

An addendum has been included at the end of the document.

**5.06 INFLIXIMAB,
Injection 120 mg in 1 mL pre-filled syringe,
Injection 120 mg in 1 mL pre-filled pen,
Remsima[®],
Celltrion Healthcare Australia Pty Ltd.**

1 Purpose of submission

- 1.1 The submission requested Section 85 and Section 100 Authority Required listing of infliximab (IFX) administered via subcutaneous (SC) injection (Remsima[®]) as a biosimilar to IFX administered via intravenous (IV) infusion. This was the first application to the PBAC for Remsima, and if listed will be the first SC formulation of IFX on the PBS. Currently, there are three formulations of IFX IV on the PBS (Remicade[®], Inflectra[®] and Renflexis[®]).
- 1.2 The submission requested listing in most indications currently approved for IFX IV, including for the treatment of adults with:
- severe active rheumatoid arthritis (RA),
 - ankylosing spondylitis (AS),
 - severe refractory Crohn's disease (CD),
 - complex refractory fistulising Crohn's disease (RFCD),
 - severe active psoriatic arthritis (PsA),
 - moderate to severe ulcerative colitis (UC), and
 - severe chronic plaque psoriasis (CPP).

The submission did not request listing for the treatment of moderate to severe UC or moderate to severe CD in patients aged 6-17 years given the lack of evidence in paediatric patients, or for the treatment of acute severe UC (one dose of IFX IV approved) given patients cannot initiate treatment with IFX SC.

For readability, the indications are referred to by their acronym only. The acronym relates to the specific patient population; e.g. RA refers to severe active RA.

- 1.3 The basis of the requested listing was a cost-minimisation analysis (CMA) to IFX IV, based on the weighted cost of treatment across each of the requested PBS indications (Table 1).

Table 1: Key components of the clinical issue addressed by the submission

Component	Description
Population	Adult patients with RA, AS, CD, RFCD, PsA, UC, and CPP .
Intervention	IFX SC (Remsima® SC)
Comparator	IFX IV (Inflectra® / also known as Remsima® IV)
Outcomes	<p>RA Primary: DAS28 change from baseline at week 22 Secondary: ACR 20 50 and 70 Safety: Key safety outcomes: AEs and discontinuations due to AEs Irritable bowel disease (CD and UC) Primary (PK): IFX Ctrough, week22 Secondary: clinical response and remission, defined by CDAI for CD and Mayo score for UC Safety: Key safety outcomes: AEs and discontinuations due to AEs</p>
Clinical claim	<p>RA: 120 mg IFX SC given every 2 weeks has superior efficacy and safety (based on discontinuation rates) compared to 3 mg/kg IFX IV given every 8 weeks. UC: 120 mg IFX SC given every 2 weeks has superior efficacy and non-inferior (similar) safety to 5 mg/kg IFX IV given every 8 weeks. CD: 120 mg IFX SC given every 2 weeks, is at least equivalent (non-inferior) in terms of safety and efficacy to 5 mg/kg IFX IV given every 8 weeks.</p> <p>Given the data presented it is concluded by extrapolation that 120 mg IFX SC given every 2 weeks, is at least equivalent (non-inferior) in terms of efficacy and safety to:</p> <ul style="list-style-type: none"> • 5 mg/kg IFX IV given every 6 weeks for AS, and • 5 mg/kg IFX IV given every 8 weeks for PsA, CPP, RFCD.

Abbreviations: ACR=American College of Rheumatology; AE=adverse event; AS=ankylosing spondylitis; CD=Crohn's disease; CDAI=Crohn's Disease Activity Index; CPP=chronic plaque psoriasis; DAS28=Disease Activity Score 28-joint; IFX=infliximab IV=intravenous; PK=pharmacokinetic outcomes; PsA=psoriatic arthritis; RA=rheumatoid arthritis; UC=ulcerative colitis; SC=subcutaneous; RFCD=refractory fistulising Crohn's disease.

Source: Table 1.2, pp3-4 of the submission.

2 Background

Registration status

- 2.1 The submission was made under the TGA/PBAC Parallel Process. The submission described IFX SC as a biosimilar product to IFX IV. In contrast, the TGA documentation described IFX SC as a new strength and route of administration of IFX. The Sponsor's application to the TGA presented clinical evidence for the indications RA, UC and CD, and requested extrapolation of evidence from these indications to AS, PsA and CPP. The TGA documents available at the time of PBAC consideration were the Clinical Evaluation report (CER; Round 2), the Delegate's Overview, and the Advisory Committee on Medicines (ACM) outcome.
- 2.2 Table 2 presents the proposed TGA indications for IFX SC. The clinical claim for these indications was extrapolated from the clinical evidence in RA, UC and CD.

Table 2: The proposed TGA indications for IFX SC as maintenance treatment in adult patients (≥18 years)

	Proposed indication of IFX SC
RA	“in combination with methotrexate, is indicated for the reduction of signs and symptoms and prevention of structural joint damage (erosions and joint space narrowing) in: <ul style="list-style-type: none"> • patients with active disease despite treatment with methotrexate, and • patients with active disease who have not previously received methotrexate. Remsima® should be given in combination with methotrexate. Efficacy and safety in Rheumatoid Arthritis have been demonstrated only in combination with methotrexate.”
AS	“indicated for the reduction of signs and symptoms and improvement in physical function in patients with active disease”
PsA	“indicated for the treatment of the signs and symptoms, as well as for the improvement in physical function in adult patients with active and progressive psoriatic arthritis who have responded inadequately to disease-modifying anti-rheumatic drug (DMARD) therapy. Remsima® may be administered in combination with methotrexate.”
CPP	“indicated for the treatment of adult patients with moderate to severe plaque psoriasis [i.e. CPP] for whom phototherapy or conventional systemic treatments have been inadequate or are inappropriate. Safety and efficacy beyond 12 months have not been established.”
CD	“indicated for the treatment of moderate to severe Crohn’s disease, to reduce the signs and symptoms and to induce and maintain clinical remission in patients who have an inadequate response to conventional therapies.”
RFCD	“indicated for reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients.”
UC	“indicated for the treatment of moderately severe to severe active ulcerative colitis in patients who have had an inadequate response to conventional therapy.”

Abbreviations: AS=ankylosing spondylitis; CD=Crohn’s disease; CPP=chronic plaque psoriasis; IFX=infliximab; PsA=psoriatic arthritis; RA=rheumatoid arthritis; RFCD=refractory fistulising Crohn’s disease;
 Source: Section 1.6.2, pp30-31 of the submission

2.3 The CER recommended registration of IFX SC in RA, UC, and CD in adults (p276-277). However, the PBAC noted that the CER did not recommend registration for AS, PsA and CPP (p277) due to inadequate demonstration of safety, and raised concerns over:

- extrapolating the safety data for IFX IV 5 mg/kg in patients with AS, PsA and CPP to IFX SC 120 mg, given that the safety of exposure to prolonged higher trough IFX concentrations in patients treated with SC 120 mg compared to IV 5 mg/kg is unknown, and
- the small number of patients in the two trials (of inflammatory bowel disease (IBD) and RA) treated with maintenance therapy IFX SC 120 mg was not adequate to confidently extrapolate safety data from these trials to AS, PsA and CPP.

The CER also noted the uncertainties raised by the European Medicines Agency (EMA) despite their positive recommendations of all the indications, and stated that the TGA was of the opinion “the uncertainties relating to the safety of Remsima 120 mg SC for the treatment of As, PsA and Ps should be satisfactorily resolved in favour of the drug before it is recommended for approval rather than after it has been approved” (p278, TGA CER Round 2).

2.4 The TGA Delegate’s Overview recommended registration of IFX SC for treatment of adult patients in RA, UC and CD based on the clinical evidence available. The Delegate

was also inclined to extrapolate the efficacy and safety of Remsima to AS, PsA and CPP, but considered further independent expert advice from the ACM.

- 2.5 The ACM advised that it is safe and allowable for extrapolation of infliximab SC indications to AS, PsA and CPP (ACM Minutes on Item No. 2.02 infliximab). The ACM expressed their support for the availability of a SC formulation, and considered it to have an overall positive benefit-risk profile for all of the proposed indications.

For more detail on PBAC's view, see section 7 PBAC outcome.

3 Requested listing

- 3.1 The requested abridged listing for IFX SC is provided below. Suggested additions are in italics and deletions are in strikethrough.

Name, restriction, manner of administration, form	Max. qty (packs)	Max. qty (units)	No. of repeats	DPMQ: Section 85	DPMQ: Section 100 (Public)	DPMQ: Section 100 (Private)	Proprietary name and manufacturer
Initial Treatment 1, 2 and 3, Balance of Supply							
Infliximab							
120 mg pre-filled syringe	2	2	2* or 3#	\$ [REDACTED] +	\$ [REDACTED]	\$ [REDACTED]	Remsima®, Celltrion Healthcare Pty Ltd
120 mg pre-filled pen	2	2	2* or 3#	\$ [REDACTED] +	\$ [REDACTED]	\$ [REDACTED]	Remsima®, Celltrion Healthcare Pty Ltd
Continuing Treatment^A, Balance of Supply							
Infliximab							
120 mg pre-filled syringe	2	2	5	\$ [REDACTED] +	\$ [REDACTED]	\$ [REDACTED]	Remsima®, Celltrion Healthcare Pty Ltd
120 mg pre-filled pen	2	2	5	\$ [REDACTED] +	\$ [REDACTED]	\$ [REDACTED]	Remsima®, Celltrion Healthcare Pty Ltd
Category/Program:	GENERAL – General Schedule (Code GE) Section 100 – Highly Specialised Drugs Program: Public & Private Hospital						
PBS indication:	Ankylosing spondylitis, complex refractory fistulising Crohn's disease, moderate to severe ulcerative colitis, severe Crohn's disease, severe active rheumatoid arthritis, severe chronic plaque psoriasis and severe psoriatic arthritis.						
Treatment phase:	Initial treatment 1						
Restriction:	<input checked="" type="checkbox"/> Authority Required – Telephone, Electronic						
Treatment criteria:	<p><u>Indications: ankylosing spondylitis, severe rheumatoid arthritis and severe psoriatic arthritis</u> Must be treated by a rheumatologist; OR Must be treated by a clinical immunologist with expertise in the management of (the indication).</p> <p><u>Indications: severe chronic plaque psoriasis</u> Must be treated by a dermatologist.</p> <p><u>Indications: complex refractory fistulising Crohn's disease, moderate to severe ulcerative colitis and severe Crohn's disease</u> Must be treated by a gastroenterologist (code 87); OR Must be treated by a consultant physician [internal medicine specialising in gastroenterology (code 81)]; OR Must be treated by a consultant physician [general medicine specialising in gastroenterology (code 82)].</p>						
Clinical criteria:	Restriction details for each indication <i>were provided</i> in an attachment to the submission. Common criteria for the following indications: ankylosing spondylitis, complex refractory						

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	<p><u>fistulising Crohn’s disease, moderate to severe ulcerative colitis and severe Crohn’s disease.</u> ‘Patient must not receive more than 12 weeks of treatment under this restriction (excluding loading dose infusions).’</p> <p><u>Common criteria for the following indications: severe chronic plaque psoriasis, rheumatoid arthritis, psoriatic arthritis</u> ‘Patient must not receive more than 16 weeks of treatment (not including loading dose infusions) under this restriction.’</p>
Population criteria:	Patient must be aged 18 years or older.
Prescriber criteria:	Restriction details for each indication <i>were provided</i> in an attachment to the submission.

Treatment phase:	Continuing treatment
Restriction:	<input checked="" type="checkbox"/> Authority Required – Telephone, Electronic, for First continuing treatment [±] . <input checked="" type="checkbox"/> Authority Required – Streamlined, for Subsequent continuing treatment [±] .
Treatment criteria:	As for Initial Treatment.
Clinical criteria:	Restriction details for each indication <i>were provided</i> in an attachment to the submission. <u>Common criteria for all indications</u> ‘Patient must have demonstrated ... an adequate response to treatment’, AND ‘Patient must not receive more than 24 weeks of treatment under this restriction.’
Administrative Advice:	Note Biosimilar preferred prescribing policy Note Prescribers must include the proprietary name (brand) on the prescription to ensure the appropriate item is approved.

* Indications include: ankylosing spondylitis, complex refractory fistulising Crohn’s disease, moderate to severe ulcerative colitis and severe Crohn’s disease.

Indications include: severe active rheumatoid arthritis, severe chronic plaque psoriasis and severe psoriatic arthritis.

^ ‘First’ and ‘subsequent’ continuing treatment for all indications except ulcerative colitis

+ Updated DPMQ. The submission requested a Section 85 DPMQ of \$ [redacted] assuming a wholesale mark-up of \$ [redacted] for AEMP >\$ [redacted]; however, the current wholesale mark-up is [redacted]% for AEMP <\$ [redacted], corresponding to a DPMQ of \$ [redacted]. This was based on the mark-up applicable from 1 January 2021.

± No distinction between first and subsequent continuing treatment for ulcerative colitis, in-line with current PBS listing of IFX IV.

Source: Attachment 2 to the submission (7 separate documents).

3.2 The Sponsor requested Section 85 and Section 100 Highly Specialised Drugs Program (HSDP) Authority Required (Telephone, Electronic; and Streamlined) listing for two formulations of IFX SC (Remsima), 120mg pre-filled syringe and 120mg pre-filled autoinjector pen, for and initial and continuing treatment of adult patients with RA, UC, AS, CD, RFCD, PsA and CPP. The Sponsor stated in the Pre-Sub-Committee Response (PSCR) that difficult to treat patients are often seen in hospital settings and for these patients, IFX treatment is initiated during their hospital stay, which is an opportunity to provide (i) the required self-injection technique training for SC use and (ii) the IFX SC script. However, the PBAC considered that only a Section 85 listing is warranted and noted that all other biologic disease-modifying drugs (bDMDs) administered via SC injections on the PBS are listed under Section 85.

3.3 The wording of the requested restrictions for IFX SC are similar to the corresponding restrictions for IFX IV, but it was assumed that the current PBS listings for IFX IV will enable the prescribing of the two IV loading doses required prior to IFX SC. The PBAC

noted that the wording of the current IFX IV restrictions may need to be amended to permit these loading doses.

- 3.4 The Sponsor requested Authority Required – Streamlined listing for subsequent continuing treatment (or ‘continuing treatment’ in UC), consistent with biosimilar brands of IFX IV and in line with the biosimilar preferred prescribing policy. The Sponsor stated in the PSCR that their request for listing is “in accordance with the Government’s Biosimilar Uptake Drivers for IFX (November 2019) and expects IFX SC to form part of the Price Disclosure data collection, alongside Remicade, Inflectra and Renflexis® (as all contain the same drug and have the same administration by “injection”)”. The PSCR also argued that “the Note relating to Biosimilar preferred prescribing policy should remain.” The ESC noted that if IFX SC is recommended for listing, it would have a separate item number because it has a different route of administration, and biosimilar policy would not apply in this case. Therefore, the administrative advice in the requested restriction noting ‘Biosimilar preferred prescribing policy’ should be deleted and the requested Streamlined listings may not be appropriate. The Sponsor further stated in the pre-PBAC response that listing IFX SC and IFX IV with different Authority levels would be confusing and unnecessarily burdensome for prescribers. The PBAC agreed with the ESC that the premise of biosimilarity for the purposes of PBS listing is flawed given the different routes of administration, where IFX SC is fixed dose and IFX IV is weight-based dosing, and there is evidence of different pharmacokinetic profiles. The PBAC considered that restrictions for IFX SC should not be based on biosimilar policy but consistency with other SC agents and/or similar indications.
- 3.5 For initial treatment, patients receive 6 weeks of IFX IV (two infusions at Week 0 and Week 2 with IV 3 mg/kg or 5 mg/kg depending on the indication), before becoming eligible for treatment with IFX SC. The requested maximum quantities of IFX SC then provide for a total of 18 weeks or 22 weeks of initial treatment with IFX depending on the indication. The stated maximum durations for initial treatment with IFX SC (i.e. ‘12 weeks’ and ‘16 weeks’) do not include the first 6 weeks of treatment with IFX IV.
- 3.6 The PBAC noted that for the CPP, AS, RA and PsA, indications, the Initial 1 restriction stating: ‘Patient must not have received PBS-subsidised treatment with a biological medicine for this condition’ should be removed since patients would already have received IFX IV.
- 3.7 For RA, CPP and PsA, patients treated with IFX SC will receive a maximum of 22 weeks of initial treatment, which is consistent with the current listing of IFX IV for these indications. For AS, CD, RFCD and UC, patients treated with IFX SC will receive a maximum of 18 weeks of initial treatment, which is consistent with the current listing of IFX IV in AS, but provides for an additional 4 weeks of initial treatment in CD, RFCD and UC (maximum of ‘3 doses’ or ‘14 weeks’). The ESC noted that the submission did not provide any justification for the additional 4 weeks of initial treatment with IFX SC in CD, RFCD and UC. The PBAC considered that the maximum duration of initial

treatment for IFX SC should be consistent with established maximums for IFX IV for all indications.

- 3.8 The PBAC advised that the IFX SC restrictions should have an initial SC restriction that allow transition from IV to SC at Week 6 onwards until assessment from Week 12, and a Balance of Supply (to initial SC and continuing SC) to complete what is required for each indication. A continuing restriction will also be required, as the ‘first and subsequent’ continuing restriction will not be applicable here.
- 3.9 The PBAC agreed with the Sponsor that the evaluation of response should remain the same as for IFX IV (even though in the PI the recommended time to response differs for some indications), in line with precedence set by IFX IV and other TNF α s.
- 3.10 For continuing treatment in all indications (for patients who respond to treatment continuation criteria), the requested maximum quantities provide up to 24 weeks of treatment. This is consistent with the current listing of IFX IV in all requested indications.
- 3.11 The PBAC agreed with the ESC that re-induction after a treatment break should not be required, whereas the requested restriction assumes SC is pre-dated by 2 doses of IV. The PBAC advised that the restriction should be consistent with the PI in allowing resumption after treatment break without re-induction.
- 3.12 The PBAC considered that existing IFX patients who have received more than 2 IV doses should be allowed to switch to IFX SC, and the limitation of patients receiving only 2 doses of IFX IV before switching to IFX SC should be resolved in the restriction.
- 3.13 In general, the PBAC considered that the listing for IFX SC should show alignment to the current concepts of initiation, continuation, balance of supply for IFX IV, and ensure assessment at precedented time points.
- 3.14 The PBAC noted that the fixed SC dose limits dose flexibility available with IFX IV: IFX is given every 6 (AS) or 8 weeks at a dose of 3 mg/kg for RA and 5 mg/kg for all other indications. Since IFX IV can be titrated from 1.5 mg/kg to 7.5 mg/kg for RA, and dose adjustments can be made up to 10 mg/kg for CD and RFCD, some patients may need to stay on IFX IV to retain dose flexibility.

For more detail on PBAC’s view, see section 7 PBAC outcome.

4 Population and disease

- 4.1 The proposed indications for IFX SC include:
 - RA, an autoimmune disease caused by chronic inflammation. Typical features of RA include deformities of the fingers and toes.

- AS (or radiographic axial spondyloarthritis), characterised by inflammation of the spine and sacroiliac joints, with inflammation and damage mainly occurring at entheses, the connective tissue between bones and ligaments or tendons.
 - PsA, an inflammatory musculoskeletal disease associated with psoriasis, which affects multiple organs including peripheral and axial joints, entheses, skin and nails and is associated with comorbidities such as osteoporosis and subclinical bowel inflammation.
 - CPP, a chronic inflammatory skin disease characterised by plaque type lesions and is associated with multiple comorbidities including irritable bowel disease (IBD).
 - CD and UC, two common types of IBD, characterised by chronic inflammation of the intestinal tract associated with imbalance of intestinal microbiota. These disorders have somewhat different pathologic and clinical characteristics, but with substantial overlap. In RFCD, the clinical manifestation of fistulas depends upon the area of involvement adjacent to the diseased bowel segment.
- 4.2 IFX is a chimeric human-murine monoclonal antibody that binds to human tumour necrosis factor alpha (TNF α), a pro-inflammatory and immunoregulatory cytokine that mediates chronic inflammation in a number of conditions. If listed, IFX SC would be used as an alternative to IFX IV and have a similar place on the clinical management algorithm.
- 4.3 The draft PI for IFX SC states that all patients must initiate treatment with IFX IV (3 mg/kg or 5 mg/kg depending on the indication) for two infusions administered at Week 0 and Week 2, before commencing IFX SC 120 mg administered every 2 weeks from Week 6. The same re-administration instructions apply to both IFX IV and IFX SC after a break in treatment, but re-induction with IFX IV is not required for patients using IFX SC. The draft PI states that to optimise clinical response during maintenance, patients with RA or CD may dose adjust up to IFX IV 7.5 mg/kg or 10 mg/kg respectively, however there is insufficient information for switching from IFX IV higher than 3 mg/kg for RA or 5 mg/kg for CD every 8 weeks (Q8W) to IFX SC formulation. There is also no information regarding switching from IFX SC formulation to IFX IV. The PBAC noted that there is insufficient information available about switching to IFX SC from higher doses of IFX IV, or from IFX SC back to IFX IV.
- 4.4 The TGA Clinical Evaluation Report (Round 2) noted that the selection of IFX SC 120 mg fixed-dose regimen was based on a pharmacokinetic modelling report which included obese patients (100-150 kg) where the simulated outcomes met the bioequivalence interval. The TGA evaluator also noted that the limited data from Study 1.6 Part 1 at Week 54 and a post-hoc analysis of Part 2 suggest that efficacy was generally comparable between SC 120 mg (n=11) and SC 240 mg (n=7) for patients with CD and between SC 120 mg (n=28) and SC 120/240 mg (n=38) for patients with UC.

5 Comparator

- 5.1 The submission nominated IFX IV (Inflectra®) as the main comparator, stating that IFX SC (Remsima) is a biosimilar formulation. Inflectra (known as Remsima IV overseas) is an approved biosimilar to the original brand Remicade. However, IFX SC has been evaluated for registration by the TGA as a new strength and route of administration (paragraph 2.1), and the PBAC noted that IFX SC is not a biosimilar and therefore the biosimilar prescribing policy should not apply to IFX SC (paragraph 3.4).
- 5.2 The evaluation considered that the nominated comparator is generally reasonable given patients must commence treatment on IFX IV before switching to IFX SC. However, IFX SC (including the IV loading doses), may also substitute for other treatments when initiating therapy thus all other bDMDs available on the PBS for the various different indications are also relevant comparators. The ESC agreed with the evaluation that IFX IV followed by IFX SC may replace a number of alternative therapies.
- 5.3 The PBAC's approach has been to recommend that new, non-inferior or therapeutically equivalent products should be PBS listed at the price of the lowest cost product in a basket of products that have been considered by the PBAC to be either non-inferior or therapeutically equivalent to each other, regardless of the market share, or clinical utility/use of the lowest cost product. This approach is consistent Section 101(3B) of the National Health Act 1953 ('The Act'), which states that "where therapy involving the use of a particular drug or medicinal preparation, or a class of drugs and medicinal preparations, is substantially more costly than an alternative therapy or alternative therapies, whether or not involving the use of other drugs or preparations, the Committee ... shall not recommend to the Minister that the drug, preparation or class be made available as pharmaceutical benefits under this Part unless the Committee is satisfied that the first-mentioned therapy, for some patients, provides a significant improvement in efficacy or reduction of toxicity over the alternative therapy or therapies." In effect, this section of the Act requires PBAC to consider what therapies could be replaced rather than what therapies will be replaced, and any currently listed bDMD could be considered an alternative therapy.
- 5.4 The PBAC considered that the nomination of IFX IV as comparator is appropriate. The PBAC considered that while there are alternative bDMDs which may be less costly, a switch from those alternative agents to IFX SC for maintenance treatment is 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 is likely to deliver improved outcomes, for some patients, compared with a switch to an alternative agent.

For more detail on PBAC's view, see section 7 PBAC outcome.

6 Consideration of the evidence

Sponsor hearing

6.1 The Sponsor requested a hearing for this item, which was presented by a gastroenterologist with expertise in IBD. The clinician discussed the morbidity associated with IBD, the role of IFX IV and IFX SC in the treatment of patients with IBD and the development of IFX anti-drug antibodies. The PBAC considered that the hearing was not informative as it did not add substantively to the evidence presented in the submission.

Consumer comments

6.2 The PBAC noted and welcomed the input from 2 organisations via the Consumer Comments facility on the PBS website, Crohn's & Colitis Australia (CCA) and the National Paediatric Medicines Forum.

6.3 CCA stated that the SC formulation is an important option for consumers because it would not require infusion in a medical facility, providing flexibility for consumers, avoidance of absence from work for treatment, and reduced travel for those particularly in remote or regional areas. For some remote or regional people who cannot travel regularly for infusions, it would provide a new treatment choice. CCA stated that the option of subcutaneous injection of IFX was welcomed by multiple consumers.

6.4 The comments from the National Paediatric Medicines Forum were not relevant to this submission, as IFX SC is not being considered for paediatric use.

Clinical trials

6.5 The literature search identified two head-to-head randomised trials comparing IFX SC (Remsima) to IFX IV (Inflixtra)¹ (Table 3):

- Study 3.5 Part 2 compared IFX SC 120 mg every 2 weeks (Q2W) to IFX IV 3 mg/kg every 8 weeks (Q8W) in patients with RA, and
- Study 1.6 Part 2 compared IFX SC 120/240 mg every 2 weeks (Q2W) to IFX IV 5 mg/kg every 8 weeks (Q8W) in patients with CD or UC.

¹ While Inflectra was the IFX IV brand used in the clinical trials, IFX SC could be used after any brand of IFX IV if the SC formulation is recommended for PBS listing.

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Table 3: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
Study 3.5 Part 2 NCT03147248	FINAL CLINICAL STUDY REPORT (PART 2) A Randomised, Parallel-Group, Phase I/III Study to Evaluate Efficacy, Pharmacokinetics and Safety between Subcutaneous CT-P13 and Intravenous CT-P13 in Patients with Active Rheumatoid Arthritis. PROTOCOL NUMBER 3.5 CT-P13. (Celltrion 2019)	12 August 2019.
Study 1.6 Part 2 NCT02883452	WEEK 30 CLINICAL STUDY REPORT (PART 2) An Open-label, Randomized, Parallel-Group, Phase I Study to Evaluate Pharmacokinetics, Efficacy and Safety between Subcutaneous CT-P13 and Intravenous CT-P13 in Patients with Active Crohn's Disease and Active Ulcerative Colitis PROTOCOL NUMBER CT-P13 1.6. (Celltrion 2018) Celltrion. Final Clinical Study Report (Part 2): An Open-label, Randomized, Parallel-Group, Phase I Study to Evaluate Pharmacokinetics, Efficacy and Safety between Subcutaneous CT-P13 and Intravenous CT-P13 in Patients with Active Crohn's Disease and Active Ulcerative Colitis. (Celltrion 2020)	August 2019 31 March 2020

Source: Table 2.5, pp45-46 of the submission.

- 6.6 The submission did not present any clinical evidence to inform the comparative efficacy and safety between IFX SC and IFX IV in RFCD, AS, PsA or CPP. The clinical claim for these indications was extrapolated from the clinical evidence in RA, UC and CD.
- 6.7 Table 4 presents the key features of the included trials.

Table 4: Key features of the included evidence

Trial	N	Design/duration	Bias	Treatment arms	Population	Key efficacy outcomes
IFX SC 120 mg vs IFX IV 3 mg/kg						
Study 3.5 Part 2 ^a	218	R, MC, DB 30wk ^b / OL extension SC switch in IV arm Wk 30	Low	SC 120 mg ^c IV 3 mg/kg ^d	Active RA	1°: DAS28 (CRP) (Wk 22) 2°: ACR20/50/70, CDAI, SDAI
IFX SC 120/240 mg vs IFX IV 5 mg/kg						
Study 1.6 Part 2 ^a	130	R, MC, OL 30wk ^e / OL extension SC switch in IV arm Wk 30	Low	SC 120 mg (<80 kg) or 240 mg (≥80 kg) ^f IV 5 mg/kg ^g	Active CD or UC	1°: PK Ctrough (Wk 22) 2°: CDAI70/100 (CD) and MSS (UC)

Abbreviations: Ctrough=trough concentration; CD=Crohn's disease; CDAI=Crohn's Disease Activity Index Assessment; DAS28 (CRP)=Disease Activity Score 28 joint counts (C-reactive protein); DB=double blind; IFX=infliximab; IV=intravenous infusion; MC=multicentre; MSS=Mayo Scoring System; OL=open label; PBO=placebo; PK=pharmacokinetic; R=randomised; RA=rheumatoid arthritis; SC=subcutaneous injection; UC=ulcerative colitis; wk=week;

^a Part 2 was designed to demonstrate non-inferiority of IFX SC vs IV in terms of efficacy (Study 3.5) and PK (Study 1.6)

^b Treatment period include dose loading phase (Wks 0 to 6) and maintenance phase (Wks 6 to 54). During dose loading, all patients received IFX IV at Wks 0 and 2. Patients were randomised to either IFX SC or IV at Wk 6. A double-dummy design was used to maintain blinding during the maintenance phase up to Wk 30. IFX IV arm switched to IFX SC via pre-filled syringe at Wk 30. All patients received open label SC during the extended maintenance phase (Wks 30 to 54).

^c During the maintenance phase, patients in the SC treatment arm were administered IFX SC at Wk 6 and every 2 weeks up to Wk 54 with PBO IV at Wk 6, 14 and 22.

^d Patients in IV treatment arm were administered 3 doses of IV 3 mg/kg at Week 6 and every 8 weeks thereafter up to Wk 22 (Wks 14 and 22) with PBO.SC at Wk 6 and every 2 weeks thereafter up to Wk 28.

^e Treatment period include Wks 0 to 6 dose loading phase and Wks 6 to 54 maintenance phase. During dose loading, all patients received IFX IV at Wks 0 and 2. Patients were randomised to either IFX SC or IV at Wk 6. IFX IV arm was then switched to SC based on body weight at Wk 30. All patients received open label SC during the extended maintenance phase (Wks 30 to 54).

^f During the maintenance phase, patients in the SC treatment arm were administered IFX SC at Wk 6 based on body weight and every 2 weeks up to Wk 54. From Wk 30, patients (weight <80 kg) receiving SC 120 mg every 2 weeks, dose escalation were allowed to SC 240 mg every 2 weeks if the patient initially respond but lost response at Wk 30, 38, 46 and 54. Dose escalation was not allowed for patients receiving SC 240 mg every 2 weeks.

^g Patients in IV treatment arm were administered 3 doses of IV 5 mg/kg at Wk 6 and every 8 weeks thereafter up to Wk 22 (Wks 14 and 22), then switched to IFX SC at Wk 30 with doses based on body weight, and further doses of SC treatment every 2 weeks up to Wk 54.

Source: constructed during the evaluation

6.8 Both trials were multicentre randomised parallel group trials comparing IFX SC to IFX IV for maintenance therapy between Week 6 and Week 30; and included extended maintenance phases from Week 30 to Week 54 where all patients on IFX IV switched to IFX SC. Specifically:

- Study 3.5 Part 2 was double-blind double-dummy trial in patients with RA, designed to demonstrate non-inferiority in terms of change (decrease) in DAS28 (CRP) at Week 22, using a pre-specified non-inferiority margin of -0.6 for the 97.5% one-sided confidence interval of the difference.
- Study 1.6 Part 2 was open label in patients with CD or UC, designed to demonstrate non-inferiority in terms of the geometric mean ratio in C-trough at Week 22, using a pre-specified non-inferiority margin of 80% for the 95% one-sided confidence interval.

6.9 All patients received IFX IV (Weeks 0 and 2), and were randomised to either IFX SC or IV at Week 6. Doses in the trials were consistent with the TGA approved/proposed doses, with the exception of the IFX SC arm in Study 1.6 Part 2. Patients <80 kg

received IFX SC 120 mg Q2W and patients ≥ 80 kg received IFX SC 240 mg Q2W; dose escalation to 240 mg Q2W was permitted after Week 30. The weight-based dosing of IFX SC in Study 1.6 Part 2 may potentially overstate the treatment effect for the proposed fixed 120 mg dose in the draft PI, but this may be more relevant for pharmacokinetic outcomes rather than the clinical outcomes given supportive evidence indicating that 120 mg is equally effective for all weights.

- 6.10 The overall risk of bias in the trials was considered low for the primary outcomes, but Study 1.6 Part 2 was a small open label pharmacokinetic trial and was not powered to test for differences in clinical outcomes. More patients discontinued on IFX IV (23.1%) compared to IFX SC (16.7%) in Study 1.6 Part 2.
- 6.11 The submission stated the trial populations were broadly generalisable to the PBS population and consistent with other trials considered by the PBAC. Overall, baseline characteristics indicated that patients in both trials may have had less severe disease than the PBS eligibility criteria, particularly for RA in Study 3.5 Part 2 demonstrated by lower CRP levels and fewer number of swollen joints. In addition, both trials excluded patients aged ≥ 75 years, those with BMI ≥ 35 kg/m² and who previously received bDMDS.

Comparative effectiveness

- 6.12 Under the requested PBS restriction for RA and IBD (CD and UC), continued treatment is dependent on demonstrating and maintaining response to therapy, assessed after a minimum of 12 weeks following initiation (and every 24 weeks ongoing thereafter).
- For RA, the PBS response criteria are similar to the American College of Rheumatology (ACR) 50% and 20% response criteria. The PBAC had previously accepted both trial outcomes as patient relevant outcomes, with a preference for ACR50 (paragraph 6.12, baricitinib Public Summary Document (PSD) July 2017 PBAC meeting).
 - For CD and UC, the PBS response criteria is similar to 'clinical remission' on Crohn's disease activity index (CDAI) and 'clinical response' on partial Mayo score respectively. The PBAC had previously accepted both outcomes as patient relevant outcomes in CD and UC (p4, infliximab (Remicade) PSD March 2007 PBAC meeting and p6, infliximab (Remicade) PSD March 2014 PBAC meeting).

For initial treatment, patient response is assessed after a minimum of 12 weeks of therapy (including loading dose) and no later than 4 weeks after completion of initial therapy (i.e. 18 weeks to 22 weeks depending on the condition).

- 6.13 Patient relevant outcomes were reported as secondary outcomes in the trials: ACR (20/50/70) response in Study 3.5 Part 2; and clinical response and clinical remission on CDAI and partial Mayo score in Study 1.6 Part 2. The submission argued despite the trials being designed to demonstrate non-inferiority on the primary outcomes,

treatment superiority can be demonstrated using secondary outcomes by statistical inference if the lower bound of the non-inferiority margin does not contain zero.

- 6.14 The PBAC has previously rejected this type of argument because “the selection of 0% as a threshold for superiority allowed any marginal statistically significant improvement ... to be judged as superiority, in the absence of demonstrating this was a clinically meaningful difference” (paragraph 6.13, baricitinib PSD July 2017 PBAC meeting). More importantly, this type of interpretation is not appropriate in this case because it ignores the risk of spurious statistical significance given the trials were not powered on secondary outcomes and did not adjust for multiplicity. The Sponsor maintained in the PSCR that treatment superiority can be demonstrated in non-inferiority trials and this interpretation can be conducted without a need for a statistical penalty for multiple testing. While it may be argued that a well powered non-inferiority trial to demonstrate non-inferiority on the primary outcome may also show treatment superiority on the primary outcome, the submission’s claim of superior effectiveness in RA and in UC were based on secondary effectiveness outcomes, which were not powered to demonstrate non-inferiority, or superiority. The primary outcomes to demonstrate non-inferiority was DAS28 (CRP) in Study 3.5 Part 2 for RA and a pharmacokinetics outcome in Study 1.6 Part 2, both assessed at Week 22 in the trials.

Comparative effectiveness of IFX SC versus IFX IV for RA

- 6.15 Table 5 summarises trial results from Study 3.5 Part 2.

Table 5: Results of DAS28 and ACR response for IFX SC vs IFX IV from Study 3.5 Part 2

Outcome	IFX SC N=165	IFX IV N=174	Difference (95%CI)	
Change from baseline DAS28 (CRP)				
LS mean change (decrease) (SE) at Wk 22 ^a	2.21 (0.22)	1.94 (0.21)	0.27 (0.02, 0.52)	
Mean change (SD) Wk 22	-2.66 (1.26)	-2.39 (1.27)	-0.27 (-0.55, 0.00)	
Mean change (SD) Wk 30	-2.99 (1.31)	-2.34 (1.27)	-0.64 (-0.93, -0.36)	
n (%) remission (<2.6) ^b Wk 30	61 (37.0)	38 (21.8)	15.2% (0.06, 0.25)	
n (%) remission + low disease activity (≥2.6 to <3.2) ^b Wk 30	88 (53.3)	67 (38.5)	14.8% (0.04, 0.25)	
Change from baseline DAS28 (ESR)				
Mean change (SD) Wk 22	-2.72 (1.28)	-2.49 (1.34)	-0.23 (-0.51, 0.05)	
Mean change (SD) Wk 30	-3.05 (1.36)	-2.44 (1.39)	-0.60 (-0.90, -0.30)	
n (%) remission (<2.6) ^b Wk 30	29 (17.6)	27 (15.5)	2.1% (-0.06, 0.10)	
n (%) remission + low disease activity (≥2.6 to <3.2) ^b Wk 30	55 (33.3)	41 (23.6)	9.7% (0.00, 0.19)	
ACR responses			RR (95%CI)	RD (95%CI)
ACR20 response				
n (%) Wk 22	139 (84.2)	137 (78.7)	1.07 (0.97, 1.18)	0.055 (-0.03, 0.14)
n (%) Wk 30	142 (86.1)	133 (76.4)	1.13 (1.02, 1.25)	0.096 (0.01, 0.18)
ACR 50 response				
n (%) Wk 22	85 (51.5)	90 (51.7)	1.00 (0.81, 1.22)	-0.002 (-0.11, 0.10)
n (%) Wk 30	106 (64.2)	87 (50.0)	1.29 (1.07, 1.55)	0.14 (0.04, 0.25)
ACR70 response				
n (%) Wk 22	46 (27.9)	49 (28.2)	0.99 (0.70, 1.39)	-0.003 (-0.10, 0.09)
n (%) Wk 30	68 (41.2)	47 (27.0)	1.53 (1.13, 2.07)	0.14 (0.04, 0.24)

Abbreviations: ACR20/50/70=American College of Rheumatology 20%/50%/70% response; CRP=C-reactive protein; DAS28=Disease Activity Score using 28 joint counts; ESR=erythrocyte sedimentation rate; IFX=infliximab; IV=intravenous; RA=rheumatoid arthritis; SC=subcutaneous; wk=week;

^a Primary efficacy outcome defined as decrease from baseline and calculated as (DAS28 [CRP] at baseline – DAS28 [CRP] at Week 22). An ANCOVA comparing the change (decrease) from baseline of DAS28 (CRP) at Week 22 between the two treatment arms, SC and IV, was conducted considering the treatment as fixed effect and country, Week 2 serum CRP concentration (≤0.6 mg/dL versus >0.6 mg/dL), and Week 6 body weight (≤100 kg versus >100 kg) as covariates. The LS means, SEs, estimate of treatment difference, and 95%CI from the ANCOVA is shown.

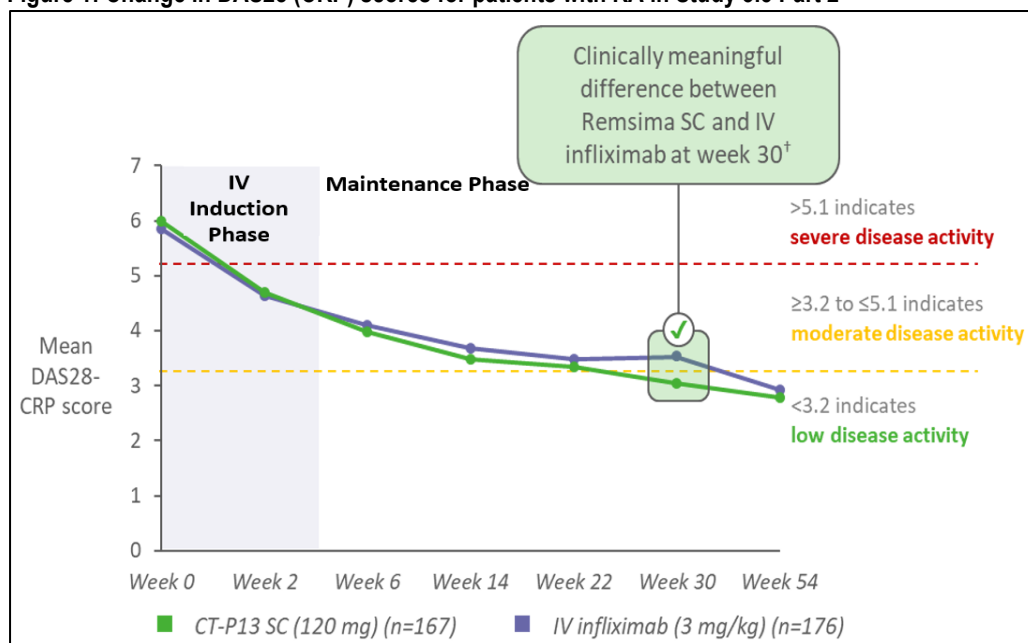
^b The submission conducted post-hoc analyses using the proportion of patients with DAS28 (CRP) and DAS28 (ESR) remission (defined as a score <2.6), low disease activity (≥2.6 to <3.2) and remission plus low disease activity (Efficacy population; LOCF analysis).

Source: Tables 2.23 to 2.26, pp84-88 of the submission and Study 3.5 Part 2 CSR – ctp1335-body.

6.16 The trial met the pre-specified non-inferiority margin for DAS28 (CRP) at Week 22 (i.e., lower limit of the two-sided 95% CI of 0.02 is within -0.6) and results at Week 30 statistically favoured IFX SC. The difference in DAS28 (CRP) at Week 30 (-0.64) was less than minimum clinically important difference (MCID) of -1.0 previously accepted by the PBAC (paragraph 6.22, infliximab (Inflectra) PSD July 2015 PBAC meeting). The PSCR argued that the result of the primary outcome DAS28 (CRP) in the RA trial of -0.64 (95% CI -0.93, -0.36; p<0.0001) showed a moderate clinically important change, given the point estimate -0.64 was greater than the MCID of -0.6, (Fransen and van Riel 2009). The ESC noted that the difference of -0.64 was less than the above mentioned MCID of -1.0 previously accepted by the PBAC, and the mean difference also may not be clinically important given the 95% CI limits of the difference were smaller than the clinically important change of approximately -1.0 for DAS28 (CRP). Figure 1 shows the

mean DAS28 (CRP) score over time, as presented in the submission, demonstrating that while there is a difference between IFX SC and IFX IV at Week 30, the 2 groups are aligned at time points before and after Week 30.

Figure 1: Change in DAS28 (CRP) scores for patients with RA in Study 3.5 Part 2



Source: Figure 2.5, p86 of the submission.

6.17 A similar trend was observed for ACR (20/50/70) response, with no difference observed at Week 22 but results at Week 30 statistically favouring IFX SC. As described above, interpretation of these secondary outcomes is problematic and there is no MCID because each outcome by definition represents a different level of response.

Comparative effectiveness of IFX SC versus IFX IV for CD and UC

6.18 Table 6 summarises efficacy results from Study 1.6 Part 2.

Table 6: Results of clinical response and clinical remission for CD (in terms of CDAI) and UC (in terms of total and partial Mayo) for IFX SC vs IFX IV from Study 1.6 Part 2.

Outcome	IFX SC ^a	IFX IV	RR (95%CI)	RD (95%CI)
CD efficacy population	N=28	N=25		
CDAI-70 response^b				
n (%) Wk 22	22 (78.6)	21 (84.0)	0.94 (0.72, 1.21)	-0.05 (-0.26, 0.15)
n (%) Wk 30	19 (67.9)	17 (68.0)	1.00 (0.69, 1.44)	-0.00 (-0.25, 0.25)
CDAI-100 response^c				
n (%) Wk 22	21 (75.0)	20 (80.0)	0.94 (0.70, 1.25)	-0.05 (-0.27, 0.17)
n (%) Wk 30	19 (67.9)	16 (64.0)	1.06 (0.72, 1.56)	0.04 (-0.22, 0.29)
CDAI remission^d				
n (%) Wk 22	17 (60.7)	15 (60.0)	1.01 (0.65, 1.57)	0.01 (-0.26, 0.27)
n (%) Wk 30	18 (64.3)	14 (56.0)	1.15 (0.74, 1.79)	0.08 (-0.18, 0.35)
UC efficacy population	N=38	N=39		
Total Mayo Wk 22^e				
n (%) response	30 (78.9)	21 (53.8)	1.47 (1.05, 2.04)	0.25 (0.05, 0.45)
n (%) remission	20 (52.6)	10 (25.6)	2.05 (1.11, 3.79)	0.27 (0.06, 0.47)
Partial Mayo Wk 22^f				
n (%) response	32 (84.2)	30 (76.9)	1.09 (0.87, 1.36)	0.07 (-0.10, 0.25)
n (%) remission	23 (60.5)	15 (38.5)	1.57 (0.98, 2.52)	0.22 (0.00, 0.44)
Partial Mayo Wk 30^f				
n (%) response	33 (86.8)	29 (74.4)	1.17 (0.94, 1.46)	0.12 (-0.05, 0.30)
n (%) remission	26 (68.4)	21 (53.8)	1.27 (0.88, 1.83)	0.15 (-0.07, 0.36)

Abbreviations: CD=Crohn's disease; CDAI=Crohn's disease activity index; IFX=infliximab; IV=intravenous; SC=subcutaneous; UC=ulcerative colitis; wk=week;

^a IFX SC treatment arm dosed based on body weight 120 mg (<80 kg) and 240 mg (≥80 kg) at Week 6.

^b CDAI-70 response defined as a decrease in CDAI score of 70 points or more from the baseline value. Baseline value was considered to be the last non-missing value before the first administration.

^c CDAI-100 response defined as a decrease in CDAI score of 100 points or more from the baseline value. Baseline value was considered to be the last non-missing value before the first administration.

^d Clinical remission was defined as an absolute CDAI score of less than 150 points.

^e Clinical response according to total Mayo score was defined as a decrease from baseline in total Mayo score ≥3 points and ≥30%, and decrease from baseline in the sub-score for rectal bleeding of ≥1 point or absolute sub-score for rectal bleeding of 0 or 1. Clinical remission according to total Mayo score was defined as a total Mayo score of <2 points with no individual sub-score exceeding 1 point.

^f Clinical response according to partial Mayo score was defined as a decrease from baseline in partial Mayo score ≥2 points, and decrease from baseline in the sub-score for rectal bleeding of ≥1 point, or an absolute sub-score for rectal bleeding of 0 or 1. Clinical remission according to partial Mayo score was defined as a partial Mayo of 1 point or lower.

Source: Tables 2.31 to 2.33, pp98-101 of the submission and Study 1.6 Part 2 CSR – Week 54

6.19 Trial results showed no difference between IFX SC (120/240 mg) and IFX IV for clinical response and clinical remission outcomes on CDAI in the CD population, and no difference for the clinical response and clinical remission outcomes on partial Mayo score in the UC population. In contrast, results for clinical response and clinical remission outcomes on total Mayo score in the UC population favoured IFX SC (120/240 mg) over IFX IV. The submission did not propose non-inferiority margins or MCIDs for the relevant outcomes of clinical response and clinical remission (on CDAI for CD and Mayo scores for UC), given non-inferiority in the trial was demonstrated on PK outcome (C-trough) (paragraph 6.17) and none has been defined for these outcomes by the PBAC.

- 6.20 As described above, interpretation of these secondary outcomes from this small open label pharmacokinetic trial is problematic. The difference observed for outcomes using total Mayo score may be explained by the higher proportion of patients discontinuing or with a missing endoscopy subscore at Week 22 in the IFX IV arm compared to IFX SC arm (28.2% vs 10.5%), given patients were coded as non-responders if they discontinued prior to a study visit or missed endoscopy subscore at a visit. The TGA evaluator considered that Study 1.6 Part 2 was a small trial and not formally powered for non-inferiority or equivalence of efficacy.
- 6.21 During the maintenance phase (Week 6 to Week 30), the mean pre-dose serum levels was higher for IFX SC (120/240 mg) compared to IFX IV. The ratio of the geometric LS means (SC/IV) of C_{trough} at Week 22 was 1154.17% (90%CI: 786.37, 1694.00). The trial met the pre-specified non-inferiority margin for the ratio of the geometric mean ratio in C_{trough} at Week 22, with the lower bound 90%CI being above the pre-defined non-inferiority margin of 80%. As noted above, the dose of IFX IV in the trial was higher than the proposed dose for some patients (i.e. >80 kg), which likely affects serum levels.

Comparative harms

- 6.22 In Study 3.5 Part 2, the incidence of any adverse events (AEs) and drug-related AEs were comparable between IFX SC and IFX IV to Week 30. Patients treated with IFX IV were more likely to experience a drug-related AEs leading to discontinuation (RD: -0.04, 95%CI: -0.08, -0.02) and an infusion-related reaction (RD: -0.03, 95%CI: -0.07, -0.01). Patients treated with IFX SC were more likely to experience injection site reactions although the difference was small (RD: 0.04, 95%CI: 0.00, 0.09).
- 6.23 In Study 1.6 Part 2, the incidence of AEs was generally comparable between IFX SC and IFX IV to Week 30, but patients treated with IFX SC were more likely to experience injection site reactions (RD: 0.14, 95%CI: 0.04, 0.24).
- 6.24 The most commonly reported AEs across the trials were injection site reactions and infections and infestations. Overall, the safety of IFX SC in the trials was generally similar to the known risks of treatment with IFX IV but the ESC noted that the TGA Clinical Evaluation raised concerns over prolonged exposure to higher trough IFX concentrations (paragraph 2.6). The ESC considered that the effect of this on the relative safety of IFX SC was uncertain.

Benefits/harms

- 6.25 There were no expected clinically meaningful differences between the IFX SC and IFX IV in efficacy and safety when used for the treatment of RA, CD and UC in the PBS population. Patients who switch from IFX IV to IFX SC will avoid the risk of infusion-related reactions but are at risk of experiencing injection site reactions.

Clinical claim

6.26 At the recommended doses for maintenance treatment (i.e. ≥ 6 weeks after initial treatment with IFX IV), the submission described IFX SC compared to IFX IV as having:

- Superior effectiveness and superior safety in RA;
- Superior effectiveness and non-inferior safety in UC;
- Non-inferior effectiveness and non-inferior safety in CD;
- Extrapolated non-inferior effectiveness and extrapolated non-inferior safety in RFC, AS, PsA and CPP.

6.27 The ESC agreed with the evaluation that the claim of superior effectiveness in RA and UC was not adequately supported:

- For RA, the claim was based on differences in outcomes, including ACR response, favouring IFX SC at Week 30. Results at Week 22, which better reflect the time point when initial response is assessed on the PBS, showed no difference between IFX SC and IFX IV. Interpretation of these secondary outcomes is also problematic as the trial did not adjust for multiplicity and the submission did not demonstrate that the differences observed were clinically meaningful. The TGA Clinical Evaluation Report (Round 2) concluded that the small differences in outcomes between IFX SC and IFX IV were unlikely to be clinically meaningful. The PSCR argued that assessment at Week 30 represents the most complete durable data, and that the PBAC had previously accepted comparative effectiveness for RA at Week 30 (paragraph 6.21, infliximab PSD, July 2015).
- For UC, the claim was based on differences favouring IFX SC in terms of clinical response and remission using total Mayo score at Week 22. Interpretation of these outcomes is problematic because the small open-label pharmacokinetic trial was not powered to test for differences in efficacy outcomes. The observed difference may be impacted by more patients in the IFX IV arm discontinuing treatment or with missing endoscopy subscores at Week 22, which were coded as treatment failures in the analysis. Clinical response or remission using partial Mayo score, which better reflects the response criteria on the PBS, showed no differences between IFX SC and IFX IV at Week 22.

On balance, the ESC agreed with the evaluation that it may be more reasonable to describe IFX SC and IFX IV as having non-inferior efficacy in RA and UC [and CD].

6.28 The ESC agreed with the evaluation that the claim of superior safety in RA was not adequately supported. The claim was based on fewer discontinuations due to drug-related AEs for IFX SC compared to IFX IV; however, these included infection and positional vertigo, which would not be considered to be dose route specific (CHMP

document for Remsima SC²). The ESC also noted that data available from this document showed there were more discontinuations in the SC arms in part 1 of this study (including 120 mg dose); no data from part 1 were presented in the submission. There was an increased risk of injection site reactions with IFX SC and the incidence of any AEs were similar in one of the trials. On balance, the ESC agreed with the evaluation that it may be more reasonable to describe IFX SC and IFX IV as having similar or non-inferior safety profiles in RA [and UC and CD].

- 6.29 The PBAC considered that the claim of superior comparative effectiveness in RA and UC was not adequately supported by the data. The PBAC considered that the claim of superior comparative safety in RA was also not adequately supported by the data. The PBAC agreed with the ESC that a conclusion of non-inferior effectiveness and safety across the RA, UC and CD indications was reasonable.
- 6.30 The PBAC considered that non-inferiority of IFX SC to IFX IV in PsA, CPP, RFCD and AS was not adequately supported given there were no clinical trials assessing the efficacy of IFX SC in patients with these conditions, and the higher dose of IFX IV is recommended for these patients.

Economic analysis

- 6.31 The submission proposed the following equi-effective doses for maintenance therapy (after two doses of IFX IV):
- 120 mg IFX SC every 2 weeks (in all indications) ≡
 - 3 mg/kg IFX IV every 8 weeks in RA
 - 5 mg/kg IFX IV every 8 weeks in UC, CD, CPP, PsA, and RFCD
 - 5 mg/kg IFX IV every 6 weeks in AS.

The nomination of equi-effective dosing for RA, UC and CD was based on clinical data from RCTs. Equi-effective dosing for AS, PsA, CPP and RFCD was extrapolated based on pharmacokinetic-pharmacodynamic modelling data, as no specific clinical studies were available for these indications.

- 6.32 The submission presented a CMA comparing IFX SC to IFX IV over a 2-year time horizon, based on the following inputs and assumptions:
- The analysis included the loading doses of IFX IV in both arms. The ESC considered this may not be a reasonable assumption and favours IFX SC. Treatment with IFX SC starts at Week 6 (or later) and patients that switch from IFX IV to IFX SC do not undergo induction therapy again with IV loading doses. The PBAC agreed with the ESC that the CMA should begin from the point of starting therapy with IFX SC

² Data available from Committee for Medicinal Products for Human Use (CHMP) document from the European Medicines Agency (EMA). https://www.ema.europa.eu/en/documents/variation-report/remsimas-h-c-2576-ii-0082-epar-assessment-report-variation_en.pdf

following the IV loading doses. The Sponsor accepted the 2-year time horizon from Week 6 in their pre-PBAC response.

- The analysis included costs offsets for the administration of IFX IV, including costs to the health system (MBS item 14245, 100% rebate) and patient time costs (■■■■■ valued at the average full-time wage). The ESC considered including patient time costs in the base case analysis is not reasonable, and the patient time costs have not been included in past comparisons when a SC formulation substitutes an IV formulation (e.g. abatacept SC vs abatacept IV; tocilizumab SC vs tocilizumab IV). The ESC and the PBAC agreed with the evaluation that while supplementary analyses may be presented that include such costs so the PBAC can consider “the impact of including production changes on the direction and extent of change on the base case”, including patient time costs in the base case is inconsistent with the Guidelines. The Sponsor accepted the exclusion of patient time costs from the CMA in their pre-PBAC response.
- The analysis inappropriately assumed there is no administration cost for IFX SC (including no patient time costs) because all patients will self-inject. This assumption is not reasonable given a proportion of patients will be unable to self-inject and require assistance. The PBAC had previously accepted that 10% of patients require assistance with injections involving ‘a visit to a doctor’ (paragraph 10, golimumab PSD for RA, March 2010). The ESC and the PBAC considered that including allowance for GP visits is required, as not all patients in the affected population will be able to self-administer IFX SC (e.g. individuals affected by severe RA in their fingers will not be able to operate the device and would require ongoing assistance for each injection). Furthermore, a proportion of patients will require assistance from a health care professional due to a change in route of administration. Thus, 10% of patients may require a GP visit over a 2-year period.

6.33 Table 7 summarises the CMA presented in the submission. The submission estimated the average weighted cost for IFX IV over two years, taking into account the number of vials and infusions required in each indication. The PBAC noted the cost of IFX IV was weighted across the 7 requested indications and that this would need to be revised to account listings for RA, UC and CD only.

Table 7: Results of the cost-minimisation analysis

Component	IFX SC	IFX IV
PBS item, max qty.	2 syringes/pens for SC injection	5 vials for IV infusion
DPMQ	IFX SC: - Section 85: \$ [REDACTED] ^d - Section 100 (Public): \$ [REDACTED] - Section 100 (Private): \$ [REDACTED]	IFX IV: - Section 100 (Public): \$1,603.55 - Section 100 (Private): \$1,651.29
AEMP	IFX SC: \$ [REDACTED] ^a / SC injection IFX IV: \$ [REDACTED] / IV vial	IFX IV: \$320.71 / IV vial
Doses	IFX SC: 49 SC injections IFX IV: 2 IV infusions	IFX IV: 15.44 ^b IV infusions
Units / dose	IFX SC: 1 syringe/pen IFX IV: 4.45 vials	IFX IV: 4.45 vials ^b
Drug cost	IFX SC: \$ [REDACTED] IFX IV: \$ [REDACTED]	IFX IV: \$22,046.89 ^b
Administration cost	IFX IV: \$202.00	IFX IV: \$1,559.57 ^b
Patient time	IFX IV: \$ [REDACTED] ^c	IFX IV: \$654.58 ^{b,c}
Total cost	\$24,261.04	\$24,261.04 ^b

Abbreviations: AEMP=Approved Ex-Manufacturer Price; DPMQ=Dispense Price Maximum Quantity; IFX=infliximab; IV=intravenous.

^a AEMP for IFX SC was calculated by dividing total drug cost for IFX SC by 49 maintenance doses (i.e.: this calculation excludes costs of the two IV induction doses required prior to SC administration)

^b Weighted across indications

^c [REDACTED]% proportion of benefit claimed by Sponsor.

^d Updated DPMQ. The submission requested a Section 85 DPMQ of \$ [REDACTED] assuming a wholesale mark-up of \$ [REDACTED] for AEMP >\$ [REDACTED]; however, the current wholesale mark-up is [REDACTED]% for AEMP <\$ [REDACTED], corresponding to a DPMQ of \$ [REDACTED]. This was based on the mark-up applicable from 1 January 2021.

(<https://www.servicesaustralia.gov.au/organisations/health-professionals/services/medicare/pbs-pharmacists/about>).

Source: Table 3.9 and 3.10, pp133-134 of the submission.

6.34 The PBAC noted that given the IV formulation is dispensed through S100 and the SC formulation will be dispensed through S85, the more frequent administration of S85 items would drive an incremental cost to government for IFX SC at the requested price.

Drug cost/patient/2-years for maintenance treatment: \$ [REDACTED]

6.35 Assuming a DPMQ of \$ [REDACTED] (AEMP of \$ [REDACTED] / SC injection) and 26 scripts required for two years of maintenance treatment with IFX SC 120 mg, exclusive of two IFX IV induction doses required prior to SC administration, the per patient cost is \$ [REDACTED]. The estimated treatment cost is overestimated because the assumptions in the CMA have been adjusted.

Estimated PBS usage & financial implications

6.36 This submission was not considered by DUSC. The submission estimated the financial implications of the proposed listing using a market share approach, assuming that IFX SC would only substitute IFX IV and there would be no impact on the rate of market growth. The submission stated this approach was supported by past DUSC Reports in AS and PsA, which found limited switching between IFX and other bDMDs.

6.37 Table 8 summarises the key inputs in the financial estimates.

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Table 8: Data sources and parameter values applied in the utilisation and financial estimates

Data	Value and Source	Comment																								
Treatment utilisation																										
Current market size of IFX IV in adult patients (Year 0)	Init. - HSD (Private) 5753T, 9654D, 10196P, 5757B, 5754W, 5758C, 5756Y	A reasonable simplification of the data, noting the following caveats: (i) the item codes for initial treatment include 'First Continuing Treatment' in six of the seven conditions; (ii) item codes for one condition (UC) includes paediatric patients; (iii) two items codes for initial treatment were incorrectly classified (10196P is Public; 10184B is Private).																								
	Init. - HSD (Public) 6448J, 9674E, 10184B, 6397Q, 9613Y, 9617E, 6496X																									
	Cont – HSD (Private) 11488P, 11489Q, 11432Q, 11412P, 11796W, 11797X, 11483J, 11487N, 11396T, 11399Y, 11595G, 11590B, 11515C, 11498E																									
	Cont. – HSD (Public) 11486M, 11482H, 11423F, 11424G, 11461F, 11459D, 11490R, 11481G, 11400B, 11389K, 11605T, 11606W, 11514B, 11497D																									
Aggregated script volumes (Jan 2019 to Dec 2019) across indications, split into initial and continuing listings for adult patients.																										
Projected IFX market growth	<table border="1"> <thead> <tr> <th></th> <th>Yr0</th> <th>Yr1</th> <th>Yr2</th> <th>Yr3</th> <th>Yr4</th> <th>Yr5</th> <th>Yr6</th> </tr> </thead> <tbody> <tr> <td>Init.</td> <td>■%</td> <td>■%</td> <td>■%</td> <td>■%</td> <td>■%</td> <td>■%</td> <td>■%</td> </tr> <tr> <td>Cont.</td> <td>■%</td> <td>■%</td> <td>■%</td> <td>■%</td> <td>■%</td> <td>■%</td> <td>■%</td> </tr> </tbody> </table>		Yr0	Yr1	Yr2	Yr3	Yr4	Yr5	Yr6	Init.	■%	■%	■%	■%	■%	■%	■%	Cont.	■%	■%	■%	■%	■%	■%	■%	Uncertain assumption that potentially favours IFX SC; figures in the submission show growth rates of 8.7% and 13.0% for 2018 and 2019 for IFX IV, respectively. The financial estimates are sensitive to growth rates.
		Yr0	Yr1	Yr2	Yr3	Yr4	Yr5	Yr6																		
Init.	■%	■%	■%	■%	■%	■%	■%																			
Cont.	■%	■%	■%	■%	■%	■%	■%																			
Assumption. Current growth (past 2-3 years) is ~11%, but the Sponsor expects this rate to decline as new bDMDs become available.																										
Market uptake of IFX SC	<table border="1"> <thead> <tr> <th></th> <th>Yr1</th> <th>Yr2</th> <th>Yr3</th> <th>Yr4</th> <th>Yr5</th> <th>Yr6</th> </tr> </thead> <tbody> <tr> <td>Init.*</td> <td>■%</td> <td>■%</td> <td>■%</td> <td>■%</td> <td>■%</td> <td>■%</td> </tr> <tr> <td>Cont.</td> <td>■%</td> <td>■%</td> <td>■%</td> <td>■%</td> <td>■%</td> <td>■%</td> </tr> </tbody> </table>		Yr1	Yr2	Yr3	Yr4	Yr5	Yr6	Init.*	■%	■%	■%	■%	■%	■%	Cont.	■%	■%	■%	■%	■%	■%	Uncertain and potentially an underestimate in the early years given the purported benefits of SC injection to patients. Also, the statement that initial scripts cannot exceed 33.3% is only true for CD, RFCD and UC; for the other indications IFX SC will replace 2 of 4 IV doses (i.e. 50% of initial scripts). The financial estimates are sensitive to uptake rates.			
		Yr1	Yr2	Yr3	Yr4	Yr5	Yr6																			
Init.*	■%	■%	■%	■%	■%	■%																				
Cont.	■%	■%	■%	■%	■%	■%																				
<p>*Initial market uptake was limited to 33.3%</p> <p>Assumed moderate levels of uptake given:</p> <ul style="list-style-type: none"> - Prescribers will not switch patients if concerned about compliance. - Some patients prefer IV. - Some patients unable to self-inject - Initial scripts cannot exceed 33.3% as IFX SC can only displace 1 of 3 IFX IV initiation doses. 																										
Script equivalence ratio IFX SC : IFX IV	<p>1.93.</p> <p>Calculated based on required numbers of scripts per year for SC to IV: No. of SC scripts / No. of weighted average IV scripts; 13 / 6.74 = 1.93</p>	Reasonable for maintenance scripts, but a minor underestimate for initial scripts. For CD, RFCD and UC, 3 IFX SC scripts will replace 1.5 IFX IV script for initial treatment (ratio = 2). For AS, RA, CPP and PsA, 4 IFX SC scripts will replace 2 IFX IV scripts for initial treatment (ratio = 2). The financial estimates are sensitive to script equivalence for initial treatment																								

Abbreviations: IFX=infliximab; DUSC=Drug Utilisation Sub-Committee; bDMD=biologic disease modifying drug; AS=ankylosing spondylitis; PsA=psoriatic arthritis; HSD=Highly Specialised Drugs; AEMP=Approved Ex-Manufacturer Price.

Source: Tables 4.1-4.6, pp136-142 of the submission.

6.38 Table 9 summarises the estimated net financial implications for the proposed listing of IFX SC on the PBS/RPBS.

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Table 9: Estimation use and financial implications of IFX SC to the PBS/RPBS and health budget

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimation of the use and financial implications of IFX SC						
IFX IV scripts (without IFX SC)	1	1	2	2	2	2
Initiation	3	3	3	3	3	3
Continuing	4	5	3	3	3	3
IFX SC, total scripts	7	4	5	6	6	1
Initiation	8	9	9	9	9	9
Continuing	7	3	4	5	5	6
IFX SC, net cost to PBS/RPBS ^a	10	11	12	13	15	16
Change in use and financial impact of IFX IV						
IFX IV, total scripts	7	7	3	3	3	4
Initiation	8	8	6	9	9	9
Continuing	9	7	7	3	3	3
IFX IV, net cost to PBS/RPBS ^a	-\$10	-\$11	-\$12	-\$12	-\$13	-\$13
Estimated financial implications for the PBS/RPBS						
Net cost to PBS/RPBS ^a	16	16	16	16	10	10
Estimated financial implications for the health budget						
Net change in MBS 14245	7	7	3	3	3	4
Net cost to MBS ^b	16	16	16	16	16	16
Net cost to health budget	16	16	16	16	16	16

Abbreviations: IFX=infliximab; IV=intravenous; SC=subcutaneous;

^a Less co-payment

^b Calculated at 80% rebate level (MBS benefit)

Source: Tables 4.8 to 4.11 pp144-147 of the submission and Excel file: IFX SC-Section 4-Base Case.

The redacted values correspond to the following ranges:

¹ 60,000 to < 70,000

² 70,000 to < 80,000

³ 20,000 to < 30,000

⁴ 30,000 to < 40,000

⁵ 40,000 to < 50,000

⁶ 50,000 to < 60,000

⁷ 10,000 to < 20,000

⁸ 500 to < 5,000

⁹ 5,000 to < 10,000

¹⁰ \$10 million to < \$20 million

¹¹ \$20 million to < \$30 million

¹² \$30 million to < \$40 million

¹³ \$40 million to < \$50 million

¹⁴ \$50 million to < \$60 million

¹⁵ \$60 million to < \$70 million

¹⁶ \$0 to < \$10 million

6.39 The estimated net financial cost of approximately \$40 million to < \$50 million to the health budget over the first 6 years of listing was not reliable and driven by: i) script relativity (slightly higher than implied in Section 3) and; ii) the requested DPMQ for IFX SC which included a price premium for patient time costs.

6.40 The PBAC considered that the requested AEMP for IFX SC is higher than justified (paragraph 6.34), resulting in an increase in the financial estimates. At the requested price however, specific factors have contributed to an underestimate of the financial impact, given:

- The analysis assumed a considerable decline in background market growth despite current trends suggesting average growth of 11% (8.7% in 2018 and 13% in 2019);
- The analysis assumed relatively moderate market uptake particularly in the initial years and for initial therapy;
- The script relativity (1.93) assumed underestimated displacement of initial scripts particularly for CD, RFCD and UC (where 3 scripts of IFX SC will replace 1 script of IFX IV). The script relativity assumed (1.93) underestimated displacement of initial scripts. The Sponsor argued in the PSCR that the initiation script ratio IFX SC:IV is 5:4 = 1.25. The calculation should be for CRFCD, MSUC, and severe CD: 3 SC scripts will replace 1.5 IV scripts (ratio=2); and for RA, CPP and PsA: 4 SC scripts will replace 2 IV scripts (ratio=2). The PSCR is incorrect because the Sponsor has omitted SC doses at Weeks 16 and 20 in the example for RA they provided. The script relativity for initial scripts (2) is only slightly higher than the value used in the submission (1.93).

Quality Use of Medicines

- 6.41 Quality Use of Medicine activities presented in the submission included educational sessions for health professionals and support programs for patients, nurse and pharmacists, which were reasonable.

For more detail on PBAC's view, see section 7 PBAC outcome.

7 PBAC Outcome

- 7.1 The PBAC recommended the listing of infliximab (IFX) subcutaneous (SC) on the General Schedule (Section 85), for the treatment of severe active rheumatoid arthritis (RA), moderate to severe ulcerative colitis (UC) and severe refractory Crohn's disease (CD) on a cost minimisation basis to IFX intravenous (IV). The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of IFX SC would be acceptable if it were cost-minimised against IFX IV.
- 7.2 The PBAC advised that the listing of IFX SC in RA, UC and CD should be based on the equi-effective dose of IFX SC 120 mg Q2W and (i) IFX IV 3 mg/kg mg Q8W in RA; and (ii) IFX IV 5 mg/kg Q8W in UC and CD.
- 7.3 The PBAC did not consider extrapolation of clinical evidence from RA, UC and CD to ankylosing spondylitis (AS), severe active psoriatic arthritis (PsA), severe chronic plaque psoriasis (CPP) and complex refractory fistulising Crohn's disease (RFCD) was adequate to support PBS listings for AS, PsA, CPP and RFCD. The PBAC noted there were no clinical trials assessing the efficacy of IFX SC in patients with these conditions, and considered it could not be assumed that IFX SC would be non-inferior to IFX IV given the higher dose of IFX IV is recommended in PsA, CPP and RFCD (5 mg/kg Q8W)

and the higher dose is recommended with more frequent administration in AS (5 mg/kg Q6W).

- 7.4 The PBAC considered that an SC formulation of IFX provides an additional patient-relevant option for maintenance therapy in RA, UC and CD. The PBAC noted that this view was reflected in the Consumer Comments for IFX SC, which emphasised benefits for consumers through not requiring infusion in a medical facility.
- 7.5 The PBAC considered that the listing for IFX SC should show alignment to the current concepts of initiation, continuation, balance of supply for IFX IV, and ensure assessment at precedented time points.
- 7.6 The PBAC noted the Sponsor requested both Section 85 and Section 100 listings for IFX SC, and requested a streamlined listing in line with biosimilar preferred prescribing policy. The PBAC considered that the requested Section 100 listing was not supported, and that only a Section 85 listing is warranted. It also considered that restrictions for IFX SC should not be based on biosimilar policy, as the premise of biosimilarity for the purposes of PBS listing is flawed given the different routes of administration and evidence of different pharmacokinetic profiles.
- 7.7 The PBAC considered that the current PBS listing for IFX IV will provide for the supply of the initial IV induction doses, and that new PBS item codes for this purpose are not necessary for IFX IV, although they may need to be amended to permit the loading doses.
- 7.8 The PBAC advised that the IFX SC restrictions should have an initial SC restriction that allow transition from IV to SC at Week 6 onwards until assessment from Week 12, and a Balance of Supply (to initial SC and continuing SC) to complete what is required for each indication. A continuing restriction will also be required, as the 'first and subsequent' continuing restriction will not be applicable here.
- 7.9 For continuing treatment, (for patients who respond to treatment continuation criteria), the requested maximum quantities provide up to 24 weeks of treatment. This is consistent with the current listing of IFX IV in all requested indications.
- 7.10 The PBAC agreed with the ESC that re-induction after a treatment break should not be required. The PBAC advised that the restriction should be consistent with the PI in allowing resumption after treatment break without re-induction.
- 7.11 The PBAC advised that patients should be able to switch back to IFX IV after receiving IFX SC, and that this should not be considered a treatment failure. Flow-on changes to the IFX IV continuing treatment restriction will be required.
- 7.12 The PBAC considered that the nomination of IFX IV as the comparator is appropriate. The PBAC considered that while there are alternative bDMARDs which may be less costly, a switch from those alternative agents to IFX SC for maintenance treatment is 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 is likely to deliver improved outcomes, for some patients, compared with a switch to an alternative agent.

- 7.13 The PBAC advised that the claim of superior effectiveness in RA was not adequately supported. The PBAC considered a statistically significant difference observed for some outcomes at week 30, but not at other time points, did not support overall superiority of IFX SC versus IFX IV. Similarly, the PBAC advised the claim of superior effectiveness in UC was not adequately supported. The PBAC noted the clinical trial on which this claim was based was a small open-label pharmacokinetic trial and the results were potentially impacted by missing data. The PBAC further noted a statistically significant difference was not observed for clinical response or remission based on the partial Mayo score.
- 7.14 The PBAC advised the claim of superior safety in RA was not adequately supported based on reduced discontinuations due to drug-related AEs for IFX SC compared to IFX IV, because these included AEs that were not dose route specific, such as infection and positional vertigo.
- 7.15 The PBAC considered that non-inferiority of IFX SC to IFX IV in RA, UC, and CD in adults was supported by the clinical evidence available. However, the PBAC considered that non-inferiority of IFX SC to IFX IV in PsA, CPP, RFCD and AS was not adequately supported given there were no clinical trials assessing the efficacy of IFX SC in patients with these conditions, and the higher dose of IFX IV being recommended for these patients. The PBAC advised that while extrapolation across indications has occurred previously for PBS listing, it was for biosimilar IV formulations, not for a SC formulation with a different route of administration.
- 7.16 The PBAC considered it is reasonable to conduct the CMA of IFX SC over a 2-year time horizon that is calculated from the point of patients starting IFX SC following IV loading doses, to exclude patient time costs, and to assume 10% of patients will require medical assistance that is included as a visit to a doctor. The PBAC also considered that the CMA should ensure there is no additional cost to the Government, noting that different fees and mark-ups apply for IFX IV (\$100) and IFX SC (\$85).
- 7.17 The PBAC considered that the use of SC IFX was potentially underestimated due to the assumed market growth, the projected uptake of IFX SC, and the Sponsor's calculation of script relativity. The PBAC considered the net cost to the PBS for IFX SC to be overestimated due to the requested AEMP being higher than justified. The PBAC considered that listing of IFX SC should not result in any additional cost to Government. The PBAC noted that the financial estimates will need to be revised to take into account listing for the RA, UC and CD indications only.
- 7.18 The PBAC recommended that the Early Supply Rule should apply.

- 7.19 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because IFX SC is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over IFX IV, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009* for Pricing Pathway A were not met.
- 7.20 The PBAC advised that IFX SC is not suitable for prescribing by nurse practitioners.
- 7.21 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

8 Recommended listing

8.1 Add new item:

Severe active rheumatoid arthritis (severe active RA)

Initial treatment, continuing treatment restrictions and balance of supply

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Name and Manufacturer
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled syringe	NEW	2	2	2	Remsima® SC Celltrion Healthcare Australia Pty Ltd
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled autoinjector pen	NEW	2	2	2	Remsima® SC Celltrion Healthcare Australia Pty Ltd

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Category / Program: General Schedule
Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Restriction Method: <input checked="" type="checkbox"/> Authority Required – non-immediate/delayed assessment by Services Australia (in-writing only via mail/postal service or electronic upload to Hobart)
Severity: Severe active
Condition: rheumatoid arthritis
PBS Indication: Severe active rheumatoid arthritis
Treatment criteria: Must be treated by a rheumatologist; OR Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Treatment Phase: Initial treatment with subcutaneous form at weeks 6, 8, 10, 12, 14 and 16
Clinical criteria: Patient must have received 2 intravenous infusions with this drug for this condition at weeks 0 and 2 under Initial 1 (new patient); OR Patient must have received 2 intravenous infusions with this drug for this condition at weeks 0 and 2 under Initial 2 (change or re-commencement of treatment after a break in biological medicine of less than 24 months); OR Patient must have received 2 intravenous infusions with this drug for this condition at weeks 0 and 2 under Initial 3 (recommencement of treatment after a break in biological medicine of more than 5 years)
AND The treatment must be given concomitantly with methotrexate at a dose of at least 7.5 mg weekly
Population criteria: Patient must be aged 18 years or older
Prescriber instruction: The authority application must be made in writing and must include: (1) a completed authority prescription form(s); and (2) a completed Rheumatoid Arthritis PBS Authority Application Form.
Prescribing Instructions: An assessment of a patient's response to an initial course of treatment must be conducted following a minimum of 12 weeks of therapy. An application for the continuing treatment must be accompanied with the assessment of response and submitted no later than 4 weeks from the date of completion of the most recent course of treatment. This will enable ongoing treatment for those who meet the continuing restriction for PBS-subsidised treatment.
Prescribing Instructions: Where a response assessment is not conducted within this 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.
Prescribing Instructions: 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.
Administrative Advice: 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. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001

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Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Name and Manufacturer
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled syringe	NEW	2	2	5	Remsima® SC Celltrion Healthcare Australia Pty Ltd
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled autoinjector pen	NEW	2	2	5	Remsima® SC Celltrion Healthcare Australia Pty Ltd

Category / Program: General Schedule
Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Restriction Method: <input checked="" type="checkbox"/> Authority Required – non-immediate/delayed assessment by Services Australia (in-writing only via mail/postal service or electronic upload to Hobart)
Severity: Severe active
Condition: rheumatoid arthritis
PBS Indication: Severe active rheumatoid arthritis
Treatment criteria: Must be treated by a rheumatologist; OR Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Treatment Phase: Continuing treatment with subcutaneous form or switching from intravenous form to subcutaneous form
Clinical criteria: Patient must have received this drug as their most recent course of PBS-subsidised biological medicine treatment for this condition; OR Patient must have received this drug in the intravenous form as their most recent course of PBS-subsidised biological medicine for this condition under the infliximab intravenous form continuing treatment restriction
AND Patient must have demonstrated an adequate response to treatment with this drug
AND The treatment must be given concomitantly with methotrexate at a dose of at least 7.5 mg weekly
AND Patient must not receive more than 24 weeks of treatment under this restriction
AND Population criteria: Patient must be aged 18 years or older
Prescribing Instruction: 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).
Prescribing Instruction:

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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.

Prescribing Instruction:

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

- (1) a completed authority prescription form(s); and
- (2) a completed Rheumatoid Arthritis PBS Authority Application Form.

The patient remains eligible to receive continuing treatment with the same biological medicine in courses of up to 24 weeks providing they continue to sustain *an adequate* response. It is recommended that a patient be reviewed in the month prior to completing their current course of treatment.

Where a response assessment is not provided, the patient will be deemed to have failed to respond to treatment with this drug, unless the patient has experienced serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.

If a patient has either failed or ceased to respond to a PBS-subsidised biological medicine for this condition 5 times, they will not be eligible to receive further PBS-subsidised treatment with a biological medicine for this condition.

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.

Administrative Advice:

No increase in the maximum quantity or number of units may be authorised.

Administrative Advice:

No increase in the maximum number of repeats may be authorised.

Administrative Advice:

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. EST Monday to Friday).

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

Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos

Or mailed to:

Services Australia
Complex Drugs
Reply Paid 9826
HOBART TAS 7001

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Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Name and Manufacturer
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled syringe	NEW	1	1	0	Remsima® SC Celltrion Healthcare Australia Pty Ltd
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled autoinjector pen	NEW	1	1	0	Remsima® SC Celltrion Healthcare Australia Pty Ltd

Category / Program: General Schedule
Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Restriction Method: <input checked="" type="checkbox"/> Authority Required – immediate/real time assessment by Services Australia (telephone/online application avenues)
Severity: Severe active
Condition: rheumatoid arthritis
PBS Indication: Severe active rheumatoid arthritis
Treatment criteria: Must be treated by a rheumatologist; OR Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Treatment Phase: Initial treatment or continuing treatment with subcutaneous form - Balance of supply
Clinical criteria: Patient must have received insufficient therapy with this drug for this condition under the Initial treatment with subcutaneous form restriction to complete 22 weeks treatment; 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
AND The treatment must be given concomitantly with methotrexate at a dose of at least 7.5 mg weekly
AND The treatment must provide no more than the balance of up to 22 weeks treatment available under the above restriction; OR The treatment must provide no more than the balance of up to 24 weeks treatment available under the above restriction
Population criteria: Patient must be aged 18 years or older
Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

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Crohn's Disease

Initial treatment, Continuing treatment restrictions and balance of supply

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Manufacturer	Name and
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled syringe	NEW	2	2	2	Remsima® SC	Celltrion Healthcare Australia Pty Ltd
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled autoinjector pen	NEW	2	2	2	Remsima® SC	Celltrion Healthcare Australia Pty Ltd

Category / Program: General Schedule
Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Restriction Method: <input checked="" type="checkbox"/> Authority Required – non-immediate/delayed assessment by Services Australia (in-writing only via mail/postal service or electronic upload to Hobart)
Severity: Severe
Condition: Crohn disease
PBS Indication: Severe Crohn disease
Treatment criteria: Must be treated by a gastroenterologist (code 87); or Must be treated by a consultant physician [internal medicine specialising in gastroenterology (code 81)]; or Must be treated by a consultant physician [general medicine specialising in gastroenterology (code 82)].
Treatment Phase: Initial treatment with subcutaneous form at weeks 6, 8, 10, 12, 14 and 16
Clinical criteria: Patient must have received 2 intravenous infusions with this drug for this condition at weeks 0 and 2 under Initial 1 (new patient); OR Patient must have received 2 intravenous infusions with this drug for this condition at weeks 0 and 2 under Initial 2 (change or re-commencement of treatment after a break in biological medicine of less than 24 months); OR Patient must have received 2 intravenous infusions with this drug for this condition at weeks 0 and 2 under Initial 3 (recommencement of treatment after a break in biological medicine of more than 5 years)
AND
Population criteria: Patient must be aged 18 years or older
Prescribing Instructions: The authority application must be made in writing and must include: (1) a completed authority prescription form(s); and (2) a completed Crohn Disease PBS Authority Application Form.
Prescribing Instructions: An assessment of a patient's response to an initial course of treatment must be conducted following a minimum of 12 weeks of therapy. An application for the continuing treatment must be accompanied with the assessment of response and submitted no later than 4 weeks from the date of completion of the most recent course of treatment. This will enable ongoing treatment for those who meet the continuing restriction for PBS-subsidised treatment.
Prescribing Instructions: Where a response assessment is not conducted within the <i>required</i> 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.
Prescribing Instructions: 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 <i>in this treatment cycle</i> . Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.

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<p>Administrative Advice: No increase in the maximum number of repeats may be authorised.</p> <p>Administrative Advice: 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. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>

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INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled autoinjector pen	NEW	2	2	5	Remsima® SC Celltrion Healthcare Australia Pty Ltd

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Category / Program: General Schedule
Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Restriction Method: <input checked="" type="checkbox"/> Authority Required – non-immediate/delayed assessment by Services Australia (in-writing only via mail/postal service or electronic upload to Hobart)
Severity: Severe
Condition: Crohn's disease
Indication: Severe Crohn's disease
Treatment Phase: Continuing treatment with subcutaneous form or switching from intravenous form to subcutaneous form
Treatment criteria:
Must be treated by a gastroenterologist; or
Must be treated by a consultant physician [internal medicine specialising in gastroenterology]; or
Must be treated by a consultant physician [general medicine specialising in gastroenterology]
Clinical criteria:
Patient must have received this drug as their most recent course of PBS-subsidised biological medicine treatment for this condition; OR
Clinical criteria:
Patient must have received this drug in the intravenous form as their most recent course of PBS-subsidised biological medicine for this condition under the infliximab intravenous form continuing treatment restriction
AND
Clinical criteria:
Patient must not receive more than 24 weeks of treatment under this restriction
AND
Clinical criteria:
Patient must have an adequate response to this drug defined as a reduction in Crohn's Disease Activity Index (CDAI) Score to a level no greater than 150 if assessed by CDAI or if affected by extensive small intestine disease;
AND
Clinical criteria:
Patient must have an adequate response to this drug defined as (a) an improvement of intestinal inflammation as demonstrated by: (i) blood: normalisation of the platelet count, or an erythrocyte sedimentation rate (ESR) level no greater than 25 mm per hour, or a C-reactive protein (CRP) level no greater than 15 mg per L; or (ii) faeces: normalisation of lactoferrin or calprotectin level; or (iii) evidence of mucosal healing, as demonstrated by diagnostic imaging findings, compared to the baseline assessment; or (b) reversal of high faecal output state; or (c) avoidance of the need for surgery or total parenteral nutrition (TPN), if affected by short gut syndrome, extensive small intestine disease or is an ostomy patient.
AND
Population criteria:
Patient must be aged 18 years or older
Prescribing Instruction:
Applications for authorisation must be made in writing and must include: (a) a completed authority prescription form; and (b) a completed Crohn Disease PBS Authority Application Form which includes the following: (i) the completed Crohn Disease Activity Index (CDAI) Score calculation sheet including the date of the assessment of the patient's condition, if relevant; or (ii) the reports and dates of the pathology test or diagnostic imaging test(s) used to assess response to therapy for patients with short gut syndrome, extensive small intestine disease or an ostomy, if relevant; and (iii) the date of clinical assessment.
Prescribing Instruction:
An application for the continuing treatment must be accompanied with the assessment of response conducted following a minimum of 12 weeks of therapy and no later than 4 weeks from the date of completion of treatment. This will enable ongoing treatment for those who meet the continuing restriction for PBS-subsidised treatment.

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Prescribing Instructions:
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.
Prescribing Instructions:
If a patient fails to demonstrate a response to treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition <i>in this treatment cycle</i> . Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.
Prescribing Instructions:
Patients are eligible to receive continuing treatment with this drug in courses of up to 24 weeks providing they continue to sustain the response.
Prescribing Instructions:
A patient may re-trial this drug after a minimum of 5 years have elapsed between the date the last prescription for a PBS-subsidised biological medicine was approved in this cycle and the date of the first application under a new cycle under the Initial 3 treatment restriction.
Prescribing Instructions:
At the time of the authority application, medical practitioners should request sufficient quantity for up to 24 weeks of treatment under this restriction.
Prescribing Instructions:
Up to a maximum of 5 repeats will be authorised.
Prescribing Instructions:
If fewer than 5 repeats are requested at the time of the application, authority approvals for sufficient repeats to complete 24 weeks treatment may be requested by telephone and authorised through the Balance of Supply treatment phase PBS restriction. Under no circumstances will telephone approvals be granted for continuing authority applications, or for treatment that would otherwise extend the continuing treatment period.
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
Administrative Advice: No increase in the maximum number of repeats may be authorised.
Administrative Advice:
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. EST Monday to Friday).
Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au
Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos
Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001

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Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Name and Manufacturer
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled syringe	NEW	2	2	0	Remsima® SC Celltrion Healthcare Australia Pty Ltd
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled autoinjector pen	NEW	2	2	0	Remsima® SC Celltrion Healthcare Australia Pty Ltd

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Restriction Type – <input checked="" type="checkbox"/> Authority Required – immediate/real time assessment by Medicare (telephone/online/emergency)
Severity: Severe
Condition: Crohn's disease
Indication: Severe Crohn's disease
Treatment Phase: Initial treatment or continuing treatment with subcutaneous form - Balance of supply
Treatment criteria:
Must be treated by a gastroenterologist; or
Must be treated by a consultant physician [internal medicine specialising in gastroenterology]; or
Must be treated by a consultant physician [general medicine specialising in gastroenterology]
AND
Clinical criteria:
Patient must have received insufficient therapy with this drug under the Initial treatment with subcutaneous form to complete 14 to 16 weeks treatment; OR
Clinical criteria:
Patient must have received insufficient therapy with this drug under the Continuing treatment to complete 24 weeks of treatment;
AND
Clinical criteria:
The treatment must provide no more than the balance of doses up to 14 to 16 weeks therapy available under Initial treatment – subcutaneous form; OR
Clinical criteria:
The treatment must provide no more than the balance of up to 24 weeks therapy available under Continuing treatment – subcutaneous form
AND
Population criteria:
Patient must be aged 18 years or older.
Prescribing Instructions:
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

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Moderate to severe ulcerative colitis

Initial treatment, Continuing treatment and Balance of supply

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Name and Manufacturer
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled syringe	NEW	2	2	2	Remsima® SC Celltrion Healthcare Australia Pty Ltd
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled autoinjector pen	NEW	2	2	2	Remsima® SC Celltrion Healthcare Australia Pty Ltd

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber Type(s): Medical Practitioners
PBS Indication: Moderate to severe ulcerative colitis
Treatment phase : Initial treatment with subcutaneous form at weeks 6, 8, 10, 12, 14 and 16
Restriction Type: Authority required - non-immediate/delayed assessment by Services Australia (in-writing only via mail/postal service or electronic upload to Hobart)
Treatment criteria: Must be treated by a gastroenterologist (code 87); or Must be treated by a consultant physician [internal medicine specialising in gastroenterology (code 81)]; or Must be treated by a consultant physician [general medicine specialising in gastroenterology (code 82)]
Clinical criteria: Patient must have received 2 intravenous infusions with this drug for this condition at weeks 0 and 2 under Initial 1 (new patient); OR
Clinical criteria: Patient must have received 2 intravenous infusions with this drug for this condition at weeks 0 and 2 under Initial 2 (change or re-commencement of treatment after a break in biological medicine of less than 24 months); OR
Clinical criteria: Patient must have received 2 intravenous infusions with this drug for this condition at weeks 0 and 2 under Initial 3 (recommencement of treatment after a break in biological medicine of more than 5 years)
AND
Population criteria: Patient must be aged 18 years or older
Prescribing Instructions: The authority application must be made in writing and must include: (1) a completed authority prescription form(s); and (2) a completed Ulcerative Colitis PBS Authority Application Form.
Prescribing Instructions: An assessment of a patient's response to an initial course of treatment must be conducted following a minimum of 12 weeks of therapy. An application for the continuing treatment must be accompanied with the assessment of response and submitted no later than 4 weeks from the date of completion of the most recent course of treatment. This will enable ongoing treatment for those who meet the continuing restriction for PBS-subsidised treatment.
Prescribing Instructions: 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.
Prescribing Instructions: If a patient fails to demonstrate a response to treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition in this treatment cycle. Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.
Administrative Advice: No increase in the maximum number of repeats may be authorised.
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.

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Administrative Advice:

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. EST Monday to Friday).

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

Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos

Or mailed to:
 Services Australia
 Complex Drugs
 Reply Paid 9826
 HOBART TAS 7001

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Proprietary Name and Manufacturer
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled syringe	NEW	2	2	5	Remsima® SC Celltrion Healthcare Australia Pty Ltd
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled autoinjector pen	NEW	2	2	5	Remsima® SC Celltrion Healthcare Australia Pty Ltd

Category / Program: General Schedule
Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Restriction Method: <input checked="" type="checkbox"/> Authority Required – immediate/real time assessment by Medicare (telephone/online/emergency)
Severity: Moderate to severe
Condition: Ulcerative colitis
Indication: Moderate to severe ulcerative colitis
Treatment Phase: Continuing treatment with subcutaneous form or switching from intravenous form to subcutaneous form
Treatment criteria:
Must be treated by a gastroenterologist; or
Must be treated by a consultant physician [internal medicine specialising in gastroenterology]; or
Must be treated by a consultant physician [general medicine specialising in gastroenterology]
Clinical criteria:
Patient must have received this drug as their most recent course of PBS-subsidised biological medicine treatment for this condition; OR
Clinical criteria:
Patient must have received this drug in the intravenous form as their most recent course of PBS-subsidised biological medicine for this condition under the infliximab intravenous form continuing treatment restriction
AND
Clinical criteria:
Patient must not receive more than 24 weeks of treatment under this restriction
AND
Clinical criteria:

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Patient must have demonstrated or sustained an adequate response to treatment by having a partial Mayo clinic score less than or equal to 2, with no subscore greater than 1 while receiving treatment with this drug,
AND
Population criteria:
Patient must be aged 18 years or older
Prescribing Instructions:
Patients who have failed to maintain a partial Mayo clinic score less than or equal to 2, with no subscore greater than 1 with continuing treatment with this drug, will not be eligible to receive further PBS-subsidised treatment with this drug.
Prescribing Instructions:
Patients are eligible to receive continuing treatment with this drug in courses of up to 24 weeks providing they continue to sustain the response.
Prescribing Instructions:
At the time of the authority application, medical practitioners should request sufficient quantity for up to 24 weeks of treatment under this restriction.
Prescribing Instructions:
Up to a maximum of 5 repeats will be authorised.
Prescribing Instructions:
An application for the continuing treatment must be accompanied with the assessment of response conducted following a minimum of 12 weeks of therapy and no later than 4 weeks from cessation of the most recent course <i>the date of completion</i> of treatment. This will enable ongoing treatment for those who meet the continuing restriction for PBS-subsidised treatment.
Prescribing Instructions:
Where a response assessment is not conducted within this <i>the required</i> 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.
Prescribing Instructions:
If a patient fails to demonstrate a response to treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition <i>in this treatment cycle</i> . Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.
Prescribing Instructions:
A patient may re-trial this drug after a minimum of 5 years have elapsed between the date the last prescription for a PBS-subsidised biological medicine was approved in this cycle and the date of the first application under a new cycle under the Initial 3 treatment restriction.
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
Administrative Advice: No increase in the maximum number of repeats may be authorised.
Administrative Advice:
Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

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Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Manufacturer	Name and
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled syringe	NEW	2	2	0	Remsima® SC	Celltrion Healthcare Australia Pty Ltd
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled autoinjector pen	NEW	2	2	0	Remsima® SC	Celltrion Healthcare Australia Pty Ltd

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Restriction Type – <input checked="" type="checkbox"/> Authority Required – immediate/real time assessment by Medicare (telephone/online/emergency)
Severity: Moderate to severe
Condition: Ulcerative colitis
Indication: Moderate to severe ulcerative colitis
Treatment Phase: Initial treatment or continuing treatment with subcutaneous form - Balance of supply
Treatment criteria:
Must be treated by a gastroenterologist; or
Must be treated by a consultant physician [internal medicine specialising in gastroenterology]; or
Must be treated by a consultant physician [general medicine specialising in gastroenterology]
AND
Clinical criteria:
Patient must have received insufficient therapy with this drug under the Initial treatment with subcutaneous form to complete 14 to 16 weeks treatment; OR
Clinical criteria:
Patient must have received insufficient therapy with this drug under the Continuing treatment to complete 24 weeks of treatment;
AND
Clinical criteria:
The treatment must provide no more than the balance of doses up to 14 to 16 weeks therapy available under Initial treatment – subcutaneous form; OR
Clinical criteria:
The treatment must provide no more than the balance of up to 24 weeks therapy available under Continuing treatment – subcutaneous form
AND
Population criteria:
Patient must be aged 18 years or older.
Prescribing Instructions:
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
Administrative Advice:
Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

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

9 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.

10 Sponsor's Comment

The Sponsor will continue to work with the PBAC to provide infliximab SC for ankylosing spondylitis, severe active psoriatic arthritis, severe chronic plaque psoriasis and complex refractory fistulising Crohn's disease.

Addendum to the November 2020 PBAC Minutes:

11 PBAC Outcome

- 11.1 A grandfathering provision for IFX SC is required for < 500 patients in a Patient Familiarisation Program.

12 Recommended listing

- 12.1 Add new item:

Severe active rheumatoid arthritis

Initial treatment restriction (Grandfather patient)

MEDICINAL PRODUCT medicinal product pack (MPP)	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Manufacturer	Name and
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled syringe	NEW	2	2	5	Remsima® SC	Celltrion Healthcare Australia Pty Ltd
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled autoinjector pen	NEW	2	2	5	Remsima® SC	Celltrion Healthcare Australia Pty Ltd

Category / Program: General Schedule
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
Restriction Method: <input checked="" type="checkbox"/> Authority Required – non-immediate/delayed assessment by Services Australia (in-writing only via mail/postal service or electronic upload/digital submission)
Severity: Severe active
Condition: rheumatoid arthritis
PBS Indication: Severe active rheumatoid arthritis
Treatment criteria: Must be treated by a rheumatologist; OR Must be treated by a clinical immunologist with expertise in the management of rheumatoid arthritis.
Treatment Phase: Initial PBS-subsidised treatment (Grandfather patient) - subcutaneous form
Clinical criteria: Patient must have previously received non-PBS subsidised treatment with this drug with the subcutaneous form for this condition prior to [1 Month 20XX, insert listing date here]
AND Patient must have previously received induction treatment consisting of 2 doses with this drug for this condition in the intravenous form
AND Patient must be receiving treatment with this drug for this condition at the time of application
AND Patient must have failed to achieve, 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
AND 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

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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 6-3 months of continuous intensive treatment with a DMARDs which, if where 2 or more of: methotrexate, (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: 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.
AND
Patient must not have already failed, or ceased to respond to, PBS-subsidised biological medicine treatment for this condition 5 times
AND
Patient must have demonstrated an adequate response to treatment with this drug OR
Patient must have demonstrated an adequate response to treatment with this drug in the intravenous form
AND
The treatment must be given concomitantly with methotrexate at a dose of at least 7.5 mg weekly
AND
Patient must not receive more than 24 weeks of treatment under this restriction
AND
Population criteria: Patient must be aged 18 years or older
Prescribing Instruction: 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.
Prescribing Instruction: 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).
Prescribing Instruction: 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.
Prescribing Instruction:

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All applications for treatment with this drug for this condition under this restriction must include baseline joint count and ESR and/or CRP as determined at the completion of a 6 month intensive DMARD trial but prior to ceasing DMARD therapy, and measurement of response to the prior course of non-PBS-subsidised therapy with this drug. This assessment must be submitted no later than 4 weeks from the cessation of that treatment course.
A Grandfathered patient 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 criteria.
Prescribing Instruction: The authority application must be made in writing and must include: (1) a completed authority prescription form(s); and (2) a completed Rheumatoid Arthritis PBS Authority Application Form.
The patient remains eligible to receive continuing treatment with the same biological medicine in courses of up to 24 weeks providing they continue to sustain <i>an adequate</i> response. It is recommended that a patient be reviewed in the month prior to completing their current course of treatment.
Where a response assessment is not provided, the patient will be deemed to have failed to respond to treatment with this drug, unless the patient has experienced serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment.
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.
Administrative advice: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
Administrative Advice: No increase in the maximum number of repeats may be authorised.
Administrative Advice: 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. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001

Severe Crohn's Disease

Initial treatment restriction (Grandfather patient)

MEDICINAL PRODUCT medicinal product pack (MPP)	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Name and Manufacturer
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled syringe	NEW	2	2	5	Remsima® SC Celltrion Healthcare Australia Pty Ltd
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled autoinjector pen	NEW	2	2	5	Remsima® SC Celltrion Healthcare Australia Pty Ltd

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

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Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
Restriction Type – <input checked="" type="checkbox"/> Authority Required – non-immediate/delayed assessment by Services Australia (in-writing only via mail/postal service or electronic upload/digital submission)
Severity: Severe
Condition: Crohn's disease
Indication: Severe Crohn's disease
Treatment Phase: Initial PBS-subsidised treatment (Grandfather patient) - subcutaneous form
Treatment criteria:
Must be treated by a gastroenterologist; or
Must be treated by a consultant physician [internal medicine specialising in gastroenterology]; or
Must be treated by a consultant physician [general medicine specialising in gastroenterology]
Clinical criteria:
Patient must have a documented history of severe Crohn disease
AND
Clinical criteria:
Patient must have previously received non-PBS subsidised therapy with this drug in the subcutaneous form for this condition prior to [1 Month 20XX, insert listing date here]
AND
Clinical criteria:
Patient must have previously received induction treatment consisting of 2 doses with this drug for this condition in the intravenous form
AND
Patient must be receiving treatment with this drug for this condition at the time of application
AND
Patient must have had a Crohn Disease Activity Index (CDAI) Score of greater than or equal to 300 prior to commencing treatment with this drug; OR
Patient must have a documented history of intestinal inflammation and have diagnostic imaging or surgical evidence of short gut syndrome if affected by the syndrome or has an ileostomy or colostomy; OR
Patient must have a documented history and radiological evidence of intestinal inflammation if the patient has extensive small intestinal disease affecting more than 50 cm of the small intestine,
AND
Clinical criteria:
Patient must have an adequate response to this drug defined as a reduction in Crohn Disease Activity Index (CDAI) Score to a level no greater than 150 if assessed by CDAI or if affected by extensive small intestine disease; OR
Clinical criteria:
Patient must have an adequate response to this drug defined as (a) an improvement of intestinal inflammation as demonstrated by: (i) blood: normalisation of the platelet count, or an erythrocyte sedimentation rate (ESR) level no greater than 25 mm per hour, or a C-reactive protein (CRP) level no greater than 15 mg per L; or (ii) faeces: normalisation of lactoferrin or calprotectin level; or (iii) evidence of mucosal healing, as demonstrated by diagnostic imaging findings, compared to the baseline assessment; or (b) reversal of high faecal output state; or (c) avoidance of the need for surgery or total parenteral nutrition (TPN), if affected by short gut syndrome, extensive small intestine or is an ostomy patient; OR
Patient must have demonstrated an adequate response to treatment with this drug in the intravenous form
AND
Population criteria:
Patient must be aged 18 years or older.
Prescribing Instructions:
Applications for authorisation must be made in writing and must include: (a) a completed authority prescription form; and (b) a completed Crohn Disease PBS Authority Application Form which includes the following: (i) the completed Crohn Disease Activity Index (CDAI) Score calculation sheet including the date of the assessment of the patient's condition, if relevant; or

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(ii) the reports and dates of the pathology test or diagnostic imaging test(s) used to assess response to therapy for patients with short gut syndrome, extensive small intestine disease or an ostomy, if relevant; and (iii) the date of the most recent clinical assessment.
Prescribing Instructions: An application for the continuing treatment must be accompanied with the assessment of response conducted up to 12 weeks after the first dose of infliximab and no later than 4 weeks from the date of completion of treatment. This will enable ongoing treatment for those who meet the continuing restriction for PBS-subsidised treatment.
Prescribing Instructions: Where a response assessment is not conducted within <i>the required</i> 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.
Prescribing Instructions: If a patient fails to demonstrate a response to treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition within this treatment cycle. Serious adverse reaction of a severity resulting in the necessity for permanent withdrawal of treatment is not considered as a treatment failure.
Prescribing Instructions: Patients are eligible to receive continuing treatment with this drug in courses of up to 24 weeks providing they continue to sustain the response.
Prescribing Instructions: A Grandfathered patient 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 criteria.
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
Administrative Advice: No increase in the maximum number of repeats may be authorised.
Administrative advice: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.
Administrative Advice: 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. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001

Moderate to severe ulcerative colitis
Initial treatment restriction (Grandfather patient)

MEDICINAL PRODUCT medicinal product pack (MPP)	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Name and Manufacturer
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled syringe	NEW	2	2	5	Remsima® SC Celltrion Healthcare Australia Pty Ltd
INFLIXIMAB SC, subcutaneous administration, 120mg pre-filled autoinjector pen	NEW	2	2	5	Remsima® SC Celltrion Healthcare Australia Pty Ltd

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
Restriction Type – <input checked="" type="checkbox"/> Authority Required - non-immediate/delayed assessment by Services Australia (in-writing only via mail/postal service or electronic upload/digital submission)

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Severity: Moderate to severe
Condition: Ulcerative colitis
Indication: Moderate to severe ulcerative colitis
Treatment Phase: Initial PBS-subsidised treatment (Grandfather patient) - subcutaneous form
Treatment criteria:
Must be treated by a gastroenterologist; or
Must be treated by a consultant physician [internal medicine specialising in gastroenterology]; or
Must be treated by a consultant physician [general medicine specialising in gastroenterology]
AND
Clinical criteria:
Patient must have previously received non-PBS subsidised therapy with this drug in the subcutaneous form for this condition prior to [1 Month 20XX, insert listing date here]
AND
Clinical criteria:
Patient must have previously received induction treatment consisting of 2 doses with this drug for this condition in the intravenous form
AND
Patient must have had a Mayo clinic score greater than or equal to 6 prior to commencing treatment with this drug; OR
Patient must have had a partial Mayo clinic score greater than or equal to 6, provided the rectal bleeding and stool frequency subscores were both greater than or equal to 2 (endoscopy subscore is not required for a partial Mayo score) prior to commencing treatment with this drug; OR
Patient must have a documented history of moderate to severe refractory ulcerative colitis prior to having commenced treatment with this drug where a Mayo clinic, partial Mayo clinic baseline assessment is not available
AND
Clinical criteria:
Patient must have demonstrated or sustained an adequate response to treatment by having a partial Mayo clinic score less than or equal to 2, with no subscore greater than 1 while receiving treatment with this drug, OR
Patient must have demonstrated an adequate response to treatment with this drug in the intravenous form
AND
Population criteria:
Patient must be aged 18 years or older.
Prescribing Instructions:
Applications for authorisation must be made in writing and must include: (a) a completed authority prescription form; and (b) a completed Ulcerative Colitis PBS Authority Application Form which includes the following: (i) the completed baseline Mayo clinic or partial Mayo clinic calculation sheet prior to initiating treatment (if available) and current Mayo clinic or partial Mayo clinic calculation sheet to demonstrate response, including the date of assessment; (ii) If the baseline Mayo or partial Mayo clinic calculation is not available, reason must be provided; and (iii) the date of commencement of this drug
Prescribing Instructions:
The current Mayo clinic or partial Mayo clinic assessment must be no more than 4 weeks old at the time of application. The baseline assessment must be from immediately prior to commencing treatment with this drug.
Prescribing Instructions:
Patients are eligible to receive continuing treatment with this drug in courses of up to 24 weeks providing they continue to sustain the response.
A Grandfathered patient 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 criteria.
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
Administrative Advice: No increase in the maximum number of repeats may be authorised.
Administrative advice:

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This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.

Administrative Advice:

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. EST Monday to Friday).

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

Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos

Or mailed to:

Services Australia

Complex Drugs

Reply Paid 9826

HOBART TAS 7001

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

13 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.

14 Sponsor's Comment

The sponsor had no comment.