR or CRP cannot be met, the application must state the reasons why this criterion cannot be satisfied. Treatment with prednisolone dosed at 7.5 mg or higher daily (or equivalent) or a parenteral steroid within the past month (intramuscular or intravenous methylprednisolone or equivalent) is an acceptable reason.
	<b>Prescribing Instructions:</b> 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.
	<b>Prescribing Instructions:</b> The authority application must be made in writing and must include: (a) a completed authority prescription form(s); and (b) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	<b>Prescribing Instructions:</b> An assessment of a patient's response to this initial course of treatment must be conducted following a minimum of 12 weeks of treatment and no later than 4 weeks from the cessation of that treatment course. If the response assessment is not conducted within these timeframes, the patient will be deemed to have failed this course of treatment.
	<b>Prescribing Instructions:</b> Where a response assessment is not conducted within the required timeframe, the patient will be deemed to have failed to respond to treatment with this drug, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.
	<b>Prescribing Instructions:</b> If a patient fails to demonstrate a response to treatment with this drug under this restriction they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition.
<b>Restriction Summary [new] / Treatment of Concept: [new]</b>	
<b>Concept ID</b> (for internal Dept. use)	<b>Category / Program:</b> GENERAL – General Schedule (Code GE)
	<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners
	<b>Restriction type:</b> <input checked="" type="checkbox"/> Authority Required (in writing only via post/HPOS upload):
	<b>Indication:</b> Severe active rheumatoid arthritis
	<b>Treatment Phase:</b> <i>Initial treatment with the subcutaneous form – Initial 2 (change or recommencement of treatment after a break in biological medicine of less than 24 months)</i>
	<b>Treatment criteria:</b>
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis
	<b>AND</b>
	<b>Clinical criteria:</b>

Public Summary Document– November 2022 PBAC Meeting

	Patient must have received prior PBS-subsidised treatment with a biological medicine for this condition
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must not have failed to respond to previous PBS-subsidised treatment with this drug for this condition
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must not have already failed, or ceased to respond to, PBS-subsidised biological medicine treatment for this condition 5 times
	<b>AND</b>
	<b>Clinical criteria:</b>
	The treatment must be given concomitantly with methotrexate at a dose of at least 7.5 mg weekly
	<b>Population criteria:</b>
	Patient must be at least 18 years of age
	<b>Prescribing Instructions:</b> 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) 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 (b) 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 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>Prescribing Instructions:</b> An application for a patient who has received PBS-subsidised treatment with this drug and who wishes to re-commence therapy with this drug, must be accompanied by evidence of a response to the patient's most recent course of PBS-subsidised treatment with this drug, within the timeframes specified below.
	<b>Prescribing Instructions:</b> Where the most recent course of PBS-subsidised treatment with this drug was approved under either of the Initial 1, Initial 2, Initial 3, first or subsequent continuing treatment restrictions, it is recommended that an assessment of a patient's response is conducted following a minimum of 12 weeks of therapy and no later than 4 weeks from the completion of the most recent course of treatment.
	<b>Prescribing Instructions:</b> An assessment of a patient's response to this initial course of treatment must be conducted following a minimum of 12 weeks of treatment and no later than 4 weeks from the cessation of that treatment course. If the response assessment is not conducted within these timeframes, the patient will be deemed to have failed this course of treatment.
	<b>Prescribing Instructions:</b> Where a response assessment is not conducted within the required timeframe, the patient will be deemed to have failed to respond to treatment with this drug, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.
	<b>Prescribing Instructions:</b> The authority application must be made in writing and must include: (a) a completed authority prescription form(s); and (b) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
	<b>Prescribing Instructions:</b>

Public Summary Document– November 2022 PBAC Meeting

	If a patient fails to demonstrate a response to treatment with this drug under this restriction, they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition.
	<b>Prescribing Instructions:</b> A patient who has demonstrated a response to a course of rituximab must have a PBS-subsidised biological therapy treatment-free period of at least 22 weeks, immediately following the second infusion, before swapping to an alternate biological medicine.
<b>Restriction Summary [new] / Treatment of Concept: [new]</b>	
<b>Concept ID</b> (for internal Dept. use)	<b>Category / Program:</b> GENERAL – General Schedule (Code GE)
	<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners
	<b>Restriction type:</b> <input checked="" type="checkbox"/> Authority Required (in writing only via post/HPOS upload):
	<b>Indication:</b> Severe active rheumatoid arthritis
	<b>Treatment Phase:</b> <i>Initial treatment with the subcutaneous form</i> – Initial 3 (recommencement of treatment after a break in biological medicine of more than 24 months)
	<b>Treatment criteria:</b>
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis
	<b>Clinical criteria:</b>
	Patient must have previously received PBS-subsidised treatment with a biological medicine for this condition
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must have a break in treatment of 24 months or more from the most recent PBS-subsidised biological medicine for this condition
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must not have failed to respond to previous PBS-subsidised treatment with this drug for this condition
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must not have already failed, or ceased to respond to, PBS-subsidised biological medicine treatment for this condition 5 times
	<b>AND</b>
	<b>Clinical criteria:</b>
	The condition must have an elevated erythrocyte sedimentation rate (ESR) greater than 25 mm per hour; or
	The condition must have a C-reactive protein (CRP) level greater than 15 mg per L
	<b>AND</b>
	<b>Clinical criteria:</b>
	The condition must have either (a) a total active joint count of at least 20 active (swollen and tender) joints; or (b) at least 4 active major joints
	<b>AND</b>
	<b>Clinical criteria:</b>
	The treatment must be given concomitantly with methotrexate at a dose of at least 7.5 mg weekly
	<b>Population criteria:</b>
	Patient must be at least 18 years of age

Public Summary Document– November 2022 PBAC Meeting

	<p><b>Prescribing Instructions:</b> Major joints are defined as (i) elbow, wrist, knee and/or ankle (assessed as swollen and tender); and/or (ii) shoulder 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><b>Prescribing Instructions:</b> All measures of joint count and ESR and/or CRP must be no more than one month old at the time of initial application.</p>
	<p><b>Prescribing Instructions:</b> 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><b>Prescribing Instructions:</b> The authority application must be made in writing and must include: (a) a completed authority prescription form(s); and (b) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).</p>
	<p><b>Prescribing Instructions:</b> An assessment of a patient's response to this initial course of treatment must be conducted following a minimum of 12 weeks of treatment and no later than 4 weeks from the cessation of that treatment course. If the response assessment is not conducted within these timeframes, the patient will be deemed to have failed this course of treatment.</p>
	<p><b>Prescribing Instructions:</b> Where a response assessment is not conducted within the required timeframe, the patient will be deemed to have failed to respond to treatment with this drug, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.</p>
	<p><b>Prescribing Instructions:</b> If a patient fails to demonstrate a response to treatment with this drug under this restriction they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition.</p>

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
INFLIXIMAB					
infliximab 120 mg/mL injection, 1 mL syringe	12553Q	2	2	5	Remsima SC
infliximab 120 mg/mL injection, 1 mL pen device	12554R	2	2	5	Remsima SC

**Restriction Summary [new] / Treatment of Concept: [new]**

<b>Concept ID</b> (for internal Dept. use)	<b>Category / Program:</b> GENERAL – General Schedule (Code GE)
	<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners
	<b>Restriction type:</b> <input checked="" type="checkbox"/> Authority Required (in writing only via post/HPOS upload):
	<b>Administrative Advice:</b> PBS AUTHORITY APPLICATIONS FOR SEVERE ACTIVE RHEUMATOID ARTHRITIS...
	<b>Administrative Advice:</b> The application should indicate which formulation eg. pre-filled pen or pre-filled syringe to ensure appropriate item is approved.
	<b>Administrative Advice:</b> No increase in the maximum quantity or number of units may be authorised.
	<b>Administrative Advice:</b>

Public Summary Document – November 2022 PBAC Meeting

	No increase in the maximum number of repeats may be authorised.
	<b>Indication:</b> Severe active rheumatoid arthritis
	<b>Treatment Phase:</b> Transitioning from non-PBS to PBS-subsidised supply - Grandfather arrangements
	<b>Treatment criteria:</b>
	Must be treated by a rheumatologist; or
	Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis
	<b>Clinical criteria:</b>
	Patient must have received non-PBS-subsidised treatment with this drug for this PBS indication prior to [Listing Date].
	<b>AND</b>
	<b>Clinical criteria:</b>
	Patient must have failed, in the 24 months immediately prior to receiving non-PBS-subsidised treatment, 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
	Patient must have failed, in the 24 months immediately prior receiving non-PBS-subsidised treatment, 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
	Patient must have failed, in the 24 months immediately prior receiving non-PBS-subsidised treatment, to achieve an adequate response to a trial of at least 3 months of continuous treatment with a DMARD where 2 of: (i) hydroxychloroquine, (ii) leflunomide, (iii) sulfasalazine, are either contraindicated according to the relevant TGA-approved Product Information or cannot be tolerated at the doses specified above in addition to having a contraindication or intolerance to methotrexate: the remaining tolerated DMARD must be trialled at a minimum dose as mentioned above; or
	Patient must have a contraindication/severe intolerance to each of: (i) methotrexate, (ii) hydroxychloroquine, (iii) leflunomide, (iv) sulfasalazine; in such cases, provide details for each of the contraindications/severe intolerances claimed in the authority application
	<b>AND</b>
	<b>Clinical criteria:</b>
	The treatment must be/have been given concomitantly with methotrexate at a dose of at least 7.5 mg weekly
	<b>Population criteria:</b>
	Patient must be at least 18 years of age
	<b>Prescribing Instructions:</b>
	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 including severity to methotrexate. The maximum tolerated dose of methotrexate must be documented in the application, if applicable.
	The application must include details of the DMARDs trialled, their doses and duration of treatment, and all relevant contraindications and/or intolerances including severity.
	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.

Public Summary Document– November 2022 PBAC Meeting

	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 including severity and dose for each DMARD must be provided in the authority application.
	<p><b>Prescribing Instructions:</b> The following criteria indicate failure to achieve an adequate response and must be demonstrated in all patients at the time of the initial application: 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 (a) a total 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 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><b>Prescribing Instructions:</b> 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><b>Prescribing Instructions:</b> If the requirement to demonstrate an elevated ESR or CRP cannot be met, the application must state the reasons why this criterion cannot be satisfied. Treatment with prednisolone dosed at 7.5 mg or higher daily (or equivalent) or a parenteral steroid within the past month (intramuscular or intravenous methylprednisolone or equivalent) is an acceptable reason.</p>
	<p><b>Prescribing Instructions:</b> 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><b>Prescribing Instructions:</b> The authority application must be made in writing and must include: (a) a completed authority prescription form(s); and (b) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).</p>
	<p><b>Prescribing Instructions:</b> An assessment of a patient's response to this initial course of treatment must be conducted following a minimum of 12 weeks of treatment and no later than 4 weeks from the cessation of that treatment course. If the response assessment is not conducted within these timeframes, the patient will be deemed to have failed this course of treatment.</p>
	<p><b>Prescribing Instructions:</b> Where a response assessment is not conducted within the required timeframe, the patient will be deemed to have failed to respond to treatment with this drug, unless the patient has experienced a serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.</p>
	<p><b>Prescribing Instructions:</b> If a patient fails to demonstrate a response to treatment with this drug under this restriction they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition.</p>
	<p><b>Administrative Advice:</b> This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.</p>
	<p><b>Administrative Advice:</b></p>

Public Summary Document – November 2022 PBAC Meeting

	Patients may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a 'Grandfathered' patient must qualify under the 'Continuing treatment with subcutaneous form or switching from intravenous form to subcutaneous form' criteria.
	<p><b>Administrative Advice:</b> Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at <a href="http://www.servicesaustralia.gov.au">www.servicesaustralia.gov.au</a> Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at <a href="http://www.servicesaustralia.gov.au/hpos">www.servicesaustralia.gov.au/hpos</a> Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>

Flow on changes to existing infliximab subcutaneous BoS restriction:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
INFLIXIMAB					
infliximab 120 mg/mL injection, 1 mL syringe	12555T	1	1	0	Remsima SC
infliximab 120 mg/mL injection, 1 mL pen device	12566J	1	1	0	Remsima SC
<b>Amend Restriction Summary [new] / Treatment of Concept: [new]</b>					
Concept ID (for internal Dept. use)	<b>Category / Program:</b> GENERAL – General Schedule (Code GE)				
	<b>Prescriber type:</b> <input checked="" type="checkbox"/> Medical Practitioners				
	<b>Restriction type:</b> <input checked="" type="checkbox"/> Authority Required (telephone/electronic):				
	<b>Administrative Advice:</b> PBS AUTHORITY APPLICATIONS FOR SEVERE ACTIVE RHEUMATOID ARTHRITIS...				
	<b>Administrative Advice:</b> <i>The application should indicate which formulation eg. pre-filled pen or pre-filled syringe to ensure appropriate item is approved.</i>				
	<b>Administrative Advice:</b> Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see <a href="http://www.servicesaustralia.gov.au/HPOS">www.servicesaustralia.gov.au/HPOS</a> ) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).				
	<b>Indication:</b> Severe active rheumatoid arthritis				
	<b>Treatment Phase:</b> Balance of supply for Initial treatment, Continuing treatment - subcutaneous form				
	<b>Treatment criteria:</b>				
	Must be treated by a rheumatologist; or				
	Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis				
	<b>AND</b>				
	<b>Clinical criteria:</b>				
	Patient must have received insufficient therapy with this drug for this condition under the Initial treatment with subcutaneous form restriction to complete 22 weeks initial treatment (intravenous and subcutaneous inclusive); or				

	Patient must have received insufficient therapy with this drug for this condition under the continuing treatment with subcutaneous form restriction to complete 24 weeks treatment
	<b>Clinical criteria:</b>
	The treatment must have been prescribed, in the most recent authority application with this drug for this condition, with a quantity that was less than available with respect to at least one of: (i) maximum units, (ii) repeats
	<b>AND</b>
	<b>Clinical criteria:</b>
	The treatment must be given concomitantly with methotrexate at a dose of at least 7.5 mg weekly
	<b>AND</b>
	<b>Clinical criteria:</b>
	The treatment must provide no more than the balance of up to 22 weeks treatment available under the Initial treatment – subcutaneous form; or
	The treatment must provide no more than the balance of up to 24 weeks treatment available under the Continuing treatment – subcutaneous form
	<b>Clinical criteria:</b>
	The treatment must provide, from the most recent authority approval with this drug for this condition, no more than the balance of: (i) 20 weeks treatment under the Initial treatment restriction, (ii) 24 weeks treatment under the Continuing treatment restriction.
	<b>AND</b>
	<b>Population criteria:</b>
	Patient must be at least 18 years of age

***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.