5.31 USTEKINUMAB
Injection 45 mg in 0.5 mL single use pre-filled syringe,
Injection 45 mg in 0.5 mL single use pre-filled pen,
Injection 90 mg in 1 mL single use pre-filled syringe,
Injection 90 mg in 1 mL single use pre-filled pen,
Stelara®,
Janssen-Cilag Pty Ltd

1 Purpose of Submission

1.1 The Category 4 submission requested the listing of ustekinumab (UST) 45 mg and 90 mg pre-filled syringe (PFS) and pre-filled pen (PFP) under the same circumstances as the Pharmaceutical Benefits Scheme (PBS) listed UST 45 mg vial.

1.2 The submission also requested amendments to the current restrictions for severe Crohn disease (CD) and severe chronic plaque psoriasis (CPP) to align with changes in the quantity required for adult patients following the proposed new listings.

1.3 The sponsor advised it intends to [redacted].

2 Background

2.1 The following three formulations of UST are currently PBS-listed. Table 1 shows the current PBS-listed forms of ustekinumab and submission's requested dose forms.

- UST 45 mg/0.5 mL injection vial is listed as an Authority Required listing for severe psoriatic arthritis (PsA), severe CD, adult and paediatric severe CPP.
- UST 90 mg/1 mL PFS is listed as an Authority Required listing for moderate to severe ulcerative colitis (MSUC) and complex refractory fistulising Crohn disease (fCD).
- UST 130 mg/26 mL injection vial is listed as Section 100 (Highly Specialised Drugs Program) Authority Required listing for severe CD, MSUC and complex refractory fCD.

Table 1: Current PBS-listed forms of ustekinumab and submission's requested dose forms

Indication	PBS listed dose forms	Recommended dosing (current PBS dose form units)	Requested additional dose forms	Recommended dosing (requested dose form units)
Adult Severe CPP	45 mg vial	≤100 kg: 45 mg (1 x 45 mg LIV) >100 kg: 90 mg (2 x 45 mg LIV) SC injection at Weeks 0 and 4, then every 12 weeks	45 mg PFS 45 mg PFP 90 mg PFS 90 mg PFP	≤100 kg: 45 mg **(1 x 45 mg PFS/PFP)** >100 kg: 90mg **(1 x 90 mg PFS/ PFP)** SC injection at Weeks 0 and 4, then every 12 weeks
Paediatric severe CPP	45 mg vial	<60 kg: 0.75 mg/kg (portion of 45 mg LIV) ≥60 to ≤100 kg: 45 mg (1 x 45 mg LIV) >100 kg: 90 mg (2 x 45 mg LIV) SC injection at Weeks 0 and 4, then every 12 weeks	45 mg PFS 90 mg PFS	<60 kg: 0.75 mg/kg (portion of 45 mg LIV) ≥60 to ≤100 kg: 45 mg **(1 x 45 mg PFS)** >100 kg: 90 mg **(1 x 90 mg PFS)** SC injection at Weeks 0 and 4, then every 12 weeks
Severe CD	45 mg vial 130 mg vial	Initiate with 260-520 mg IV infusion (2-4 x 130 mg LIV) 90 mg SC injection at Week 8, then every 8 to 12 weeks (2 x 45 mg LIV)	90 mg PFS 90 mg PFP	Initiate with 260-520 mg IV infusion (2-4 x 130 mg LIV) 90 mg SC injection at Week 8, then every 8 or 12 weeks **(1 x 90 mg PFS/PFP)**
Severe PsA	45 mg vial	45 mg SC injection at Weeks 0 and 4, then every 12 weeks (1 x 45 mg LIV)	45 mg PFS 45 mg PFP	45 mg SC injection at Weeks 0 and 4, then every 12 weeks **(1 x 45 mg PFS/PFP)**
Moderate to severe UC	90 mg PFS 130 mg vial	Initiate with 260-520 mg IV infusion (2-4 x 130 mg LIV) 90 mg SC injection at Week 8, then every 8 to 12 weeks (1 x 90 mg PFS)	90 mg PFP	Initiate with 260-520 mg IV infusion (2-4 x 130 mg LIV) 90 mg SC injection at Week 8, then every 8 or 12 weeks (1 x 90 mg PFS/**PFP**)
Complex refractory fCD	90 mg PFS 130 mg vial	Initiate with 260-520 mg IV infusion (2-4 x 130 mg LIV) 90 mg SC injection at Week 8, then every 8 to 12 weeks (1 x 90 mg PFS)	90 mg PFP	Initiate with 260-520 mg IV infusion (2-4 x 130 mg LIV) 90 mg SC injection at Week 8, then every 8 or 12 weeks (1 x 90 mg PFS/**PFP**)

Source: Main submission body (pg 7)

2.2 The submission stated that the PFS and PFP forms would improve ease of administration and patient compliance, especially for patients who are needle phobic. The submission also stated that product needs to be manually drawn from the current PBS-listed injection vial form, depending on the dose required and then administered, whereas no preparation is required before administration for the PFS and PFP forms which would reduce risk of dosing error, excessive drug exposure, bacterial contamination from unsterile technique and accidental needle stick injuries. The PFS and PFP forms would also improve ease of administration for patients with CPP and CD requiring 90 mg UST due to the administration of only one injection each time.

2.3 The Therapeutic Goods Administration (TGA) Clinical Evaluation Report (pg 2) stated that "The formulation of ustekinumab was identical for the PFS and vial presentations". It also stated on page 7 that "Within study comparison (C0743T09)

suggest that serum ustekinumab levels after switch to administration via PFS from liquid in vial are comparable".

2.4 The TGA File Note (pg 3) stated that "The CNTO1275EDI1001 (an open-label, randomized, parallel-group) study demonstrated bioequivalence between the UST PFS and PFP as the 90% confidence intervals of the geometric mean ratios for Cmax and AUCinf fell within the standard bioequivalence range of 80% to 120%". The TGA stated that the PFP has not been studied in the paediatric population and is not recommended for use by paediatric patients. The submission did not request the PFP form for paediatric patients.

Registration status

2.5 UST PFS (45 mg and 90 mg) and PFP (45 mg and 90 mg) were TGA-registered on 19 August 2010 and 9 November 2023, respectively, for:

- plaque psoriasis (adult and paediatric)
- psoriatic arthritis (PsA)
- Crohn disease
- ulcerative colitis

2.6 The TGA approved Product Information (PI) recommended the following UST doses.

- 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.
- Psoriatic Arthritis: 45 mg administered at Weeks 0 and 4, then every 12 weeks thereafter. Some patients with a body weight greater than 100 kg received a 90 mg dose in clinical trials and observed a clinical benefit.
- Crohn disease and ulcerative colitis (UC): the initial dose is administered intravenously with a tiered dose based on body weight. UST should then be administered subcutaneously with a first dose of 90 mg, 8 weeks after the initial IV dose, then every 8-12 weeks thereafter. The submission stated that the recommended treatment regimens for fCD are the same as for CD.

Previous PBAC consideration

2.7 UST 45 mg PFS and UST 45 mg and 90 mg PFP have not been previously considered by the PBAC.

2.8 UST 90 mg PFS was previously considered and recommended by the PBAC:

- For CD and severe CPP at its July 2022 meeting (the submission noted that this listing was not progressed as the sponsor could not proceed with the terms of the recommendation)
- For MSUC at its July 2022 meeting (PBS-listed on 1 May 2023)
- For complex refractory fistulising CD at its July 2023 meeting (PBS-listed on 1 January 2024)

3 Requested listing

3.1 The submission requested the following new listing and changes to the existing restriction for severe CPP and CD. Suggested additions are in italics and deletions are in strikethrough. A shortened version of the restriction is presented below:

Severe PsA

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
Initial treatment					
USTEKINUMAB					
ustekinumab 45 mg/0.5 mL injection, pre-filled syringe	*NEW*	*1*	*1*	*2*	*Stelara*
ustekinumab 45 mg/0.5 mL injection, pre-filled pen	*NEW*	*1*	*1*	*2*	*Stelara*
Continuing treatment					
USTEKINUMAB					
ustekinumab 45 mg/0.5 mL injection, syringe	*NEW*	*1*	*1*	*1*	*Stelara*
ustekinumab 45 mg/0.5 mL injection, pen device	*NEW*	*1*	*1*	*1*	*Stelara*

Severe CPP

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
Initial treatment paediatric CPP					
USTEKINUMAB					
ustekinumab 45 mg/0.5 mL injection, pre-filled syringe	*NEW*	*1*	*1*	*2*	*Stelara*
ustekinumab 90 mg/mL injection, 1 mL pre-filled syringe	*NEW*	*1*	*1*	*2*	*Stelara*
Continuing treatment paediatric CPP					
USTEKINUMAB					
ustekinumab 45 mg/0.5 mL injection, pre-filled syringe	*NEW*	*1*	*1*	*1*	*Stelara*
ustekinumab 90 mg/mL injection, 1 mL pre-filled syringe	*NEW*	*1*	*1*	*1*	*Stelara*
Continuing treatment, balance of supply paediatric CPP					

USTEKINUMAB					
ustekinumab 45 mg/0.5 mL injection, pre-filled syringe	*NEW*	*1*	*1*	*0*	*Stelara*
ustekinumab 90 mg/mL injection, 1 mL pre-filled syringe	*NEW*	*1*	*1*	*0*	*Stelara*
Initial treatment adult CPP					
USTEKINUMAB					
ustekinumab 45 mg/0.5 mL injection, pre-filled syringe	*NEW*	*1*	*1*	*2*	*Stelara*
ustekinumab 45 mg/0.5 mL injection, pre-filled pen	*NEW*	*1*	*1*	*2*	*Stelara*
ustekinumab 90 mg/mL injection, 1 mL pre-filled syringe	*NEW*	*1*	*1*	*2*	*Stelara*
ustekinumab 90 mg/0.5 mL injection, pre-filled pen	*NEW*	*1*	*1*	*2*	*Stelara*
Continuing treatment adult CPP					
USTEKINUMAB					
ustekinumab 45 mg/0.5 mL injection, pre-filled syringe	*NEW*	*1*	*1*	*1*	*Stelara*
ustekinumab 45 mg/0.5 mL injection, pre-filled pen	*NEW*	*1*	*1*	*1*	*Stelara*
ustekinumab 90 mg/mL injection, 1 mL pre-filled syringe	*NEW*	*1*	*1*	*1*	*Stelara*
ustekinumab 90 mg/0.5 mL injection, pre-filled pen	*NEW*	*1*	*1*	*1*	*Stelara*

Restriction Summary: 14457 / Treatment of Concept: 14442	
Concept ID (for internal Dept. use)	**Category / Program:** GENERAL – General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners
	Restriction Type: ☒Authority Required
	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 treatment - Initial 2, Face, hand, foot (change or re-commencement of treatment after a break in biological medicine of less than 5 years) Initial treatment - Initial 3, Face, hand, foot (re-commencement of treatment after a break in biological medicine of more than 5 years)
	Prescriber 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.
Restriction Summary 11368 / Treatment of Concept: 8891	
Concept ID (for internal Dept. use)	**Category / Program:** GENERAL – General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners
	Restriction Type: ☒Authority Required

	Indication: Severe chronic plaque psoriasis
	Treatment Phase: Continuing treatment, Whole body Continuing treatment, Face, hand, foot
	Prescriber 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 repeats will be authorised.

Abbreviation: CPP - chronic plaque psoriasis

Severe CD

MEDICINAL PRODUCT **medicinal product pack**	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
Initial 1,2,3, continuing treatment, balance of supply					
USTEKINUMAB					
Initial treatment (Week 8)					
ustekinumab 90 mg/mL injection, 1 mL pre-filled syringe	*NEW*	*1*	*1*	*0*	*Stelara*
ustekinumab 90 mg/mL injection, pre-filled pen	*NEW*	*1*	*1*	*0*	*Stelara*
Continuing treatment (24 week)					
USTEKINUMAB					
ustekinumab 90 mg/mL injection, 1 mL pre-filled syringe	*NEW*	*1*	*1*	*2*	*Stelara*
ustekinumab 90 mg/mL injection, pre-filled pen	*NEW*	*1*	*1*	*2*	*Stelara*
Restriction Summary 9195 / Treatment of Concept: 9176					
Concept ID (for internal Dept. use)	**Category / Program:** GENERAL – General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners				
	Restriction Type: ☒Authority Required				
	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)				
	Prescriber 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~~ *with* no repeats.				
	Prescriber 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.				

MSUC

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
Initial treatment					
USTEKINUMAB					
ustekinumab 90 mg/0.5 mL injection, pre-filled pen	*NEW*	*1*	*1*	*0*	*Stelara*
Continuing treatment					
USTEKINUMAB					
ustekinumab 90 mg/0.5 mL injection, pre-filled pen	*NEW*	*1*	*1*	*1*	*Stelara*

Complex refractory fCD

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
Continuing treatment					
USTEKINUMAB					
ustekinumab 90 mg/0.5 mL injection, pre-filled pen	*NEW*	*1*	*1*	*2*	*Stelara*
Initial treatment					
USTEKINUMAB					
ustekinumab 90 mg/0.5 mL injection, pre-filled pen	*NEW*	*1*	*1*	*0*	*Stelara*

3.2 The pre-PBAC response stated that Stelara 45 mg and 90 mg PFS and PFP should not be considered equivalent to the Wezlana 45 mg vial as they are different dose forms with different modes of administration. Similarly, the pre-PBAC response stated that Stelara 45 mg and 90 mg PFP should not be considered equivalent to the Wezlana 45 mg and 90 mg PFS for the same reason.

4 Comparator

4.1 The nominated comparator for UST 45 mg PFS and PFP in the adult and paediatric CPP population (patients that require UST 45 mg) was 1 x UST 45 mg vial. The nominated comparator for UST 90 mg PFS and PFP in the adult and paediatric CPP (patients that require UST 90 mg) and severe CD populations was 2 x UST 45 mg vial. The nominated comparator for UST 90 mg PFP in MSUC and fCD populations was 1 x UST 90 mg PFS.

4.2 The submission noted at its July 2022 meeting, the PBAC recommended listing UST 90 mg PFS for the treatment of CD and CPP on a cost-minimisation basis with the least costly biological disease modifying anti-rheumatic drug (bDMARD) for these conditions (Paragraph 6.2, Ustekinumab (Stelara) Public Summary Document (PSD), July 2022). The submission requested that the proposed listing of UST 45 mg and 90 mg PFS and PFP should not be cost-minimised to the least costly bDMARDs as the listing may likely result in cost savings to the government and would not replace any other bDMARDs on the PBS. The pre-PBAC response reiterated this and further

emphasized that biologics are selected by clinicians based on the drug class, molecule efficacy and safety, which are unaffected by the proposed listing of UST PFS and PFP.

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

5 Consideration of the evidence

Sponsor hearing

5.1 There was no sponsor hearing.

Consumer comments

5.2 The PBAC noted and welcomed the input from Crohn and Colitis Australia (CCA) via the Consumer Comments facility on the PBS website. CCA highlighted the benefits of UST PFS and PFP, which include increased flexibility for patients as UST PFS and PFP forms would not require infusion in a medical facility, therefore decreasing the need to travel, particularly for patients in remote and regional areas. The input also included comments from its members which stated that the UST pre-filled options are effective, convenient to administer and reduce the risk of dosing errors.

Clinical claim

5.3 The submission claimed non-inferior comparative effectiveness and safety of UST 45 mg and 90 mg PFS and PFP compared with UST 45 mg vial and UST 90 mg PFS for their respective indications.

5.4 This claim was based on the TGA's satisfaction of comparable effectiveness and safety of UST 45 mg and 90 mg PFS and PFP with UST 45 mg vial.

5.5 The PBAC considered that the claim of non-inferior comparative effectiveness and safety to UST 45 mg vial based on the TGA's evaluation was reasonable.

Pricing implications

5.6 The submission stated that there is currently a Special Pricing Arrangement (SPA) in place for UST 45 mg vial in the adult severe CPP, paediatric severe CPP, adult severe CD, PsA and UC indications and a Risk Sharing Arrangement (RSA) for paediatric CPP.

5.7 The submission noted that the compound patent for UST expires on 28 July 2024, and that following the expiration of its patent, biosimilars will seek to be listed on the PBS. PBS listing of a biosimilar brand may trigger a 25% first new brand (FNB) statutory price reduction due to a change in the formulary allocation of UST from F1 to F2. The submission noted that should a biosimilar be PBS-listed, its existing SPAs containing indication specific pricing for UST will collapse, and a weighted average price will be set per dose form across all indications. The PBAC noted that a biosimilar brand of UST (Wezlana®), sponsored by Amgen, was considered at the March 2024 PBAC meeting.

5.8 The submission further stated that under Section 99ACB or 99ACD of the *National Health Act 1953,* a 25% FNB statutory price reduction may apply if UST 45 mg and

90 mg PFS and PFP were to be PBS-listed before the first UST biosimilar because the new dose forms are not considered as new presentations. The submission stated that UST will not be eligible for ministerial discretion or other exemption from Section 99ACB or 99ACD of the *National Health Act 1953* as it's been listed on the PBS for over 10 years (first listed on 1 March 2010).

5.9 The submission stated that the proposed prices of UST PFS and PFP did not include the implications of F2 transition and associated FNB reductions due to the uncertainty relating to a possible biosimilar listing.

Economic analysis

5.10 The submission presented a cost-minimisation approach of UST 45 mg and 90 mg PFS and PFP compared with UST 45 mg vial and 90 mg PFS. The equi-effective doses were estimated as:

- Adult and paediatric CPP (patients that require UST 45 mg) and PsA: 1 x UST 45 mg PFS and PFP = 1 x UST 45 mg vial
- Adult and paediatric CPP (patients that require UST 90 mg) and severe CD: 1 x UST 90 mg PFS and PFP = 2 x UST 45 mg vial
- MSUC and fCD: 1 x UST 90 mg PFP = 1 x UST 90 mg PFS.

5.11 For adult and paediatric severe CPP, the current effective price per dose is [redacted] For these CPP indications, the SPA rebate applied to UST 45 mg [redacted] For adult severe CD, the SPA rebate [redacted] For PsA, UC and fCD, the SPA rebate [redacted]

5.12 The submission stated that if UST 90 mg PFS and PFP are PBS-listed, [redacted] for the SPA rebate will no longer be applicable as patients would start using either the 45 mg or 90 mg PFS and PFP, and the effective price per unit of UST 45 mg for the SPA will reflect the current effective price per dose, which is $[redacted] for adult severe CPP and $[redacted] for paediatric severe CPP.

5.13 Table 2 and 3 present the current and proposed indication-specific effective ex-manufacturer's prices of UST respectively.

Table 2: Current indication specific confidential effective price of ustekinumab SC presentations

	Indication	Current effective price per dose ($)	Current average effective price per unit ($)
UST 45mg vial	CPP (adult)	[redacted]	[redacted]% on 90 mg)*
	CPP (paediatric)	[redacted]	[redacted]% on 90 mg)**
	PsA	[redacted]	[redacted]
	CD (maintenance)	[redacted]	[redacted]
UST 90mg PFS	UC (maintenance)	[redacted]	[redacted]
	fCD (maintenance)	[redacted]	[redacted]

Source: Table 9 of the submission main body

Abbreviations: UST – Ustekinumab, CPP – Chronic plaque psoriasis, PsA - Psoriatic arthritis, CD – Crohn disease, UC - Ulcerative colitis, fCD - Fistulising Crohn's disease

*Weighted average price across 45 mg and 90 mg dose utilisation [redacted]% x $[redacted] + [redacted]% x $[redacted])

**Weighted average price across 45 mg and 90 mg dose utilisation ([redacted]% x $[redacted] + [redacted]% x $[redacted])

Table 3: Proposed indication specific confidential effective price of UST SC presentations

	Indication	Indication Specific Confidential Effective Price per unit ($)
Ustekinumab 45mg vial*	CPP (paediatric)	
Ustekinumab 45mg PFS, PFP#	CPP (adult) CPP (paediatric) PsA	
Ustekinumab 90mg PFS, PFP#	CPP (adult) CPP (paediatric) CD (maintenance) UC (maintenance)~ fCD (maintenance)~,%	

Source: Table 10 of the submission main body (modified)

Abbreviations: UST – Ustekinumab, LIV – Liquid in vial, PFS – Pre-filled syringe, PFP – Pre-filled pen, CPP – Chronic plaque psoriasis, PsA - Psoriatic arthritis, CD – Crohn disease, UC - Ulcerative colitis, fCD - Fistulising Crohn's disease

* [redacted] (see section 6)

PFP not requested for paediatric CPP

~ Requesting listing for 90 mg PFP only as 90 mg PFS is available on PBS for UC and under listing process for fCD

%fCD has been PBS-listed on 1 January 2024.

5.14 The submission requested an equivalent published approved ex-manufacturer price (AEMP) of UST 45 mg and 90 mg PFS and PFP as that of the currently listed UST 45 mg vial.

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

Estimated PBS usage and financial implications

5.16 The submission adopted a market share approach to estimate the net financial impact of listing UST 45 mg and 90 mg PFS and PFP. The submission claimed that there would be no change in the number of patients treated and treatment duration as the proposed listing is only expected to replace the existing UST 45 mg vial or 90 mg PFS presentations.

5.17 The submission presented the estimated substitution rates of UST PFS and PFP for existing UST presentation in each indication as below.

Table 4: Estimated substitution rate for UST PFS and PFP in each indication

Medicine and indication	Substitution rate
Ustekinumab (adult CPP) 45 mg pre-filled syringe for subcutaneous injection – Initiating	[redacted]%
Ustekinumab (adult CPP) 90 mg pre-filled pen for subcutaneous injection – Initiating	[redacted]%
Ustekinumab (adult CPP) 45 mg pre-filled pen for subcutaneous injection – Initiating	[redacted]%
Ustekinumab (adult CPP) 90 mg pre-filled syringe for subcutaneous injection – Initiating	[redacted]%
Ustekinumab (adult CPP) 45 mg pre-filled syringe for subcutaneous injection – Continuing	[redacted]%
Ustekinumab (adult CPP) 45 mg pre-filled pen for subcutaneous injection – Continuing	[redacted]%
Ustekinumab (adult CPP) 90 mg pre-filled pen for subcutaneous injection – Continuing	[redacted]%
Ustekinumab (adult CPP) 90 mg pre-filled syringe for subcutaneous injection – Continuing	[redacted]%
Ustekinumab (PsA) 45 mg pre-filled syringe for subcutaneous injection – Initiating	20.00%
Ustekinumab (PsA) 45 mg pre-filled pen for subcutaneous injection – Initiating	80.00%
Ustekinumab (PsA) 45 mg pre-filled syringe for subcutaneous injection – Continuing	20.00%
Ustekinumab (PsA) 45 mg pre-filled pen for subcutaneous injection – Continuing	80.00%
Ustekinumab (CD) 90 mg pre-filled syringe for subcutaneous injection – All	20.00%
Ustekinumab (CD) 90 mg pre-filled pen for subcutaneous injection – All	80.00%
Ustekinumab (paediatric CPP) 45 mg pre-filled syringe for subcutaneous injection – Continuing	[redacted]%
Ustekinumab (paediatric CPP) 90 mg pre-filled syringe for subcutaneous injection – Continuing	[redacted]%
Ustekinumab (paediatric CPP) 45 mg pre-filled syringe for subcutaneous injection – Initiating	[redacted]%
Ustekinumab (paediatric CPP) 90 mg pre-filled syringe for subcutaneous injection – Initiating	[redacted]%
Ustekinumab (UC) 90 mg pre-filled pen for subcutaneous injection – Initiating	100.00%
Ustekinumab (UC) 90 mg pre-filled pen for subcutaneous injection – Continuing	100.00%
Ustekinumab (fCD) 90 mg pre-filled pen for subcutaneous injection - Initiating	100.00%
Ustekinumab (fCD) 90 mg pre-filled pen for subcutaneous injection - Continuing	100.00%

Source: Table 13 of the submission main body

Abbreviations: UST – Ustekinumab, PFS – pre-filled syringe, PFP – pre-filled pen, CPP – Chronic plaque psoriasis, PsA - Psoriatic arthritis, CD – Crohn disease, UC - Ulcerative colitis, fCD - fistulising Crohn disease

5.18 Table 5 presents the estimated extent of use, cost of listing UST 45 mg and 90 mg PFS and PFP and the net financial implications to the PBS/RPBS.

5.19 The submission estimated that the proposed listing of UST 45 mg and 90 mg PFS and PFP would either result in a cost saving of $0 to < $10 million (at the published price) or be cost neutral (at the effective price) to the PBS/RPBS over a period of six years.

Table 5: Net change in prescriptions of UST SC presentations from Year 1 to Year 6

Year	2024	2025	2026	2027	2028	2029
Change in number of scripts						
Proposed market (45 mg vial, PFS, PFP; 90 mg PFS, PFP)	[redacted][7]	[redacted][8]	[redacted][9]	[redacted][10]	[redacted][11]	[redacted][12]
Current market (45 mg vial, 90 mg PFS)	-[redacted][7]	-[redacted][8]	-[redacted][9]	-[redacted][10]	-[redacted][11]	-[redacted][12]
Estimated financial implications of proposed market - 45 mg vial, PFS, PFP; 90 mg PFS, PFP (published prices)						
Cost to PBS/RPBS less co-payment (45 mg vial, PFS, PFP; 90 mg PFS, PFP)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][3]
Estimated financial implications of current market – 45 mg vial, 90 mg PFS (published prices)						
Cost to PBS/RPBS less co-payment (Current market - 45 mg vial, 90 mg PFS)	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]
Net financial implications (published prices)						
Net cost to PBS/RPBS	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]
Estimated financial implications of proposed market - 45 mg vial, PFS, PFP; 90 mg PFS, PFP (effective prices)						
Cost to PBS/RPBS less co-payment (45 mg vial, PFS, PFP; 90 mg PFS, PFP)	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][1]
Estimated financial implications of current market – 45 mg vial, 90 mg PFS (effective prices)						
Cost to PBS/RPBS less co-payment (Current market - 45 mg vial, 90 mg PFS)	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]
Net financial implications (effective prices)						
Net cost to PBS/RPBS	[redacted][6]	[redacted][6]	[redacted][6]	[redacted][6]	[redacted][6]	[redacted][6]

Source: Merged table 14 and 15 of the submission main body

Abbreviations: UST – Ustekinumab, SC – Subcutaneous, PFS – Pre-filled syringe, PFP – Pre-filled pen, M – Million

The redacted values correspond to the following ranges

[1] *$200 million to < $300 million*

[2] *$300 million to < $400 million*

[3] *$400 million to < $500 million*

[4] net cost saving

[5] *$100 million to < $200 million*

[6] *$0 to < $10 million*

[7] *50,000 to < 60,000*

[8] *60,000 to < 70,000*

[9] *70,000 to < 80,000*

[10] *80,000 to < 90,000*

[11] *90,000 to < 100,000*

[12] *100,000 to < 200,000*

5.20 As a Category 4 submission, the financial estimates analysis has not been independently evaluated.

Risk-Sharing Arrangement (RSA)

5.21 The submission requested for the UST 45 mg and 90 mg PFS presentations to join the existing RSA for the paediatric population for severe CPP. This was on the basis that these new presentations are expected to replace the use of UST 45 mg vial and not expand the overall UST and biologics market for this indication. The submission estimated that the annual subsidisation cap following the proposed listing will remain unchanged. The PBAC noted the proposal for UST 45 mg and 90 mg PFS forms to join

the existing RSA for the paediatric population for severe CPP and considered that it was appropriate.

Quality use of medicine

5.22 The submission stated that, in line with the Australian National Medicines Policy and the National Strategy for Quality Use of Medicines (QUM), several measures including monitoring of treatments outcomes and providing education/training for prescribers, patients/caregiver and nurses would be implemented to ensure the appropriate use of UST PFS and PFP in clinical practice.

6 PBAC Outcome

6.1 The PBAC recommended the listing of UST 45 mg and 90 mg PFS and PFP under the same circumstances as the currently listed UST 45 mg vial for the treatment of severe psoriatic arthritis (PsA), severe chronic plaque psoriasis (CPP), severe Crohn disease (CD), moderate to severe ulcerative colitis (MSUC) and complex refractory fistulising Crohn disease (fCD) on the PBS. The PBAC also recommended amendments to the current restrictions for severe CD and severe CPP to align with changes in the quantity required for adult patients following the proposed new listings. The PBAC made its recommendation based on, among other matters, its assessment that the cost-effectiveness of UST would be acceptable if it were cost-minimised to the least costly alternative (bDMARD) for each of the above-mentioned indications, based on previously advised equi-effective doses.

6.2 The PBAC considered that the nominated comparators were appropriate. However, the PBAC noted that other relevant comparators could include any of the currently PBS-listed bDMARDs for each of the five indications. The PBAC noted that the submission and pre-PBAC response claimed that the listing of 45 mg and 90 mg PFS and PFP should not be cost-minimised to the least costly bDMARD. The PBAC noted it could only recommend listing UST 45 mg and 90 mg PFS and PFP 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)).

6.3 The PBAC noted there was no evidence provided in the submission to demonstrate that UST 45 mg and 90 mg PFS and PFP provide, for some patients, a significant improvement in efficacy or reduction in toxicity compared to any of the other alternative bDMARDs for severe PsA, severe CPP, severe CD, MSUC and complex refractory fCD. As such, in accordance with Section 101(3B) of the *National Health Act 1953*, the PBAC considered that UST 45 mg and 90 mg PFS and PFP should be cost-minimised to the least costly accepted alternative bDMARD for each indication.

6.4 The PBAC considered that the claim of non-inferior comparative effectiveness and safety to UST 45 mg vial and UST 90 mg PFS for the respective indications was appropriate.

6.5 The PBAC noted that the TGA determined UST PFS to be equivalent to UST vial and further noted that the TGA file note stated that the open-label, randomized, parallel-group study, CNTO1275EDI1001, demonstrated bioequivalence between UST PFS and PFP.

6.6 The PBAC considered the equi-effective doses to be as follows:

- 1 x UST 45 mg PFS or PFP = 1 x UST 45 mg vial
- 1 x UST 90 mg PFS or PFP = 2 x UST 45 mg vial
- 1 x UST 90 mg PFP = 1 x UST 90 mg PFS

6.7 The PBAC noted the concerns raised in the pre-PBAC response regarding the equivalence of Stelara PFS and PFP to Wezlana injection vial as well as between Stelara PFP and Wezlana PFS presentation. The PBAC considered, under Section 101(4AACD) of the *National Health Act 1953,* equivalent strengths and forms of Stelara and Wezlana (i.e., Stelara PFS and Wezlana PFS; Stelara and Wezlana injection vial) should be treated as equivalent to each other for the purposes of substitution (i.e. 'a' flagged in the schedule).

6.8 The PBAC noted the submission's claim that the proposed listing is only expected to replace the existing UST 45 mg vial or 90 mg PFS presentations. The PBAC therefore considered that the proposed listing would be cost neutral to the PBS/RPBS.

6.9 The PBAC noted that UST 45 mg and 90 mg PFS and PFP would replace UST 45 mg vial and that the sponsor [redacted]. The PBAC noted that UST 45 mg and 90 mg PFP are not TGA approved for the paediatric population and noted the sponsor's intention for [redacted].

6.10 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because UST 45 mg and 90 mg PFS and PFP are not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over UST 45 mg vial, 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.

6.11 While not a matter for PBAC, the Committee noted that listing of the new forms of the 45 mg PFS and PFP may trigger a FNB reduction. The PBAC noted that the Department would take into consideration relevant PBS pricing policies, alongside the PBAC's advice, when progressing this recommendation to listing.

6.12 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 forms of ustekinumab as follows (indicative listing shown below includes changes made to the current prescribing instructions for severe CPP, CD, MSUC and fCD):

Severe PsA

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
Initial treatment					
USTEKINUMAB					
ustekinumab 45 mg/0.5 mL injection, pre-filled syringe	NEW	1	1	2	Stelara
ustekinumab 45 mg/0.5 mL injection, pre-filled pen	NEW	1	1	2	Stelara
Continuing treatment					
USTEKINUMAB					
ustekinumab 45 mg/0.5 mL injection, syringe	NEW	1	1	1	Stelara
ustekinumab 45 mg/0.5 mL injection, pen device	NEW	1	1	1	Stelara

Severe CPP

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
Initial treatment paediatric CPP					
USTEKINUMAB					
ustekinumab 45 mg/0.5 mL injection, pre-filled syringe	NEW	1	1	2	Stelara
ustekinumab 90 mg/mL injection, 1 mL pre-filled syringe	NEW	1	1	2	Stelara
Continuing treatment paediatric CPP					
USTEKINUMAB					
ustekinumab 45 mg/0.5 mL injection, pre-filled syringe	NEW	1	1	1	Stelara
ustekinumab 90 mg/mL injection, 1 mL pre-filled syringe	NEW	1	1	1	Stelara
Continuing treatment, balance of supply paediatric CPP					
USTEKINUMAB					
ustekinumab 45 mg/0.5 mL injection, pre-filled syringe	NEW	1	1	0	Stelara
ustekinumab 90 mg/mL injection, 1 mL pre-filled syringe	NEW	1	1	0	Stelara
Initial treatment adult CPP					
USTEKINUMAB					
ustekinumab 45 mg/0.5 mL injection, pre-filled syringe	NEW	1	1	2	Stelara

ustekinumab 45 mg/0.5 mL injection, pre-filled pen	NEW	1	1	2	Stelara
ustekinumab 90 mg/mL injection, 1 mL pre-filled syringe	NEW	1	1	2	Stelara
ustekinumab 90 mg/0.5 mL injection, pre-filled pen	NEW	1	1	2	Stelara
Continuing treatment adult CPP					
USTEKINUMAB					
ustekinumab 45 mg/0.5 mL injection, pre-filled syringe	NEW	1	1	1	Stelara
ustekinumab 45 mg/0.5 mL injection, pre-filled pen	NEW	1	1	1	Stelara
ustekinumab 90 mg/mL injection, 1 mL pre-filled syringe	NEW	1	1	1	Stelara
ustekinumab 90 mg/0.5 mL injection, pre-filled pen	NEW	1	1	1	Stelara

Restriction Summary: 14457 / Treatment of Concept: 14442	
Concept ID (for internal Dept. use)	**Category / Program:** GENERAL – General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners
	Restriction Type: ☒Authority Required
	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 treatment - Initial 2, Face, hand, foot (change or re-commencement of treatment after a break in biological medicine of less than 5 years) Initial treatment - Initial 3, Face, hand, foot (re-commencement of treatment after a break in biological medicine of more than 5 years)
	Prescriber 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.
Restriction Summary 11368 / Treatment of Concept: 8891	
Concept ID (for internal Dept. use)	**Category / Program:** GENERAL – General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners
	Restriction Type: ☒Authority Required
	Indication: Severe chronic plaque psoriasis
	Treatment Phase: Continuing treatment, Whole body Continuing treatment, Face, hand, foot
	Prescriber 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 repeats will be authorised.

Severe CD

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
Initial 1,2,3, continuing treatment, balance of supply					
USTEKINUMAB					
Initial treatment (Week 8)					
ustekinumab 90 mg/mL injection, 1 mL pre-filled syringe	NEW	1	1	0	Stelara
ustekinumab 90 mg/mL injection, pre-filled pen	NEW	1	1	0	Stelara
Continuing treatment (24 week)					
USTEKINUMAB					
ustekinumab 90 mg/mL injection, 1 mL pre-filled syringe	NEW	1	1	2	Stelara
ustekinumab 90 mg/mL injection, pre-filled pen	NEW	1	1	2	Stelara
Restriction Summary 9195 / Treatment of Concept: 9176					
Concept ID (for internal Dept. use)	**Category / Program:** GENERAL – General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners				
	Restriction Type: ☒Authority Required				
	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)				
	Prescriber 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~~ *with* no repeats.				
	Prescriber 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.				

MSUC

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
Initial treatment					
USTEKINUMAB					
ustekinumab 90 mg/0.5 mL injection, pre-filled pen	NEW	1	1	0	Stelara
Continuing treatment					
USTEKINUMAB					
ustekinumab 90 mg/0.5 mL injection, pre-filled pen	NEW	1	1	1	Stelara
Restriction Summary 13926 / Treatment of Concept: 13975					

Concept ID (for internal Dept. use)	**Category / Program:** GENERAL – General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners
	Restriction Type: ☒Authority Required
	Indication: Moderate to severe ulcerative colitis
	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)
	Prescriber 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 the subsequent first dose~~, containing a quantity of 1 pre-filled syringe of 90 mg and~~ *with* no repeats.

Complex refractory fCD

MEDICINAL PRODUCT medicinal product pack	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
Continuing treatment					
USTEKINUMAB					
ustekinumab 90 mg/0.5 mL injection, pre-filled pen	NEW	1	1	2	Stelara
Initial treatment					
USTEKINUMAB					
ustekinumab 90 mg/0.5 mL injection, pre-filled pen	NEW	1	1	0	Stelara
Restriction Summary 14775 / Treatment of Concept: 14787					
	Indication: Complex refractory Fistulising Crohn disease				
	Treatment Phase: Initial treatment - Initial 1 (new patient or recommencement of treatment after a break in biological medicine of more than 5 years) Initial treatment - Initial 2 (change or recommencement of treatment after a break in biological medicine of less than 5 years) Initial 1 (new patient or recommencement of treatment after a break in biological medicine of more than 5 years), Initial 2 (change or recommencement of treatment after a break in biological medicine of less than 5 years) - balance of supply				
	Prescriber 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 1 vial or pre-filled syringe of 90 mg and~~ *with* no repeats.				

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.