

5.20 USTEKINUMAB, Injection 90 mg in 1 mL pre-filled syringe, Stelara[®], Janssen-Cilag Pty Ltd

1 Purpose of Submission

- 1.1 The Category 4 submission sought to list a 90 mg in 1 mL pre-filled syringe (PFS) form of ustekinumab (Stelara[®]) for the treatment of patients with Crohn disease and severe chronic plaque psoriasis requiring a 90 mg dose of ustekinumab, under the same conditions as the current 45 mg vial for injection (vial) form of ustekinumab.

2 Background

- 2.1 Ustekinumab 45 mg in 0.5 mL injection (vial) is currently available as an Authority Required listing on the PBS for severe psoriatic arthritis; severe Crohn disease; and adult and paediatric severe chronic plaque psoriasis.
- 2.2 The submission indicated that the PFS form of ustekinumab would be more convenient for patients than the current vial form as it reduces the time required for preparation of the dose for administration. The submission stated that the product needs to be drawn from the vial(s) depending on the dose required and then administered, whereas no preparation is required before administration for the PFS form.
- 2.3 The Therapeutic Goods Administration (TGA) Clinical Evaluation Report for ustekinumab provided as an attachment to the submission states that “The formulation of ustekinumab was identical for the PFS and LIV (liquid in vial) presentations”. It also stated “Within study comparison (C0743T09) suggest that serum ustekinumab levels after switch to administration via PFS from LIV are comparable”.

Registration status

- 2.4 Ustekinumab was registered by the TGA in the Australian Register of Therapeutic Goods (ARTG) on 28 July 2009 for the treatment of moderate to severe chronic plaque psoriasis. Ustekinumab was subsequently registered in the ARTG for the treatment of psoriatic arthritis in adults, Crohn disease in adults and ulcerative colitis in adults.
- 2.5 The recommended doses of ustekinumab from the Stelara Product Information are:
- Plaque psoriasis (adults): 45 mg administered at weeks 0 and 4, then every 12 weeks thereafter. Alternatively, 90 mg administered over weeks 0 and 4, then every 12 weeks thereafter may be used in patients with a body weight greater than 100 kg.

- Plaque psoriasis (paediatrics, 6 years and older): the recommended dose is based on body weight, and is administered at weeks 0 and 4, then every 12 weeks thereafter. The recommended dose is 0.75 mg/kg for patients weighing <60 kg, 45 mg for patients weighing ≥60 kg to ≤100 kg, and 90 mg for patients weighing >100 kg.
- Crohn disease: the initial dose is administered intravenously with a tiered dose based on body weight. After the initial intravenous (IV) dose Stelara is administered subcutaneously at a dose of 90 mg 8 weeks after the initial IV dose, then every 8-12 weeks thereafter.

Previous PBAC consideration

2.6 Ustekinumab 45 mg vial was previously considered by the PBAC:

- For severe chronic plaque psoriasis in adults at its November 2009 meeting (recommended)
- For severe Crohn disease in adults at its March 2017 meeting (recommended)
- For paediatric patients with severe chronic plaque psoriasis at its March 2021 meeting (recommended)

2.7 Ustekinumab 90 mg PFS has not been considered by the PBAC previously. However, the submission stated that the pivotal trials included in the ustekinumab submissions for chronic plaque psoriasis and Crohn disease used a 90 mg PFS form of ustekinumab and claimed therefore that the PBAC has already considered the safety and efficacy of the 90 mg PFS form.

2.8 A request to list ustekinumab 90 mg on the PBS for the treatment of ulcerative colitis was also considered at the July 2022 PBAC meeting.

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

3 Requested listing

3.1 The submission requested the following new listing. Suggested additions are in italics and deletions are in strikethrough. A shortened version of the restriction is presented, which includes the relevant prescribing instructions where key changes or additions are made.

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MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
Initial 1,2,3, continuing treatment CD					
USTEKINUMAB ustekinumab injection 90 mg in 1 mL pre-filled syringe	NEW	1	1	0	Stelara
Initial 1,2,3 whole body, or, face/hand/foot, balance of supply paediatric CPP					
USTEKINUMAB ustekinumab injection 90 mg in 1 mL pre-filled syringe	NEW	1	1	2	Stelara
Initial 1,2,3 whole body, or, face/hand/foot, balance of supply adult CPP					
USTEKINUMAB ustekinumab injection 90 mg in 1 mL pre-filled syringe	NEW	1	1	2	Stelara
Continuing treatment whole body, or, face/hand/foot, grandfather treatment paediatric CPP					
USTEKINUMAB ustekinumab injection 90 mg in 1 mL pre-filled syringe	NEW	1	1	1	Stelara
Balance of supply continuing treatment whole body, or, face/hand/foot paediatric CPP					
USTEKINUMAB ustekinumab injection 90 mg in 1 mL pre-filled syringe	NEW	1	1	0	Stelara
Continuing treatment whole body, or face/hand/foot, balance of supply adult CPP					
USTEKINUMAB ustekinumab injection 90 mg in 1 mL pre-filled syringe	NEW	1	1	1	Stelara

CD: Crohn disease; CPP: chronic plaque psoriasis

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Restriction Summary [new] / Treatment of Concept: [new]	
	Category / Program: GENERAL – General Schedule
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required (in writing only via post/HPOS upload)
	Indication: Severe Crohn disease
	Treatment Phase: Initial treatment - Initial 1 (new patient) Initial treatment - Initial 2 (change or recommencement of treatment after a break in biological medicine of less than 5 years) Initial treatment - Initial 3 (recommencement of treatment after a break in biological medicine of more than 5 years)
	Prescribing Instructions: Two completed authority prescriptions should be submitted with every initial application for this drug. One prescription should be written under S100 (Highly Specialised Drugs) for a weight-based loading dose, containing a quantity of up to 4 vials of 130 mg and no repeats. The second prescription should be written under S85 (General) for 2 vials of 45 mg and no repeats a total dose of 90 mg and no repeats.
	Prescribing Instructions: A maximum quantity of a weight based loading dose is up to 4 vials with no repeats and the subsequent first dose of 90 mg (2 vials of 45 mg) with no repeats provide for an initial 16 week course of this drug will be authorised.
	Prescribing Instructions: Where fewer than 6 5 vials in total are requested at the time of the application, authority approvals for a sufficient number of vials based on the patient's weight to complete dosing at weeks 0 and 8 may be requested by telephone through the balance of supply restriction.

- 3.2 For chronic plaque psoriasis, a maximum quantity of one 90 mg PFS with 2 repeats for initial treatment was requested for a patient requiring 90 mg ustekinumab. For continuing treatment, a maximum quantity of one 90 mg PFS with 1 repeat was requested for a patient requiring 90 mg ustekinumab and is sufficient for 24 weeks of treatment, with patients receiving SC ustekinumab every 12 weeks. This was appropriate.
- 3.3 The current listing of ustekinumab 45 mg vial for chronic plaque psoriasis has a maximum quantity of 1 with 2 repeats, and the continuing treatment listing has a maximum quantity of 1 with 1 repeat.
- 3.4 The submission proposed no changes to the chronic plaque psoriasis restriction.
- 3.5 The sponsor stated that if ustekinumab 90 mg PFS was PBS-listed for chronic plaque psoriasis and Crohn disease, it would replace the use of ustekinumab 45 mg vials to make up a 90 mg dose. It was expected that a transition period would occur whereby patients would transition from using 2 x ustekinumab 45 mg vials to 1 x 90 mg PFS. The submission stated this would likely be at least 6 months given the 24 week duration of the continuing treatment authority. The sponsor stated that in time, the PBS-listing for ustekinumab 45 mg vial in Crohn disease may no longer be required. The ustekinumab 45 mg vial PBS-listing would continue to be required for chronic plaque psoriasis as the 45 mg dose would be used for patients who weigh ≤100 kg.

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

4 Comparator

4.1 The submission proposed to list a new strength and form of ustekinumab and compared this to the currently listed 45 mg strength of the same drug. This was appropriate, however ustekinumab could replace any of the current PBS-listed bDMARDs for Crohn disease and chronic plaque psoriasis. These could include:

- adalimumab, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab and tildrakizumab for chronic plaque psoriasis
- adalimumab, infliximab and vedolizumab for Crohn disease.

4.2 The PBAC noted it could only recommend listing ustekinumab 90 mg PFS at a higher price than the alternative therapy or therapies if it was satisfied that it provided, for some patients, a significant improvement in efficacy or reduction of toxicity over the alternative therapy or therapies (*National Health Act 1953, Section 101(3B)*). The alternative therapies in this case includes other bDMARDs outlined in paragraph 4.1.

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

5 Consideration of the evidence

Sponsor hearing

5.1 There was no hearing for this item.

Consumer comments

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

Clinical trials

5.3 The submission included the following clinical trials:

- PHOENIX-1, PHOENIX-2 and ACCEPT for adult chronic plaque psoriasis
- CADMUS and CADMUS Jr for paediatric plaque psoriasis
- UNITI-1, UNITI-2 and IM-UNITI for Crohn disease

5.4 These trials were the pivotal trials previously included in the ustekinumab submissions for adult chronic plaque psoriasis, paediatric plaque psoriasis and Crohn disease.

5.5 As a Category 4 submission, no evaluation of the clinical evidence was undertaken.

Clinical claim

5.6 The submission claimed non-inferior comparative effectiveness and non-inferior comparative safety of ustekinumab 90 mg PFS compared with ustekinumab 45 mg vial.

5.7 The PBAC considered that the claim of non-inferior comparative effectiveness was reasonable.

5.8 The PBAC considered that the claim of non-inferior comparative safety was reasonable.

Economic analysis

5.9 As a Category 4 submission, the economic analysis has not been independently evaluated.

5.10 The submission presented a cost-minimisation analysis of ustekinumab 90 mg compared with ustekinumab 45 mg. The equi-effective doses were estimated as ustekinumab 90 mg PFS = 2 x ustekinumab 45 mg vial.

5.11 The submission provided the current indication-specific effective prices of ustekinumab 45 mg and the requested prices of ustekinumab 90 mg PFS for adult and paediatric severe chronic plaque psoriasis patients who need the 90 mg dose and for the maintenance treatment of adult severe Crohn disease, which are presented in the below.

Table 1. Current indication-specific effective ex-manufacturer prices of ustekinumab

Indication/listing	Current price per dose	Average price per 45 mg LIV unit for all patients (for SPA rebate)	Price per 45 mg LIV unit for patients on 90 mg	Requested price for 90 mg PFS
Adult severe CPP	\$ [REDACTED]	\$ [REDACTED] ([REDACTED] % on 90 mg)	\$ [REDACTED]	\$ [REDACTED]
Paediatric severe CPP	\$ [REDACTED]	\$ [REDACTED] ([REDACTED] % on 90 mg)	\$ [REDACTED]	\$ [REDACTED]
Adult severe CD (maintenance)	\$ [REDACTED]	\$ [REDACTED] ([REDACTED] on 90 mg)	\$ [REDACTED]	\$ [REDACTED]

CD: Crohn disease, CPP: chronic plaque psoriasis, LIV: liquid-in-vial, PFS: pre-filled syringe, SPA: Special Pricing Arrangement
 Source: Submission Main Body p.22

Drug cost/patient/year

5.12 Using the requested effective prices outlined in paragraph 5.17, the estimated drug cost/patient per year is:

- \$ [REDACTED] for adult chronic plaque psoriasis, based on ongoing treatment every 12 weeks
- \$ [REDACTED] for paediatric chronic plaque psoriasis, based on ongoing treatment every 12 weeks
- \$ [REDACTED] for Crohn disease, based on ongoing treatment every 8 weeks.

5.13 The submission stated that there is a Special Pricing Arrangement (SPA) in place for ustekinumab 45 mg in the adult severe chronic plaque psoriasis, paediatric severe chronic plaque psoriasis and adult severe Crohn disease indications. For adult and paediatric severe chronic plaque psoriasis, the cost per full dose at the effective price is [REDACTED]. For these chronic plaque psoriasis indications, the SPA rebate applied to ustekinumab 45 mg [REDACTED]. For adult severe Crohn disease, the SPA rebate [REDACTED].

5.14 The submission stated that if ustekinumab 90 mg PFS is PBS-listed, [REDACTED] [REDACTED] [REDACTED] [REDACTED] for the SPA rebate will no longer be applicable as patients on the 90 mg dose will start

using the 90 mg PFS, and the effective price per unit of ustekinumab 45 mg for the SPA rebate will reflect the current effective price per dose, which is \$| for adult severe chronic plaque psoriasis and \$| for paediatric severe chronic plaque psoriasis.

- 5.15 The submission stated that there is a Risk-Sharing Arrangement (RSA) with annual subsidisation caps in place for ustekinumab 45 mg in paediatric severe chronic plaque psoriasis. The sponsor proposed that ustekinumab 90 mg join the existing RSA for paediatric severe chronic plaque psoriasis.

Estimated PBS utilisation and financial implications

- 5.16 The requested published AEMP for ustekinumab 90 mg, 1 of \$3,809.08, is equivalent to the published AEMP for ustekinumab 45 mg, 1 as at 1 May 2022. The requested effective prices are \$| for adult severe chronic plaque psoriasis, \$| for paediatric severe chronic plaque psoriasis, and \$| for adult severe Crohn disease.
- 5.17 The submission stated that at the effective prices, the PBS-listing of ustekinumab 90 mg is expected to be cost neutral for the PBS/RPBS.

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

6 PBAC Outcome

- 6.1 The PBAC recommended the listing of ustekinumab injection 90 mg in 1 mL pre-filled syringe for the treatment of patients with Crohn disease and severe chronic plaque psoriasis requiring a 90 mg dose of ustekinumab, under the same circumstances as the current PBS-listed ustekinumab 45 mg vial for these indications.
- 6.2 The PBAC noted the TGA considered ustekinumab PFS to be equivalent to ustekinumab vial. The PBAC considered the equi-effective doses to be ustekinumab 90 mg PFS and 2 x ustekinumab 45 mg vials.
- 6.3 The PBAC noted that other relevant comparators for the treatment of severe chronic plaque psoriasis could include adalimumab, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab and tildrakizumab. Other relevant comparators for the treatment of Crohn disease could include adalimumab, infliximab and vedolizumab. The PBAC noted that no evidence of superiority against any of the other alternative therapies was provided.
- 6.4 The PBAC recommended listing ustekinumab 90 mg PFS for the treatment of Crohn disease and chronic plaque psoriasis on a cost-minimisation basis with the least costly biological disease modifying anti-rheumatic drug (bDMARD) for these conditions. In making its recommendation, the PBAC accepted that any of the currently PBS-listed bDMARDs for Crohn disease and severe chronic plaque psoriasis could be an alternative therapy to ustekinumab 90 mg.
- 6.5 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because ustekinumab 90 mg PFS is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over

ustekinumab 45 mg vial or other products listed on the PBS for Crohn disease and severe chronic plaque psoriasis, 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 2022* for Pricing Pathway A were not met.

- 6.6 The PBAC noted that this submission is not eligible for an Independent Review because it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

- 7.1 Add new item:

(N.B. A shortened version of the restriction is presented, which includes the relevant prescribing instructions where key changes are made to the restrictions of the current PBS-listed ustekinumab 45 mg vial.)

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MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
Initial 1,2,3, continuing treatment CD, balance of supply					
USTEKINUMAB ustekinumab injection 90 mg in 1 mL pre-filled syringe	NEW	1	1	0	Stelara
Initial 1,2,3 whole body, or, face/hand/foot, balance of supply paediatric CPP					
USTEKINUMAB ustekinumab injection 90 mg in 1 mL pre-filled syringe	NEW	1	1	2	Stelara
Initial 1,2,3 whole body, or, face/hand/foot, balance of supply adult CPP					
USTEKINUMAB ustekinumab injection 90 mg in 1 mL pre-filled syringe	NEW	1	1	2	Stelara
Continuing treatment whole body, or, face/hand/foot, grandfather treatment paediatric CPP					
USTEKINUMAB ustekinumab injection 90 mg in 1 mL pre-filled syringe	NEW	1	1	1	Stelara
Balance of supply continuing treatment whole body, or, face/hand/foot paediatric CPP					
USTEKINUMAB ustekinumab injection 90 mg in 1 mL pre-filled syringe	NEW	1	1	0	Stelara
Continuing treatment whole body, or face/hand/foot, balance of supply adult CPP					
USTEKINUMAB ustekinumab injection 90 mg in 1 mL pre-filled syringe	NEW	1	1	1	Stelara

CD: Crohn disease; CPP: chronic plaque psoriasis

Copy Restriction Summaries from Severe Crohn Disease

Initial treatment - Initial 1 (new patient) - Restriction Summary 9772 / ToC: 9710: Authority Required

Initial treatment - Initial 2 (change or recommencement) - Restriction Summary 9746 / ToC: 9655: Authority Required

Initial treatment - Initial 3 (recommencement of treatment) - Restriction Summary 9709 / ToC: 9656: Authority Required

Continuing treatment - Restriction Summary 9747 / ToC: 9657: Authority Required

Balance of Supply - Restriction Summary 9797 / ToC: 9711: Authority Required

For Initial 1, 2 and 3, edit the following prescribing instructions. These changes should flow-on to the current Initial 1, 2 and 3 ustekinumab CD listings: 11164N, 1182M, 11178H

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	Category / Program: GENERAL – General Schedule
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required (in writing only via post/HPOS upload)
	Indication: Severe Crohn disease
	Treatment Phase: Initial treatment - Initial 1 (new patient) Initial treatment - Initial 2 (change or recommencement of treatment after a break in biological medicine of less than 5 years) Initial treatment - Initial 3 (recommencement of treatment after a break in biological medicine of more than 5 years)
	Prescribing Instructions: Two completed authority prescriptions should be submitted with every initial application for this drug. One prescription should be written under S100 (Highly Specialised Drugs) for a weight-based loading dose, containing a quantity of up to 4 vials of 130 mg and no repeats. The second prescription should be written under S85 (General) for 2 vials of 45 mg and no repeats a total dose of 90 mg and no repeats.
	Prescribing Instructions: A maximum quantity of a weight based loading dose is up to 4 vials with no repeats and the subsequent first dose of 90 mg (2 vials of 45 mg) with no repeats provide for an initial 16 week course of this drug will be authorised.
	Prescribing Instructions: Where fewer than € 5 vials in total are requested at the time of the application, authority approvals for a sufficient number of vials based on the patient's weight to complete dosing at weeks 0 and 8 may be requested by telephone through the balance of supply restriction.

Copy Restriction Summaries from Severe chronic plaque psoriasis

Whole body

Initial treatment - Initial 1 (new patient) - Restriction Summary 11169 / ToC: 11086: Authority Required
 Initial treatment - Initial 2 (change or recommencement) - Restriction Summary 11085 / ToC: 11153: Authority Required
 Initial treatment - Initial 3 (recommencement of treatment) - Restriction Summary 11135 / ToC: 11161: Authority Required

Face, hand, foot

Initial treatment - Initial 1 (new patient) - Restriction Summary 11136 / ToC: 11137: Authority Required
 Initial treatment - Initial 2 (change or recommencement) - Restriction Summary 11144 / ToC: 11119: Authority Required
 Initial treatment - Initial 3 (recommencement of treatment) - Restriction Summary 11118 / ToC: 11145: Authority Required

Balance of Supply Initial - Restriction Summary 11092 / ToC: 11120: Authority Required

For Initial 1, 2 and 3 (both whole body and face, hand, foot) edit the following prescribing instructions. These changes should flow-on to the current Initial 1, 2 and 3 ustekinumab CPP listings: 9304Q, 9305R, 12664M, 12669T

Public Summary Document – July 2022 PBAC Meeting

	Category / Program: GENERAL – General Schedule
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required (in writing only via post/HPOS upload)
	Indication: Severe chronic plaque psoriasis
	Treatment Phase: Initial treatment - Initial 1, Whole body (new patient) Initial treatment - Initial 2, Whole body (change or re-commencement of treatment after a break in biological medicine of less than 5 years) Initial treatment - Initial 3, Whole body (re-commencement of treatment after a break in biological medicine of more than 5 years) Initial treatment - Initial 1, Face, hand, foot (new patient) Initial 2, Face, hand, foot (change or re-commencement of treatment after a break in biological medicine of less than 5 years) Initial 3, Face, hand, foot (re-commencement of treatment after a break in biological medicine of more than 5 years)
	Population criteria: Patient must be aged 18 years or older.
	Prescribing Instructions: At the time of the authority application, medical practitioners should request the appropriate number of vials, based on the weight of the patient, to provide sufficient for a single injection. Up to a maximum of 2 repeats will be authorised.

Whole body

Continuing treatment whole body (adult) - Restriction Summary 11368 / ToC: 8891: Authority Required

Continuing treatment whole body (paediatric) - Restriction Summary 12311 / ToC: 12311: Authority Required

Face, hand, foot

Continuing treatment face, hand, foot (adult) - Restriction Summary 11347 / ToC: 8987: Authority Required

Continuing treatment face, hand, foot (paediatric) - Restriction Summary 12322 / ToC: 12302: Authority Required

Balance of supply continuing (adult) - Restriction Summary 8829 / ToC: 6696: Authority Required,

Balance of supply - Continuing treatment (Whole body, or, face/hand/foot) Restriction Summary 12285 / ToC: 12285: Authority Required

Restriction Summary [new] / Treatment of Concept: [new]	
	Category / Program: GENERAL – General Schedule
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required (in writing only via post/HPOS upload)
	Indication: Severe chronic plaque psoriasis
	Treatment Phase: Continuing treatment, Whole body Continuing treatment, Face, hand, foot
	Population criteria: Patient must be aged 18 years or older.
	Prescribing Instructions: At the time of the authority application, medical practitioners should request the appropriate number of vials, based on the weight of the patient, to provide sufficient for a single injection. Up to a maximum of 1 repeat will be authorised.

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

8 Context for Decision

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

9 Sponsor's Comment

The sponsor had no comment.