5.08 GUSELKUMAB,
Solution for I.V. infusion 200 mg in 20 mL vial,
Injection 100 mg in 1 mL single use pre-filled pen,
Injection 200 mg in 2 mL single use pre-filled pen,
Injection 100 mg in 1 mL single use pre-filled syringe,
Injection 200 mg in 2 mL single use pre-filled syringe,
Tremfya®,
Janssen-Cilag Pty Ltd.

1 Purpose of submission

1.1 The Category 2 submission requested Section 100 (Highly Specialised Drugs Program) and General Schedule Authority Required (in writing) Pharmaceutical Benefits Scheme (PBS) listings of guselkumab (GUS) for the treatment of adults with severe Crohn's disease (CD). This was the second submission for this indication; the first submission was considered by the PBAC in July 2025.

1.2 Listing was requested on the basis of a cost-utility analysis versus ustekinumab (UST). Table 1 summarises the key components of the clinical claim.

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

Component	Description
Population	Adults with severe Crohn's disease. The requested listing is consistent with the other biologics listed on the PBS for the treatment of severe CD.
Intervention	Induction regimen - Guselkumab 200 mg intravenously (IV) at week 0, 4, and 8, or - Guselkumab 400 mg subcutaneously (SC) at week 0, 4, and 8 Maintenance regimen - Guselkumab 200 mg SC at week 12, and then every 4 weeks, or - Guselkumab 100 mg SC at week 16 and then every 8 weeks
Comparator	Ustekinumab
Outcomes	Primary outcomes: clinical outcomes (clinical response and clinical remission)[a] and safety (any AE, SAEs, serious infection and discontinuation due to AE) Supportive outcomes: endoscopic outcomes (endoscopic response and endoscopic remission)[a]
Clinical claim	On the totality of the evidence presented in the submission: - In the induction phase, guselkumab 200 mg IV is non-inferior to guselkumab 400 mg SC in terms of efficacy and safety. - Guselkumab is superior to ustekinumab in terms of efficacy. - Guselkumab is non-inferior to ustekinumab in terms of safety.

Blue shading indicates information previously seen by the PBAC.

Source: Table 1.1, p15 of the submission.

AE=adverse events; CDAI=Crohn's disease Activity Index; SAE=serious adverse events; SES-CD=simplified endoscopic activity score for CD.

a In the GALAXI trials: Clinical response was defined as a CDAI reduction of ≥100 points from baseline; Clinical remission was defined as CDAI points <150

b In the GALAXI trials: Endoscopic response was defined as a ≥50% improvement from baseline in the SES-CD or SES-CD score≤2; Endoscopic remission was defined as SES-CD ≤ 4 and a ≥2-point reduction from baseline and no subscore >1 in any individual component

2 Background

Registration status

2.1 GUS was registered by the TGA on 19 July 2025 for the following indication:

"TREMFYA is indicated for the treatment of adult patients with moderately to severely active Crohn's disease who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic treatment."

Previous PBAC consideration

2.2 In July 2025, the PBAC recommended GUS for the treatment of adults with severe CD, on the basis that GUS be cost minimised to UST over two years. The PBAC considered that, while GUS was non-inferior in terms of effectiveness compared to UST for the outcomes of clinical remission and response, it was likely superior in terms of endoscopic outcomes in the maintenance treatment setting. However, the PBAC was unable to recommend on a cost-effectiveness basis. The PBAC considered the economic model was uninformative, noting it included short-term and long-term benefits for clinical remission that were not supported by the available clinical trial data, and the assumed link between endoscopic remission, longer term clinical remission and quality of life was not adequately supported and quantified. In the absence of an appropriate model comparing GUS and UST based on endoscopic outcomes, the PBAC was unable to determine the magnitude of price premium for

GUS over UST that would be cost-effective. The PBAC also considered GUS was highly unlikely to be cost effective at the price requested in the submission as the cost per patient over two years was more than [redacted] that of UST (paragraphs 7.1, 7.8 and 7.9, guselkumab PSD July 2025 PBAC meeting).

2.3 The July 2026 submission asserted that listing on a cost-minimisation basis to PBS-listed b/tsDMARDs including UST would undervalue innovation and therefore was not commercially viable to the sponsor, as the current prices for comparator treatments of CD are much lower than prices initially considered cost-effective. The submission requested that the price of GUS correspond to a similar two-year treatment cost as other PBS-listed treatments for CD when they were initially considered cost-effective (i.e. $[redacted] for GUS, compared to an estimated $[redacted] for IFX and $[redacted] for UST). At the current prices, the two-year cost of all current PBS-listed b/tsDMARDs for CD ranges between approximately $12,000 to $16,000 (see Table 4). The pre-subcommittee response (PSCR) stated that the requested price for GUS is reasonable in the context of historical prices at which therapies were originally considered cost-effective and listed for CD, but is not achievable via cost-minimisation to a substantially eroded comparator such as UST whose price no longer reflects value or innovation. The ESC considered the justification for the requested price was not valid, as decisions regarding the allocation of today's health resources should be done using today's costs, not historical prices. The pre-PBAC response clarified that the requested price for GUS is not based on historical prices but is derived from the cost-effectiveness model presented in the submission.

2.4 In response to the PBAC comments, the submission presented new supportive evidence on the relationship between endoscopic remission, clinical remission and quality of life, and addressed issues identified with the modelled economic evaluation. Aside from narrowing the focus of the clinical and economic comparisons to UST (rather than all PBS-listed b/tsDMARDs), the submission requested the same effective price, presented the same clinical evidence and maintained the clinical claim of superiority versus UST (and by extension, all other PBS-listed treatments). Table 2 summarises the key concerns identified in the July 2025 submission and how the submission addresses the concerns.

Table 2: Summary of key matters of concern and how the July 2026 submission addressed them

Component	Matter of concern raised at the July 2025 PBAC meeting	How the July 2026 submission addresses the concern
Clinical evidence & clinical claim	The key clinical evidence presented in the submission for GUS was from three head-to-head randomised trials comparing GUS to UST and PBO for induction and maintenance treatment (GALAXI 1, GALAXI 2 and GALAXI 3). The PBAC considered that, based on direct evidence, while GUS was non-inferior in terms of effectiveness compared to UST for the outcomes of clinical remission and response, it was likely superior in terms of endoscopic outcomes in the maintenance treatment setting (para 7.1, guselkumab PSD July 2025). The submission also presented indirect evidence comparing GUS versus the nominated comparators for induction and maintenance treatment. The PBAC considered these analyses were largely uninformative due to significant transitivity issues (e.g., different trial designs, patient populations, outcome definitions, timing of endpoint assessment) and, in particular, due to the use of imputed data to inform the maintenance analysis (para 7.7, guselkumab PSD July 2025).	No new clinical data were presented in the submission. The submission maintained the clinical claim that GUS was superior in terms of effectiveness and non-inferior in terms of safety compared with UST, the nominated main comparator (and by extension all other PBS-listed b/tsDMARDs). The indirect evidence presented in the July 2025 submission comparing GUS versus PBS-listed b/tsDMARDs for induction and maintenance treatment were not presented in the July 2026 submission. However, the results of the indirect evidence were used inform the July 2026 submission's modelled economic evaluation for the efficacy of subsequent treatments.
Economic evaluation	The submission presented a cost utility analysis comparing GUS to the nominated comparators weighted according to market share. The PBAC noted the model included short-term and long-term benefits for clinical remission that were not supported by the clinical trial data presented. Additionally, the PBAC noted the model assumed a link between endoscopic remission, longer term clinical remission and quality of life that had not been adequately supported or quantified. The PBAC considered that the model was uninformative. In the absence of an appropriate economic model comparing GUS and UST based on endoscopic outcomes, the PBAC was unable to determine the magnitude of price premium for GUS over UST that would be cost effective. The PBAC also considered GUS was highly unlikely to be cost effective at the price requested in the submission as the cost per patient over 2 years was more than [redacted] that of UST and the benefit in endoscopic remission observed in the trial was limited to a risk difference of 9% to 14% at 48 weeks. Unable to recommend on a cost-effectiveness basis, the PBAC recommended GUS be cost minimised to UST over 2 years (para 7.8, guselkumab PSD July 2025).	The submission requested the same price as the previous submission, and used the same modelling approach. To justify the modelling approach the submission presented new evidence from the published literature as well as trial data to quantify the relationship between endoscopic outcomes and longer-term outcomes (hospitalisation, quality of life and longer-term clinical remission). The submission presented a revised base-case, which included parameter changes, including: • Average cost and efficacy of subsequent treatment was estimated for basket of treatments (rather than specific treatments). • Treatment benefits related to non-significant differences in clinical remission were removed. • The utility weight for active-disease was increased (from 0.45 to 0.513), reflecting the CDAI distribution at Week 12 in GALAXI.

Source: Table 1.5, pp34-35 of the submission, guselkumab PSD July 2025 PBAC meeting.
Blue shading indicates information previously seen by the PBAC.
ADA=adalimumab; b/tsDMARD=biologic/targeted synthetic disease modifying anti-rheumatic drug; CD=Crohn's disease; GUS=guselkumab; IFX=infliximab; IV=intravenous; PFP=pre-filled pen; PFS=pre-filled syringe; PBO=placebo; SC=subcutaneous; SPA=special pricing arrangement; UST=ustekinumab; UPA=upadacitinib; VDZ=vedolizumab; QxW=every x week;

2.5 In August 2025, the National Institute for Health and Care Excellence (NICE)[1] recommended GUS for previously treated moderately to severely active CD in adults when i) conventional or biologic treatment has not worked or cannot be tolerated, and ii) TNF-inhibitor has not worked, cannot be tolerated or is not suitable. NICE recommend the use of the least expensive treatment option of the suitable treatments including GUS, risankizumab and VDZ, taking into account administration costs, dosages, price per dose and commercial arrangements.

2.6 In September 2025, Canada's Drug Agency (CDA-AMC)[2] recommended that GUS be reimbursed for the treatment of adult patients with moderately to severely active CD on conditions including a price reduction. The CDA-AMC considered there was insufficient evidence to justify a cost premium for GUS over the least costly relevant advanced therapy reimbursed for adult patients with moderately to severely active CD.

2.7 The PSCR stated these outcomes are not directly transferable to the Australian context and that while GUS has been recommended in these jurisdictions, those decisions were made within fundamentally different HTA and pricing environments.

3 Requested listing

MEDICINAL PRODUCT medicinal product pack	Dispensed Price for Max. Qty	Max. qty packs	Max. qty units	№.of Rpts	Available brands
GUSELKUMAB					
Initial treatment 200 mg / 20 mL, solution for IV infusion	Published: $3,452.89 (public); $3,501.77 (private) Effective: $[redacted] (public); $[redacted] (private)	1	1	2	TREMFYA® Janssen-Cilag Pty Ltd
Initial treatment 200 mg / 2 mL, solution for injection in pre-filled pen (Ypsomate® 2mL)	Published: $7,068.71 Effective: $[redacted]	1	2	2	
Initial treatment 200 mg / 2 mL, solution for injection in pre-filled syringe (Ultrasafe® 2mL)	Published: $7,068.71 Effective: $[redacted]	1	2	2	
Continuing 100 mg / 1 mL, solution for injection in pre-filled pen (One Press® 1mL)	Published: $3,615.82 Effective: $[redacted]	1	1	2	
Continuing 100 mg / 1 mL, solution for injection in pre-filled syringe (Ultrasafe® 1mL)	Published: $3,615.82 Effective: $[redacted]	1	1	2	
Continuing 200 mg / 2 mL, solution for injection in pre-filled pen (Ypsomate® 2mL)	Published: $3,615.82 Effective: $[redacted]	1	1	5	

[1] National Institute for Health and Care Excellence (NICE). Guselkumab for previously treated moderately to severely active Crohn's disease. Technology appraisal guidance. 28 August 2025. Available from: https://www.nice.org.uk/guidance/ta1095. [Accessed on: 08/04/2026].

[2] Canada Drug Agency (CDA-AMC). Reimbursement Recommendation - Guselkumab (Tremfya). September 2025. Available from: https://www.cda-amc.ca/sites/default/files/DRR/2025/SR0882-Tremfya_FINAL_Recommendation.pdf. [Accessed on 08/04/2026].

Continuing 200 mg / 2 mL, solution for injection in pre-filled syringe (Ultrasafe® 2mL)	Published: $3,615.82 Effective: $[redacted]	1	1	5	
Category / Program: Section 100 - Highly Specialised Drugs (public/private), IV infusion Section 85 – General Schedule, SC injection					
Restriction type: ☒Authority Required (in writing)					
Indication: Severe Crohn disease					
Treatment Phase: Initial 1 (new patient)					
Clinical criteria:					
Patient must have confirmed severe Crohn disease					
AND					
Patient must have failed to achieve an adequate response to prior systemic therapy (corticosteroids and at least 3 months of immunosuppressive therapy)					
AND					
Patient must have severity of disease activity with CDAI ≥300; OR CDAI ≥220 with extensive small intestine disease					
AND					
Evidence of intestinal inflammation; OR in high faecal output state; OR require surgery or total parenteral nutrition as the next therapeutic option					
AND					
The treatment must not exceed a total of 3 doses to be administered at weeks 0, 4 and 8 under this restriction					
Treatment criteria:					
Must be treated by a gastroenterologist or consultant physician [specialising in gastroenterology]					
Population criteria:					
Patient must be aged 18 years or older					
Prescribing Instructions: Any one of the baseline criteria may be used to determine response to an initial course of treatment and eligibility for continued therapy, according to the criteria included in the continuing treatment restriction. However, the same criterion must be used for any subsequent determination of response to treatment, for the purpose of eligibility for continuing PBS subsidised therapy.					
Prescribing Instructions: A maximum quantity and number of repeats to provide for an initial course of this drug consisting of two pre-filled subcutaneous injections of 200 mg per dose (400mg in total), administered at weeks 0, 4 and 8, will be authorised. **(FOR HSD LISTING: A maximum quantity and number of repeats to provide for an initial course of this drug consisting of a single 200 mg dose (via IV infusion) administered at weeks 0, 4 and 8, will be authorised)**					
Prescribing Instructions: If fewer than 2 repeats are requested at the time of the application, authority approvals for sufficient repeats to complete the 3 doses of this drug 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 initial authority applications, or for treatment that would otherwise extend the initial treatment period.					
Prescribing Instructions: An application for the continuing treatment must be accompanied with the assessment of response conducted up to 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.					

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 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.
Treatment Phase: Initial 2 (change or recommencement of treatment after a break in biological medicine of less than 5 years)
Clinical criteria:
Patient must have received prior PBS-subsidised treatment with a biologic for this condition in this treatment cycle
AND
Patient must not have failed PBS-subsidised therapy with this drug for this condition more than once in the current treatment cycle
AND
The treatment must not exceed a total of 3 doses to be administered at weeks 0, 4 and 8 under this restriction
Treatment Phase: Initial 3 (recommencement of treatment after a break in biological medicine of more than 5 years)
Clinical criteria:
Patient must have received prior PBS-subsidised treatment with a biological medicine for this condition
AND
Patient must have confirmed severe Crohn disease
AND
Patient must have a Crohn Disease Activity Index (CDAI) Score of greater than or equal to 300 that is no more than 4 weeks old at the time of application; 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, together with a Crohn Disease Activity Index (CDAI) Score greater than or equal to 220 and that is no more than 4 weeks old at the time of application
AND
Evidence of intestinal inflammation; OR in high faecal output state; OR require surgery or total parenteral nutrition as the next therapeutic option
AND
The treatment must not exceed a total of 3 doses to be administered at weeks 0, 4 and 8 under this restriction
Category / Program: Section 85 – General Schedule, SC injection
Restriction type: ☒Authority Required (in writing)
Indication: Severe Crohn disease
Treatment Phase: Continuing
Clinical criteria:
Patient must have previously received PBS-subsidised treatment with this drug for this condition
AND
Patient must have shown adequate response as CDAI <150; OR show an improvement of intestinal inflammation/ reversal of high faecal output state/avoidance of TPN
AND
Patient must not receive >24 weeks of treatment

Prescribing Instructions:
An application for continuing treatment with this drug must include a measurement of response to the most recent course of PBS-subsidised therapy. This assessment must be conducted no later than 4 weeks from the cessation of that treatment course. If the application is the first application for continuing treatment with this drug, it must be accompanied by an assessment of response to a minimum of 12 weeks of treatment with the initial treatment course.
Category / Program: Section 100 - Highly Specialised Drugs (public/private), IV infusion Section 85 – General Schedule, SC injection
Treatment Phase: Transitioning from non-PBS to PBS-subsidised supply - Grandfather arrangements (for patients transitioning through induction doses)
Clinical criteria:
Patient must have confirmed severe Crohn disease
AND
Patient must have previously received non-PBS-subsidised treatment with this drug for this condition prior to [LISTING DATE]
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 had short gut syndrome with diagnostic imaging or surgical evidence, or have had an ileostomy or colostomy; and must have had evidence of intestinal inflammation; and must have had evidence of failure to achieve an adequate response to prior systemic therapy as specified below prior to commencing treatment with this drug; or
Patient must have had extensive intestinal inflammation affecting more than 50 cm of the small intestine as evidenced by radiological imaging; and must have had a Crohn Disease Activity Index (CDAI) Score greater than or equal to 220; and must have had evidence of failure to achieve an adequate response to prior systemic therapy as specified below prior to commencing treatment with this drug
Category / Program: Section 85 – General Schedule, SC injection
Treatment Phase: Transitioning from non-PBS to PBS-subsidised supply - Grandfather arrangements (for patients transitioning through maintenance doses)
Clinical criteria:
Patient must have a documented history of severe Crohn disease
AND
Clinical criteria:
Patient must have previously received non-PBS-subsidised treatment with this drug for this condition prior to [LISTING DATE]
AND
Clinical criteria:
Patient must be receiving treatment with this drug for this condition at the time of application
AND
Clinical criteria:
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
Category / Program: Section 100 - Highly Specialised Drugs (public/private), IV infusion Section 85 – General Schedule, SC injection
Treatment Phase: Balance of supply
Clinical criteria:

Patient must have received insufficient therapy with this drug for this condition under the Initial 1, 2 or 3 restriction to complete the 3 doses (the initial infusion regimen at 0, 4 and 8 weeks); or Patient must have received insufficient therapy with this drug under the Continuing treatment restriction to complete 24 weeks of treatment
AND
The treatment must provide no more than the balance of up to 12 weeks therapy available under Initial 1, 2 or 3 treatment; or The treatment must provide no more than the balance of up to 24 weeks treatment available under Continuing treatment

Blue shading indicates information previously seen by the PBAC.
Source: Table 1.9, p45 and Table 1.10 p47 of the submission.

3.1 Consistent with the July 2025 submission, the submission requested listing for four formulations of GUS: (i) Section 100 (Highly Specialised Drugs Program) listing of GUS 200 mg in 20 mL vial for IV infusion, and (ii) General Schedule Authority Required (in writing) listing of GUS 100 mg and 200 mg pre-filled syringe (PFS) and GUS 100 mg and 200 mg SC pre-filled pen (PFP) for SC injection.

3.2 For initial treatment with either 200 mg IV or 400 mg (2 x 200 mg) SC, the maximum quantity with two repeats (total three doses) allows for up to a maximum 12 weeks of treatment. This provides all patients with the recommended three doses of induction treatment at Weeks 0, 4 and 8. Patients who demonstrate an adequate response to therapy after at least 12 weeks of induction could switch to either 100 mg SC every eight weeks (Q8W) starting from Week 16 or 200 mg SC every four weeks (Q4W) starting from Week 12. For continuing patients, the requested maximum quantity of 100 mg SC or 200 mg SC with five repeats (total six doses) allows for 24 weeks of maintenance treatment at the recommended dose.

3.3 The submission proposed a Special Pricing Arrangement (SPA). The proposed published EMP of $3,452.89 for all dose forms (GUS 200 mg / 20 mL vial, 200 mg PFS/PFP, and 100 mg PFS/PFP) and the proposed effective prices were unchanged from July 2025 submission (see Table 3). The effective EMP per 100 mg PFS/ PFP (pricing quantity of one) for psoriatic arthritis is $[redacted] and $[redacted] for chronic plaque psoriasis.

Table 3: Proposed effective AEMP of GUS for severe CD

GUS	Treatment phase	Proposed effective EMP July 2025 and July 2026
GUS 200 mg / 20 mL IV (one vial per pack)	Initial	$[redacted]
GUS 200 mg PFS/PFP SC (two injections per pack)	Initial	$[redacted]
GUS 100 mg PFS/PFP SC (one injection per pack)	Continuing	$[redacted]
GUS 200 mg PFS/PFP SC (one injection per pack)	Continuing	$[redacted]

Blue shading represents information previously considered by the PBAC.
Source: Table 4.29, p438 of the July 2025 submission, and Table 4.32, p217 of the submission.
GUS=guselkumab; IV=intravenous; SC=subcutaneous; SPA=special pricing arrangement.

3.4 The requested restriction criteria were largely unchanged in the submission compared to the July 2025 submission, but included minor amendments to the Clinical Criteria and Prescribing Instructions proposed by the Secretariat to the July 2025 submission for consistency with other PBS-listed b/tsDMARDs. The submission also separated the initial and continuing grandfather restriction as proposed by the Secretariat, but the submission stated that the sponsor now expected 750 patients (up from 463 patients)

would be enrolled in an early access program, which was expected to commence six months (up from three months) prior to PBS listing of GUS.

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

4 Population and disease

4.1 CD is an incurable, progressive inflammatory bowel disease (IBD) characterised by chronic transmural inflammation of the gastrointestinal tract, most commonly affecting any portion of the gastrointestinal tract from the mouth to the perianal area. Symptom burden increases as disease severity increases from mild to moderate or severe active disease. CD runs a relapsing and remitting course.

4.2 CD activity index score (CDAI) is commonly used to assess the severity of CD and response to treatment in clinical trials and routine practice. Improvement in CDAI score (i.e. CDAI <150) is the established outcome measure for determining continued eligibility to b/tsDMARDs for CD on the PBS. Historically, the PBAC has based their recommendations for listing of b/tsDMARDs for the treatment of severe CD on the proportion of patients achieving 'clinical remission' (often defined as CDAI <150) as well as 'clinical response' (often defined as ≥100 point or ≥70 point reduction in CDAI from baseline, i.e. CR-100 or CR-70).

4.3 At the July 2025 PBAC meeting, the PBAC noted that the treatment guidelines for CD refer to the importance of achieving endoscopic healing and in 2022 the FDA implemented a requirement for endoscopic remission as a co-primary endpoint with clinical remission in clinical trials. Endoscopic outcomes are commonly defined using either the CD Endoscopic Index of Severity (CDEIS) and the Simple Endoscopic Score for CD (SES-CD). The SES-CD evaluates four key endoscopic items: ulcer size, proportion of ulcerated surface, proportion of affected surface, and the presence and type of stenosis, each scored on a scale of 0 to 3, and a total score ranging 0 (inactive) to 56 (severe disease activity). However, the definitions of 'endoscopic remission' (also called endoscopic healing) and 'endoscopic response' vary across the literature. The GALAXI trials measured the SES-CD and defined endoscopic remission as SES-CD ≤2 or SES-CD ≤4 with at least 2-point reduction from baseline and no subscore greater than 1 in any individual subcomponent, and endoscopic response as ≥50% improvement from baseline in SES-CD or SES-CD ≤2. The submission stated that endoscopic outcomes (intestinal inflammation) were only moderately correlated with clinical outcomes (clinical symptoms), and intestinal inflammation in the absence of clinical symptoms was associated with long-term disease related complications and lower quality of life.

4.4 The proposed clinical management algorithm was unchanged and positioned GUS as an alternative treatment to other b/tsDMARDs available on the PBS for the treatment of severe CD. GUS is a fully human anti-interleukin (IL)-23 monoclonal antibody that neutralizes inflammation at the source of IL-23 production. The recommended induction dosage is GUS 200 mg IV infusion or 400 (2x200) mg SC injection at Weeks 0, 4 and 8. The recommended maintenance dose is GUS 200 mg Q4W SC injection

starting at Week 12 (i.e., 400 mg over eight weeks) or 100 mg Q8W SC injection starting at Week 16 (i.e., 100 mg over eight weeks).

4.5 If listed, GUS would become the sixth b/tsDMARD available on the Pharmaceutical Benefits Scheme (PBS) for severe CD and the second interleukin (IL) inhibitor. The ESC noted GUS has a slightly different mechanism of action to UST, the other PBS listed IL inhibitor.

4.6 The PSCR stated that where cost-effectiveness has been demonstrated across the indicated population, as in the case of GUS, restricting access to a subset represents a cost-containment measure rather than an evidence-based clinical distinction, and is therefore not an appropriate basis for defining PBS access. The PSCR acknowledged that, in practice, it is often not feasible to fully confine utilisation to a narrowly defined subgroup where there is robust evidence of efficacy for a much broader population. Thus, it is assumed that in any such circumstance that the PBAC would require an RSA to address the financial risk of utilisation beyond the intended population. However, the PSCR considered this would expose the sponsor to significant unmanageable financial risk. Under these conditions, the sponsor stated it would not be able to proceed. The sponsor indicated it would only consider a more restricted PBS listing (than currently proposed) for GUS in CD in the absence of an RSA.

5 Comparator

5.1 The submission nominated UST as the main comparator. The previous submission nominated all current PBS-listed b/tsDMARDs (UST, ADA, IFX, UPA and VDZ), as the relevant comparators. The PBAC had previously considered GUS (IL-23 inhibitor) may be more likely to substitute for UST (IL-12/23 inhibitor), which accounted for 40% of the market and has a similar mechanism of action (paragraph 7.4, guselkumab PSD July 2025 PBAC meeting). The PBAC had also previously considered that the indirect evidence comparing GUS versus other b/tsDMARDs presented in the July 2025 submission were largely uninformative (paragraph 7.7, guselkumab PSD July 2025 PBAC meeting).

5.2 The submission argued that, given that the PBAC had previously accepted non-inferior effectiveness and safety between all currently PBS-listed b/tsDMARDs (UST, ADA, IFX, UPA and VDZ) (paragraph 7.4, upadacitinib PSD July 2023 PBAC meeting), the clinical claim of superior effectiveness versus UST could be extended to all PBS-listed b/tsDMARDs. The submission noted that the PBAC had previously considered that GUS was non-inferior in terms of clinical remission and response to UST, but it was likely superior in terms of endoscopic outcomes in the maintenance treatment setting (paragraph 7.1, guselkumab PSD July 2025 PBAC meeting).

5.3 Consistent with the July 2025 submission, the July 2026 submission requested a substantial price premium for GUS over UST and all other currently PBS-listed b/tsDMARDs. Table 4 presents the estimated treatment costs over two years across the alternative therapies based on the unit costs presented in the financial estimates of the submission. The ustekinumab prices applied in July 2025 were the indication

specific effective prices and the prices applied in July 2026 are the published weighted prices (which are higher than the indication specific effective prices).

Table 4: Comparison of treatment costs over the first two years for GUS and PBS-listed comparator biologics for severe CD using the submission's effective AEMP

Drug	Dosing	Doses over two years	July 2025 submission		July 2026 submission	
			Effective AEMP	Cost over two years [a]	Effective AEMP	Cost over two years [a]
GUS	200 mg IV wk 0, 4, 8 induction -> 200 mg SC Q4W maintenance	3 IV + 23 SC	200 mg IV: $[redacted]	$[redacted]	200 mg IV: $[redacted]	$[redacted]
	200 mg IV wk 0, 4, 8 induction -> 100 mg SC Q8W maintenance	3 IV + 11 SC	100 mg SC: $[redacted]	$[redacted]	100 mg SC: $[redacted]	$[redacted]
	2x200 mg SC wk 0, 4, 8 induction -> 200 mg SC Q4W maintenance	3 SC + 23 SC	200 mg SC: $[redacted]	$[redacted]	200 mg SC: $[redacted]	$[redacted]
	2x200 mg SC wk 0, 4, 8 induction -> 100 mg SC Q8W maintenance	3 SC + 11 SC	2 x 200 mg SC: $[redacted]	$[redacted]	2 x 200 mg SC:$[redacted]	$[redacted]
Other biologics						
IFX IV	5 mg/kg IV wk 0, 2, 6 induction -> 5 mg/kg IV Q8W maintenance	14.3 IV infusions (57 vials)	100 mg IV: $186.16[a]	$10,611.12 $11,963.45	100 mg IV: $186.16	$10,611.12 $12,239.90
IFX IV/SC	5 mg/kg IV wk 0, 2 and 120 mg SC wk 6, 8, 10, 12 induction -> 120 mg SC Q2W	2 IV (8 vials) + 49 SC [b]	100 mg IV: $186.16 120 mg SC (PFP): $226.30[c]	$12,577.98 $12,767.78	100 mg IV: $186.16 120 mg SC (PFP, 100%): $252.40 120 mg SC (PFS, 0%): $332.80 [d]	$13,856.88 $14,085.48
UST Q12W	130 mg IV weight-based[c] wk 0, and 90 mg SC wk 8 induction -> 90 mg SC Q12W maintenance	1 IV (3 vials) + 8.3 SC (8.3×90 mg vials or 16.6 × 45 mg vials)	130 mg IV: $[redacted] 45 mg SC: $[redacted]	$[redacted] $[redacted]	130 mg IV: $[redacted] 45 mg SC (50%): $[redacted] 90 mg SC (50%): $[redacted]	$[redacted] $[redacted]
UST Q8W	130 mg IV weight-based[c] wk 0, and 90 mg SC wk 8 induction -> 90 mg SC Q8W maintenance	1 IV (3 vials) + 12 SC (12×90 mg vials or 24 × 45 mg vials)	130 mg IV: $[redacted] 45 mg SC: $[redacted]	$[redacted] $[redacted]	130 mg IV: $[redacted] 45 mg SC (50%): $[redacted] 90 mg SC (50%): $[redacted]	$[redacted] $[redacted]
ADA	160 mg (2 x 80 mg) SC wk 0 and 80 mg SC wk 2, then 40 mg SC Q2W wk 4, 6, 8, 10, 12, 14 induction -> 40 mg SC Q2W maintenance	1	3 x 80 mg SC: $618.90 [c]	$11,908.49	3 x 80 mg SC: $618.90 [c, e]	$11,723.15
		6	40 mg SC: $505.95 [c]		40 mg SC: $444.17 [c, e]	
VDZ IV/SC	300 mg IV wk 0, 2, then 108 mg SC wk 6, 8, 10, 12, 14, 16 induction -> 108mg SC Q2W maintenance	2 IV + 49 SC	2 x 108 mg SC: $[redacted]	$[redacted] $[redacted]	2 x 108 mg SC: $[redacted] (with 5% SPR= $[redacted] [used]) [f]	$[redacted] $[redacted]
VDZ IV	300 mg IV wk 0, 2, 6, induction -> 300 mg IV Q8W maintenance	14.25 IV	300 mg IV: $[redacted]	$[redacted] $[redacted]	300 mg IV: $[redacted] (with 5% SPR= $[redacted] [used]) [f]	$[redacted] $[redacted]
UPA	45 mg D induction -> 30 mg D maintenance	26	45 mg oral (28 tabs): $[redacted]	$[redacted]	45 mg oral (28 tabs): $[redacted] (with 5% SPR= $[redacted] [used]) [f]	$[redacted]
		26	30 mg oral (28 tabs): $[redacted]	$[redacted]	30 mg oral (28 tabs): $[redacted] (with 5% SPR= $[redacted] [used]) [f]	$[redacted]
	45 mg D induction -> 15 mg D maintenance	26	15 mg oral (28 tabs): $[redacted]	$[redacted]	15 mg oral (28 tabs): $[redacted] (with 5% SPR= $[redacted] [used]) [f]	$[redacted]

Blue shading represents information previously considered by the PBAC.

Source: calculated during the evaluation using the prices reported in Attachment 3.2 Guselkumab CD Economic Model.xlsx.

ADA=adalimumab; D=daily; PFP=pre-filled pen; PFS=pre-filled syringe; GUS=guselkumab; IFX=infliximab; IV=intravenous; QxW=every x week; SC=subcutaneous; UPA=upadacitinib; UST=ustekinumab; VDZ=vedolizumab.

[a] Drug cost plus administration cost (MBS item 14245, July 2025 submission: $94.90, July 2026: $114.3).

[b] The submission assumed an average of 4 IFX IV vials dispensed per script, which equates to average patient weight of 80 kg.

[c] IFX and ADA are on F2 formulary, their effective prices are assumed to be the published prices.

[d] The economic analysis did not incorporate the price of the IFX SC pre-filled syringe ($332.80). As the proportion of use of this dosage form relative to the SC pre-filled pen is unknown to the evaluators, it was excluded from the cost estimations.
[e] The July 2026 submission incorrectly assumed an 11.71% price reduction due to simplified price disclosure (SPD) for ADA (reduced prices were $546.43 for 80 mg, and $392.16 for 40 mg). The non-reduced prices were used in this analysis.
[f] The 5% anniversary statutory price reduction (SPR) was applied in the financial analysis section, but not in the economic analysis. The reduced price was used in this table.

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

6 Consideration of the evidence

Sponsor hearing

6.1 There was no hearing for this item.

Consumer inputs

6.2 The PBAC noted and welcomed the input from individuals (38), health care professionals (35) and organisations (5) via the Office of Health Technology Assessment Consultation Hub. Health professionals noted guselkumab's efficacy in moderate to severe Crohn's disease, particularly its ability to achieve clinical remission, endoscopic response, and endoscopic remission. Contributors noted current therapies often reach a "therapeutic ceiling", leaving many patients without durable disease control. In this context, guselkumab was described as an important new option for patients who have had prior biologic exposure or failed existing therapies. Health professionals described guselkumab as safe and well-tolerated with no major safety concerns. Health professionals that treat paediatric patients highlighted important quality-of-life concerns for children and adolescents, which included impacts on: growth, puberty, school participation, peer relationships and psychological wellbeing, reinforcing the burden of under-treated disease in children can be especially profound. Some contributors noted that without PBS-listing, access may depend on clinical trials, compassionate access or hospital funding (particularly for paediatric patients), creating inequity between patients and services. Cost to government was acknowledged by some contributors but needed to be weighed against the costs of uncontrolled disease, including hospitalisation, surgery, steroid toxicity and reduced productivity.

6.3 Two individuals who have used guselkumab noted the quality of life benefits they experienced with treatment, including improved symptom control. Many individuals described the symptoms of uncontrolled Crohn's disease including pain, fatigue and diarrhoea and the impact on everyday activities including the ability to work and socialise. Individuals considered guselkumab was an important additional treatment option, particularly for people who had failed, become non-responsive to or could not tolerate existing therapies. Individuals with a family member impacted by Crohn's disease noted the significant impact uncontrolled disease has on the broader family. The importance and benefit of a fully subcutaneous treatment regimen was noted.

6.4 The Gastroenterological Society of Australia (GESA) supported access to an IL-23 p19 inhibitor for Crohn's disease. The input stated the lack of access represents a

significant treatment gap compared to other jurisdictions. The input highlighted guselkumab's superior endoscopic outcomes compared to ustekinumab and potential benefit for patients with a severe inflammatory burden. Additionally, GESA provided advice to PBAC regarding the areas of highest clinical need in CD. GESA identified two high need groups:

- First line advanced-therapy[3] treatment for severe, high-risk CD: adults with severe CD with objective evidence of active inflammation who have been assessed as having severely aggressive phenotype placing them at high risk of near-term surgery, irreversible bowel damage and/ or intestinal failure. The ESC noted there was limited clinical evidence to support GUS preventing the need for intervention in this population.
- Advanced-therapy experienced moderate to severe CD: adults with moderate to severe CD with objective evidence of active inflammation who have had an inadequate response, loss of response, intolerance or contraindication to at least one prior advanced therapy. The ESC noted it was unclear whether patients should trial more than one advanced therapy to be considered appropriate for GUS, noting several advanced therapies with different mechanism of action are currently approved on the PBS.

6.5 Input received from Crohn's and Colitis Australia and its Scientific, Medical and Quality of Care Committee supported the PBS listing of guselkumab for severe Crohn's disease, noting the need for medicines with different mechanisms of action.

6.6 Crohn's and Colitis Australia provided patient testimonials that emphasised the burden of uncontrolled Crohn's disease and the need for additional treatment options.

6.7 Crohn's Colitis Cure stated that many people experience a suboptimal response or intolerance to current therapies and noted the importance of additional treatment options being available.

6.8 The Gastroenterological Nurses College of Australia (GENCA) noted the mechanise of action of guselkumab is different to ustekinumab. Input stated that funding guselkumab would expand treatment choice, improve clinical and quality-of-life outcomes, reduce treatment burden, and support equitable access to contemporary care.

Clinical trials

6.9 No new clinical data were presented in the submission. The submission was based on three head-to-head randomised trials comparing GUS to UST and placebo (PBO) for induction and maintenance treatment: GALAXI 1, GALAXI 2 and GALAXI 3. The submission did not present the indirect evidence comparing GUS to the other PBS-

[3] The letter stated advanced therapy included ant-TNF therapy, anti-integrin therapy, JAK inhibition and IL-12/23 p40 inhibition. The ESC noted this corresponds to all currently PBS-listed b/tsDMARDs.

listed b/tsDMARDs that was presented in the July 2025 submission because UST was nominated as the main comparator. Although the July 2026 submission did not present or discuss the indirect evidence presented in the July 2025 submission, the results of the 'Australian NMA' were used to inform key transition probabilities for subsequent treatments in the modelled economic evaluation. The ESC noted the PBAC had previously considered the indirect evidence largely uninformative due to significant transitivity issues (e.g., different trial designs, patient populations, outcome definitions, timing of endpoint assessment) and, in particular, due to the use of imputed data to inform the maintenance analysis (paragraph 7.7, GUS PSD, July 2025 PBAC meeting).

6.10 Details of the trials presented in the submission are provided in Table 5 below.

Table 5: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
Guselkumab vs placebo and ustekinumab trials		
GALAXI 1 (NCT03466411)	A Phase 2/3, Randomized, Double-blind, Placebo- and Active-controlled, Parallel-group, Multicenter Protocol to Evaluate the Efficacy and Safety of Guselkumab in Participants with Moderately to Severely Active Crohn's Disease - 48-WeekClinical Study Report (GALAXI 1; Phase 2). Sandborn et al. (2022). Guselkumab for the Treatment of Crohn's Disease: Induction Results From the Phase 2 GALAXI-1 Study. Silvio Danese et al. (2024). Efficacy and safety of 48 weeks of guselkumab for patients with Crohn's disease: maintenance results from the phase 2, randomised, double-blind GALAXI-1 trial.	20 October 2023 Gastroenterology, 162:1650-1664 e8 Lancet Gastroenterol Hepatol, 9: 133-146
GALAXI 2 (NCT03466411)	A Phase 2/3, Randomized, Double-blind, Placebo- and Active-controlled, Parallel-group, Multicenter Protocol to Evaluate the Efficacy and Safety of Guselkumab in Participants with Moderately to Severely Active Crohn's Disease GALAXI - 48-WeekClinical Study Report (GALAXI2; Phase 3). Remo Panaccione, Danese, et al. (2024). Efficacy and safety of guselkumab therapy in patients with moderately to severely active Chron's Disease: Results of the GALAXI 2 2 & 3 Phase 3 Studies.	19 March 2024 Gastroenterology, 166:5, Supplement (1057b-1057b2)
GALAXI 3 (NCT03466411)	A Phase 2/3, Randomized, Double-blind, Placebo- and Active-controlled, Parallel-group, Multicenter Protocol to Evaluate the Efficacy and Safety of Guselkumab in Participants with Moderately to Severely Active Crohn's Disease GALAXI - 48-WeekClinical Study Report (GALAXI3; Phase 3). Remo Panaccione, Danese, et al. (2024). Efficacy and safety of guselkumab therapy in patients with moderately to severely active Chron's Disease: Results of the GALAXI 2 2 & 3 Phase 3 Studies.	18 March 2024 Gastroenterology, 166:5, Supplement (1057b-1057b2)

Blue shading indicates information previously seen by the PBAC.
Source: Table 2.6, pp59-60 of the submission.

6.11 The key features of the GALAXI trials are summarised in Table 6.

Table 6: Key features of the included direct head-to-head evidence – induction and maintenance treatment

Trial	N	Design	Bias	Population	Treatment	Outcome(s)
GUS vs UST and PBO						
GALAXI 1 [induction + maintenance]	309[e]	P2, MC, R, PC, DB 48 wks / LTE 4y [IP: 12 wks + MP: 36 wks], Type 1+2 TT LTE 2-4y	*Low*	CDAI ≥220 and ≤450; Biologic naïve and experienced (non-responders excluded)	GUS 200mg IV Wk 0, 4, 8 IP -> 200mg SC Q4W MP GUS 600mg IV Wk 0, 4, 8 IP -> 200mg SC Q4W MP GUS 1200mg IV WK 0, 4, 8 IP ->200mg SC Q4W MP UST 6mg/kg IV WK 0 IP -> 90mg SC Q8W MP PBO[a]	1°: CDAI score 2°: clinical remission and response (CDAI)[c], endoscopic remission and response (SES-CD)[d]
GALAXI 2 [induction + maintenance]	508	P3, MC, R, PC, DB 48 wks / LTE 4y [IP: 12 wks + MP: 36 wks], Type 1+2 TT LTE 2-4y	*Low*	CDAI ≥220 and ≤450; Biologic naïve and experienced (non-responders excluded)	GUS 200mg IV Wk 0, 4, 8 IP -> 200mg SC Q4W MP GUS 200mg IV Wk 0, 4, 8 IP -> 100mg SC Q8W MP UST 6mg/kg IV Wk 0 -> 90mg SC Q8W MP PBO[a]	1°: clinical response (CDAI), clinical remission (CDAI) and endoscopic response (SES-CD)[b c] 2°: endoscopic remission (SES-CD)[b d]
GALAXI 3 [induction + maintenance]	513	P3, MC, R, PC, DB 48 wks / LTE 4y [IP: 12 wks + MP: 36 wks], Type 1+2 TT LTE 2-4y	*Low*	CDAI ≥220 and ≤450; Biologic naïve and experienced (non-responders excluded)	GUS 200mg IV Wk 0, 4, 8 IP -> 200mg SC Q4W MP GUS 200mg IV Wk 0, 4, 8 IP -> 100mg SC Q8W MP UST 6mg/kg IV Wk 0 -> 90mg SC Q8W MP PBO[a]	1°: clinical remission (CDAI)[b c] 2°: endoscopic response (SES-CD)[b d]

Source: Table 2.7, pp64-65 of the submission.

CD=Crohn's disease; CDAI=CD activity index; DB=double blind; GUS=guselkumab; IP=induction phase; ITC=indirect treatment comparison; LTE=long-term extension; MC=multi-centre; MP=maintenance phase; NMA=network meta-analysis; OL=open label; PBO=placebo; PC=placebo-controlled; P2=Phase 2 trial; P3=Phase 3 trial; QxW=every x week; R=randomised; SES-CD=Endoscopic Score for Crohn's Disease; TT=treat-through; UST=ustekinumab; S3=section 3 of the submission; wk=week; y=year; i=analysis with imputed data to adjust for trial design;

[a] At Wk 12, PBO responders continued PBO treatment from Week 12 through Wk 44. PBO non-responders crossed over to receive active treatment with UST IV induction dose at Wk 12 (weight-based) and maintenance UST SC from Wk 20 through Wk 44.

[b] Region-specific co-primary endpoints were: i) clinical remission at Wk 12 and ii) endoscopic response at Wk 12. Global co-primary endpoints were: i) clinical response at Wk 12 and clinical remission at Wk 48 and ii) clinical response at Wk 12 and endoscopic response at Wk 48.

[c] clinical remission: CDAI <150 and clinical response: reduction from baseline of ≥100-point in CDAI score or CDAI score <150 (clinical remission).

[d] Endoscopic remission: SES-CD ≤4 with at least a 2-point reduction from baseline and no subscore greater than 1 in any individual subcomponent (global definition) or SES-CD ≤2 (region-specific definition) and endoscopic response: ≥50% improvement from baseline in the SES-CD or SES-CD score ≤2.

[e] Primary efficacy analysis set included 309 patients who were randomized and received ≥1 dose of study drug (including partial dose), and whose induction dosing was not discontinued due to treatment pause. Total 360 randomised, of which 51 patients had induction dosing discontinued due to a safety event.

6.12 GALAXI 1, GALAXI 2 and GALAXI 3 trials were all multicentre (including Australia), randomised, placebo-controlled, double-blind trials with a treat-through design where patients with moderate to severe CD were randomised to GUS, UST or PBO for 48 weeks. In each trial, patients randomised to GUS or UST remained on the same treatment for induction (Weeks 0-12) and maintenance therapy (Weeks 12-48) irrespective of induction response. In contrast, only patients randomised to PBO who achieved clinical response at Week 12 remained on PBO until the end of the trial and patients with non-response at Week 12 crossed over to UST. Patients who completed GALAXI 1, GALAXI 2 and GALAXI 3 may enter long-term extension for additional 4 years of treatment (Week 48 to Week 252).

Comparative effectiveness

6.13 Table 7 presents the key outcomes of clinical remission, clinical response, endoscopic remission and endoscopic response for induction and maintenance in GALAXI 1, GALAXI 2 and GALAXI 3 comparing GUS to UST.

Table 7: Summary of head-to-head evidence: GUS vs UST (GALAXI 1, GALAXI 2 and GALAXI 3)

	GUS n/N (%)	UST n/N (%)	OR (95%CI)	RR (95%CI)	RD (95%CI)
Induction, GUS IV vs UST IV					
Clinical remission (Wk12)					
GALAXI 1, 2, 3 meta-analysis	309/643 (48.1)	166/354 (46.9)	1.08 (0.80, 1.44)	1.04 (0.89, 1.21)	0.02 (-0.05, 0.09)
Clinical response (Wk12)					
GALAXI 1, 2, 3 meta-analysis	406/643 (63.1)	213/354 (60.2)	1.17 (0.89, 1.53)	1.06 (0.96, 1.18)	0.04 (-0.03, 0.1)
Endoscopic remission (Wk12)					
GALAXI 1, 2, 3 meta-analysis	147/643 (22.9)	63/354 (17.8)	1.32 (0.95, 1.83)	1.24 (0.95, 1.62)	0.05 (0, 0.1)
Endoscopic response (Wk12)					
GALAXI 1, 2, 3 meta-analysis	238/643 (37.0)	116/354 (32.8)	1.2 (0.91, 1.57)	1.12 (0.93, 1.34)	0.04 (-0.02, 0.1)
Maintenance, GUS 100 vs UST 90					
Clinical remission (Wk48)					
GALAXI 1, 2, 3 meta-analysis	226/347 (65.1)	220/354 (62.1)	1.14 (0.84, 1.55)	1.05 (0.94, 1.17)	0.03 (-0.04, 0.1)
GALAXI 2, 3 meta-analysis	187/286 (65.4)	183/291 (62.9)	1.11 (0.79, 1.57)	1.04 (0.92, 1.17)	0.02 (-0.05,0.10)
Clinical response (Wk48)					
GALAXI 1, 2, 3 meta-analysis	256/347 (73.8)	247/354 (69.8)	1.22 (0.88, 1.69)	1.06 (0.96, 1.16)	0.04 (-0.03, 0.11)
GALAXI 2, 3 meta-analysis	211/286 (73.8)	204/291 (70.1)	1.20 (0.83, 1.72)	1.05 (0.95, 1.16)	0.04 (-0.04, 0.11)
Endoscopic remission (Wk48)					
GALAXI 1, 2, 3 meta-analysis	106/347 (30.5)	76/354 (21.5)	**1.61 (1.14, 2.28)**	**1.40 (1.07, 1.82)**	**0.09 (0.03, 0.16)**
GALAXI 2, 3 meta-analysis	95/286 (33.2)	72/291 (24.7)	**1.51 (1.05, 2.17)**	**1.34 (1.03, 1.74)**	**0.09 (0.01, 0.16)**
GALAXI 2, 3 meta-analysis[a]	*72/286 (25.2)*	*48/291 (16.5)*	**1.70 (1.13, 2.56)**	**1.53 (1.10, 2.12)**	**0.09 (0.02, 0.15)**
Endoscopic response (Wk48)					
GALAXI 1, 2, 3 meta-analysis	164/347 (47.3)	127/354 (35.9)	**1.60 (1.18, 2.17)**	**1.31 (1.09, 1.56)**	**0.11 (0.04, 0.19)**
GALAXI 2, 3 meta-analysis	137/286 (47.9)	108/291 (37.1)	**1.59 (1.12, 2.17)**	**1.28 (1.04, 1.58)**	**0.11 (0.03, 0.19)**
Clinical remission (Wk48) | induction remission (Wk12)					
GALAXI 1, 2, 3 meta-analysis	140/171 (81.9)	134/165 (81.2)	1.27 (0.71, 2.28)	1.04 (0.95, 1.15)	0.04 (-0.04, 0.11)
GALAXI 2, 3 meta-analysis	114/133 (85.7)	112/137 (81.8)	1.33 (0.69, 2.56)	1.04 (0.94, 1.16)	0.04 (-0.05, 0.12)
Durable clinical remission[c] (clinical remission Wk12-48)					
GALAXI 1, 2, 3 meta-analysis	169/347 (48.7)	152/354 (42.9)	1.26 (0.94, 1.70)	1.13 (0.96, 1.33)	0.06 (-0.02, 0.13)
GALAXI 2, 3 meta-analysis	138/286 (48.3)	122/291 (41.9)	1.29 (0.87, 1.90)	1.15 (0.93, 1.43)	0.06 (-0.03, 0.16)
Sustained clinical remission[d] (clinical remission Wk12&48)					

	GUS n/N (%)	UST n/N (%)	OR (95%CI)	RR (95%CI)	RD (95%CI)
GALAXI 1, 2, 3 meta-analysis	140/347 (40.3)	134/354 (37.9)	1.11 (0.82, 1.51)	1.07 (0.89, 1.28)	0.03 (-0.05, 0.10)
GALAXI 2, 3 meta-analysis	114/286 (39.9)	112/291 (38.5)	1.06 (0.76, 1.48)	1.04 (0.85, 1.27)	0.01 (-0.07, 0.09)
Maintenance, GUS 200 vs UST 90					
Clinical remission (Wk48)					
GALAXI 1, 2, 3 meta-analysis	289/420 (68.8)	220/354 (62.1)	**1.38 (1.02, 1.87)**	**1.12 (1.01, 1.24)**	**0.07 (0.01, 0.14)**
GALAXI 2, 3 meta-analysis	208/296 (70.3)	183/291 (62.9)	1.40 (0.99, 1.97)	1.12 (1.00, 1.26)	0.07 (0.00, 0.15)
Clinical response (Wk48)					
GALAXI 1, 2, 3 meta-analysis	319/420 (76.0)	247/354 (69.8)	1.38 (1.00, 1.90)	1.09 (1.00, 1.19)	0.06 (0.00, 0.13)
GALAXI 2, 3 meta-analysis	225/296 (76.0)	204/291 (70.1)	1.35 (0.94, 1.96)	1.09 (0.99, 1.20)	0.06 (-0.01, 0.13)
Endoscopic remission (Wk48)					
GALAXI 1, 2, 3 meta-analysis	141/420 (33.6)	76/354 (21.5)	**2.15 (1.24, 3.7)**	**1.70 (1.14, 2.53)**	**0.14 (0.07, 0.22)**
GALAXI 2, 3 meta-analysis	110/296 (37.2)	72/291 (24.7)	**1.80 (1.18, 2.75)**	**1.51 (1.18, 1.93)**	**0.12 (0.02, 0.23)**
GALAXI 2, 3 meta-analysis[a]	*60/296 (20.3)*	*48/291 (16.5)*	1.29 (0.85, 1.96)	1.23 (0.87, 1.73)	0.04 (-0.02, 0.10)
Endoscopic response (Wk48)					
GALAXI 1, 2, 3 meta-analysis	212/420 (50.5)	127/354 (35.9)	**1.90 (1.41, 2.55)**	**1.43 (1.20, 1.69)**	**0.15 (0.09, 0.22)**
GALAXI 2, 3 meta-analysis	156/296 (52.7)	108/291 (37.1)	**1.90 (1.36, 2.64)**	**1.41 (1.18, 1.70)**	**0.16 (0.08, 0.24)**
Clinical remission (Wk48) | induction remission (Wk12)					
GALAXI 1, 2, 3 meta-analysis	177/203 (87.2)	134/165 (81.2)	1.65 (0.92, 2.94)	1.08 (0.98, 1.18)	0.06 (-0.01, 0.14)
GALAXI 2, 3 meta-analysis	124/141 (87.9)	112/137 (81.8)	1.59 (0.81, 3.12)	1.07 (0.97, 1.18)	0.06 (-0.03, 0.14)
Durable clinical remission[c] (clinical remission Wk12-48)					
GALAXI 1, 2, 3 meta-analysis	213/420 (50.7)	152/354 (42.9)	**1.35 (1.01, 1.80)**	1.17 (1.00, 1.36)	0.07 (0.00, 0.15)
GALAXI 2, 3 meta-analysis	149/296 (50.3)	122/291 (41.9)	**1.40 (1.01, 1.95)**	**1.20 (1.01, 1.43)**	0.08 (0.00, 0.16)
Sustained clinical remission[d] (clinical remission Wk12&48)					
GALAXI 1, 2, 3 meta-analysis	177/420 (42.1)	134/354 (37.9)	1.20 (0.90, 1.61)	1.11 (0.93, 1.33)	0.04 (-0.03, 0.11)
GALAXI 2, 3 meta-analysis	124/296 (41.9)	112/291 (38.5)	1.15 (0.83, 1.60)	1.09 (0.89, 1.33)	0.03 (-0.05, 0.11)

Blue shading indicates information previously seen by the PBAC. The **bold** text indicates statistical significance p<0.05.
Risk statistics calculated using Review Manager (version 5.3).
Source: Table 2.19, p83, Table 2.21, p89, Tables 2.22 and 2.23, pp91-92 of the submission. Attachment 2.9 GALAXI GUS vs UST – meta-analysis.xlsx.
GUS=guselkumab; SES-CD=simplified endoscopic activity score for CD; UST=ustekinumab; wk=week;
a region-specific definition of endoscopic remission (SES-CD score ≤2).
b calculated during the evaluation using RevMan v.5.3.
c Durable clinical remission defined as CDAI <150 for ≥80% of all visits between Week 12 and Week 48 [i.e., at least 8 of 10 visits]), which must include Week 48.
d Sustained clinical remission defined as clinical remission at both Weeks 12 and 48.

6.14 The head-to-head evidence of GALAXI 1, GALAXI 2 and GALAXI 3 showed:

- For induction treatment (i.e. Week 12), no difference between GUS and UST in terms of clinical remission or clinical response. Comparisons versus PBO (not presented in the table or figure) confirmed that both GUS and UST were more effective than PBO across both outcomes at the same time point.
- For maintenance treatment (i.e. Week 48), generally no difference between GUS 100 mg SC, GUS 200 mg SC and UST in terms of clinical remission and clinical response outcomes, with the exception of a few comparisons that favoured GUS 200 mg SC over UST on maintenance of clinical remission and durable clinical remission. In contrast, GUS 100 mg SC and GUS 200 mg SC were generally more effective than UST in terms of endoscopic remission and endoscopic response outcomes.

6.15 At the July 2025 PBAC meeting, the PBAC considered "it remained unclear if achieving endoscopic remission (as defined in the GALAXI trials) at Week 48 leads to better longer-term outcomes for patients. Given the lack of significant differences in key outcomes for clinical remission, the correlation between endoscopic and clinical remission for GUS versus UST remained uncertain" (paragraph 7.6, guselkumab PSD July 2025 PBAC meeting). In response, the submission sought to validate the independent causal relationship between endoscopic outcomes and improvements in longer term outcomes (e.g., surgery and hospitalisation rates, clinical remission and quality of life), based on analyses of trial data and reviews of the published literature. The submission attempted to answer the following key questions: (1) do clinical symptoms correlate with endoscopic disease activity? (2) does endoscopic disease activity independently predict longer term benefits?

6.16 To address the first question, the submission identified nine key published studies (Lewis 2020[4], Campbell 2025[5], Cellier 1994[6], Durko 2013[7], Kucharski 2016[8], Takenaka 2025[9], Rutgeerts 2006[10], Taleban 2016[11], Takabayashi 2021[12]) that investigated the correlation between clinical outcomes (including CDAI score, clinical

[4] Lewis JD, Rutgeerts P, Feagan BG, D'haens G, Danese S, Colombel JF, Reinisch W, Rubin DT, Selinger C, Bewtra M, Barcomb L, Lacerda AP, Wallace K, Butler JW, Wu M, Zhou Q, Liao X, & Sandborn WJ. Correlation of Stool Frequency and Abdominal Pain Measures With Simple Endoscopic Score for Crohn's Disease. Inflammatory bowel diseases. 2020. 26(2):304-313.

[5] Campbell I, Brownson E, Wirz A, Seenan JP, MacDonald J, Gerasimidis K, P0645 CDAI underestimates disease activity in overweight patients with Crohn's Disease when compared to endoscopic assessment. Journal of Crohn's and Colitis. 2025. 19(suppl 1):i1267

[6] Cellier C, Sahmoud T, Froguel E, Adenis A, Belaiche J, Bretagne JF, Florent C, Bouvry M, Mary JY, & Modigliani R. (1994). Correlations between clinical activity, endoscopic severity, and biological parameters in colonic or ileocolonic Crohn's disease. A prospective multicentre study of 121 cases. The Groupe d'Etudes Thérapeutiques des Affections Inflammatoires Digestives. Gut. 1994. 35(2): 231-235.

[7] Durko L, Stasikowska-Kanicka OA, Wagrowska-Danilewicz M, Danilewicz M, & Małecka-Panas EI. (2013). An analysis of the correlation of clinical, endoscopic and histological classifications in Crohn's disease. Przeglad gastroenterologiczny. 2013. 8(6):377-382.

[8] Kucharski M, Karczewski J, Mańkowska-Wierzbicka D, Karmelita-Katulska K, Kaczmarek E, Iwanik K, Rzymski P, Grzymisławski M, Linke K, Dobrowolska A. Usefulness of Endoscopic Indices in Determination of Disease Activity in Patients with Crohn's Disease. Gastroenterol Res Pract. 2016. 2016:7896478.

[9] Takenaka K, Hisamatsu T, Kobayashi T, Yamamoto H, Ohmiya N, Hayashi R, Matsuoka K, Saruta M, Andoh A, Fukata N, Watanabe K, Imaeda H, Hirai F, Matsumoto T, Hirakawa A, Yano T, Matsuura M, Okamoto R, Ohtsuka K, Watanabe M. Inadequate Efficacy of Biologics for Treating Proximal Ileal Lesions in Crohn's Disease: A Prospective Multicenter Study. Clin Gastroenterol Hepatol. 2025. 23(11):1991-2000.

[10] Rutgeerts P, Diamond RH, Bala M, Olson A, Lichtenstein GR, Bao W, Patel K, Wolf DC, Safdi M, Colombel JF, Lashner B, Hanauer SB. Scheduled maintenance treatment with infliximab is superior to episodic treatment for the healing of mucosal ulceration associated with Crohn's disease. 2006. 63(3):433-42; quiz 464.

[11] Taleban S, Stewart KO, Li DK, Singh P, Pardi DS, Sturgeon HC, Yajnik V, Xavier RJ, Ananthakrishnan AN, Khalili H. Clinical Activity and Quality of Life Indices Are Valid Across Ulcerative Colitis But Not Crohn's Disease Phenotypes. Dig Dis Sci. 2016. 61(9):2627-35.

[12] Takabayashi K, Hosoe N, Kato M, Hayashi Y, Nanki K, Fukuhara K, Mikami Y, Mizuno S, Sujino T, Mutaguchi M, Naganuma M, Yahagi N, Ogata H, Kanai T. Significance of endoscopic deep small bowel evaluation using balloon-assisted enteroscopy for Crohn's disease in clinical remission. J Gastroenterol. 2021. 56(1):25-33.

remission/response and Harvey-Bradshaw Index) and endoscopic outcomes (including SES-CD score, endoscopic remission/response, and CDEIS) at Week 12 to 52. Most studies conducted a Spearman's rank correlation (or similar) and reported low to moderate associations between the two broad types of outcomes. Consistent with the GALAXI trials, two studies (Takabayashi 2021, Rutgeerts 2006) also found a small proportion of patients with clinical remission had averse endoscopic findings (and vice versa). Based on this evidence, the submission argued that clinical remission alone is insufficient for a complete assessment of disease activity.

6.17 To explore the relationship between endoscopic outcomes and longer-term outcomes, the submission presented several published analyses of pooled GALAXI and IM-UNITI trial data (some analyses reported in Neff-Baro 2024[13] and Sanon 2026[14]) as well as multiple literature reviews. The three key longer-term outcomes considered included:

- Surgery and hospitalisation. The submission presented Kaplan-Meier plots of the time to surgery or hospitalisation during the long-term follow up period for patients with versus without endoscopic response at end of maintenance (Week 44/48), in pooled data from (i) GALAXI 1 and IM-UNITI, and (ii) GALAXI 2, GALAXI 3 and IM-UNITI (Figure 1). In one of the two analyses, the log rank test showed significantly lower risk of longer-term surgery or hospitalisation in patients with endoscopic response at the end of maintenance. Similarly, in one of the two analyses, a Cox model controlling for treatment arm, clinical remission status at the end of maintenance and 'trial-level differences' found the risk of surgery or hospitalisation was significantly lower in those who had achieved endoscopic response compared to those who did not achieve endoscopic response (hazard ratio (HR)=1.42, 95%CI: 0.179, 0.946, p=0.0365). The published literature (Takabayashi 2021, Takenaka 2025, Allez 2002[15]) also found improved endoscopic outcomes was associated with a reduction in CD-related hospitalisation and

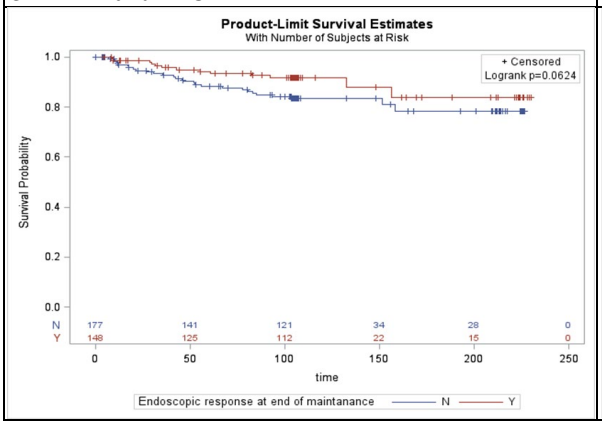
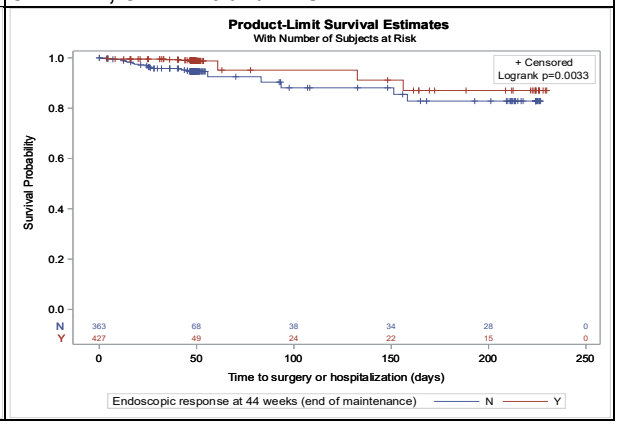
[13] Neff-Baro S, Gauthier A, Sanon M, Kachroo S, Wirth D, Gurjar K, Eisele L, Naessens D. Endoscopic improvement at 1 year and association with long-term disease outcome: a pooled clinical trial analysis in Crohn's Disease. MP153. UEG Conference 2024 October 12-15.

[14] Sanon M, Neff-Baro S, Gauthier A, Naessens D, Vetter ML, Eisele L, Dignass A, Feagan B. Association Between 1-Year Endoscopic Outcomes and Long-Term Clinical and Patient-Relevant Outcomes in Crohn's Disease. JCC Plus. 2026. 1:e70014. doi.org/10.1002/jcc5.70014.

[15] Allez M, Lemann M, Bonnet J, Cattan P, Jian R, Modigliani R. Long term outcome of patients with active Crohn's disease exhibiting extensive and deep ulcerations at colonoscopy. Am J Gastroenterol. 2002. 97(4):947-53.

surgeries, including in patients with clinical response after induction (Panaccione 2025[16], Feagan 2024[17], Rutgeerts 2006).

Figure 1: Kaplan-Meier of time to hospitalisation/surgery by endoscopic response status[a] in the long term follow up period (IM-UNITI, GALAXI 1, GALAXI 2 and GALAXI 3)

GALAXI 1 and IM-UNITI	GALAXI 2, GALAXI 3 and IM-UNITI
	

Source: Figures 3.6 and 3.7, pp124-125 of the submission, Neff-Baro 2024. pptx.

CD=Crohn's disease; CDAI=Crohn's disease Activity Index; CI=confidence intervals; EOM=end of maintenance; GUS=guselkumab; IBDQ=Inflammatory Bowel disease Questionnaire; LTE=long-term extension; OR=odds ratio; SES-CD=simplified endoscopic activity score for CD;

a Cox regression was adjusted for treatment arm, clinical remission status at end of maintenance, and trial-level differences using a random effect.

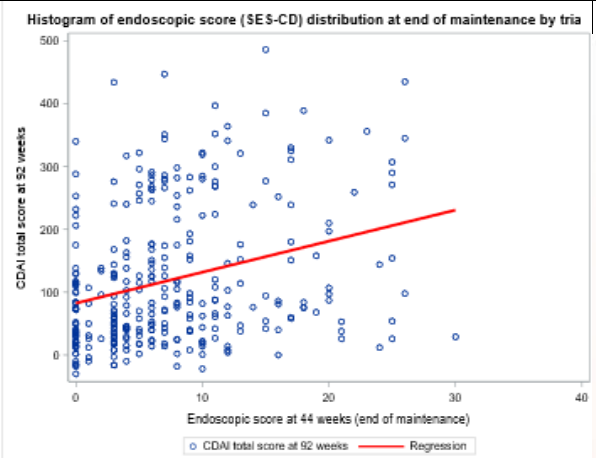
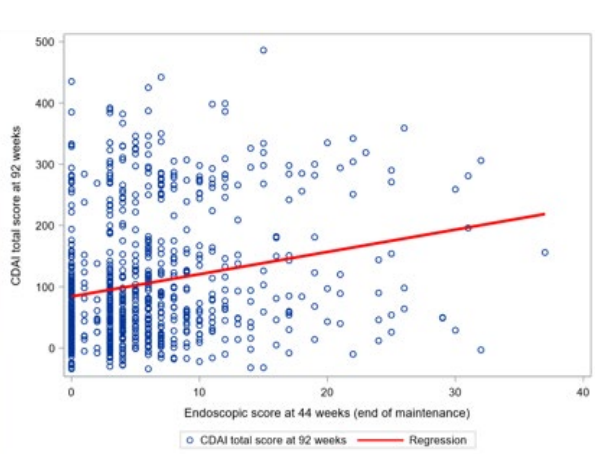
- CDAI score and clinical remission. The submission presented scatter plots of endoscopic score (SES-CD) at the end of maintenance (Week 44/48) and CDAI score at Week 92/96 in pooled data from (i) GALAXI 1 and IM-UNITI, and (ii) GALAXI 2, GALAXI 3 and IM-UNITI (Figure 2). Linear mixed models, controlling for treatment arm and clinical remission at end of maintenance found a 1-point decrease in SES-CD at Week 44/48 corresponds to a statistically significant 2.14-point to 3.31-point decrease in CDAI score at Week 92/96 on average, indicating that better endoscopic status at end of maintenance is associated with lower symptom burden in the longer term. Based on the pooled data from GALAXI 1 and IM-UNITI, a multivariate mixed logistic regression model controlling for treatment arm and clinical remission at end of maintenance, similarly found patients with endoscopic response at the end of maintenance were more likely to have clinical remission at Week 92/96 (OR = 1.91, 95%CI: 1.11, 3.28). The published literature also indicated that endoscopic remission was associated with lower rates of

[16] Panaccione R, Ma C, Jairath V, Dignass A, Joshi N, Clark R, Griffith J, Kligys K, Semwal M, Smith Z, Mitchell D, Nunag D, Ferrante M. Achievement of Endoscopic Remission After Induction Reduces Hospitalization Burden in Crohn's Disease: Findings From a Pooled Post Hoc Analysis of Risankizumab and Upadacitinib Phase III Trials. J Crohns Colitis. 2025. 19(2):jjae128.

[17] Feagan BG, Colombel JF, Panaccione R, Schreiber S, Ferrante M, Kamikozuru K, Ma C, Lee WJ, Griffith J, Joshi N, Kligys K, Kalabic J, Xuan S, Dubinsky M. Early Endoscopic Outcomes After Risankizumab Are Associated With Fewer Hospitalizations and Surgeries in Crohn's Disease. Gastro Hep Adv. 2024. 4(1):100544.

disease relapse and steroid-free clinical remission in the long-term (Baert 2010[18], Ungaro 2020[19], Frøslie 2007[20]), though most studies did not control for clinical remission status.

Figure 2: Scatterplot of endoscopic activity (SES-CD) at Week 44 and clinical disease activity (CDAI) at Week 92 (IM-UNITI, GALAXI 1, GALAXI 2 and GALAXI 3)[a]

GALAXI 1 and IM-UNITI	GALAXI 2, GALAXI 3 and IM-UNITI
	

Source: Figures 3.4 and 3.5, pp121-122 of the submission.
CD=Crohn's disease; CDAI=Crohn's disease Activity Index; GUS=guselkumab; SES-CD=simplified endoscopic activity score for CD;
a Linear mixed-effects model with a normal distribution was adjusted on treatment arm, clinical remission at end of maintenance and endoscopic score at end of maintenance with a random trial effect.

- Quality of life. The submission presented scatterplots of endoscopic activity (SES-CD) at the end of maintenance (Week 44/48) and inflammatory bowel disease questionnaire (IBDQ) score at Week 92/96 in data pooled from: (i) GALAXI 1 and IM-UNITI, and (ii) GALAXI 2, GALAXI 3 (Figure 3). Linear mixed models, controlling for treatment arm and clinical remission at the end of maintenance, found SES-CD score at Week 44/48 was not predictive of IBDQ score at Week 92/96. The submission stated whilst the effect was not statistically significant, the trend towards significance suggests that improvement in endoscopic outcomes was still likely to be associated with improved quality of life. Based on the pooled data from

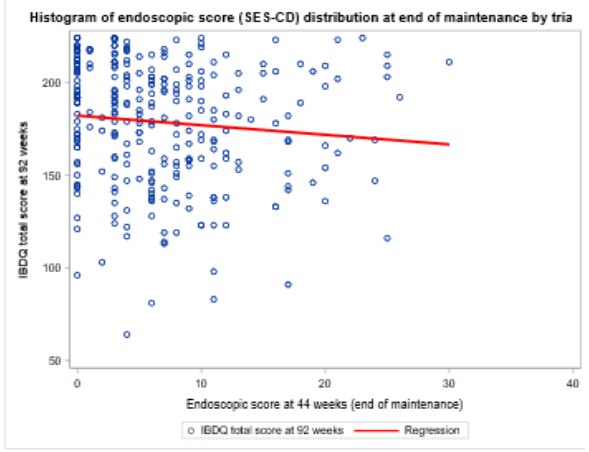
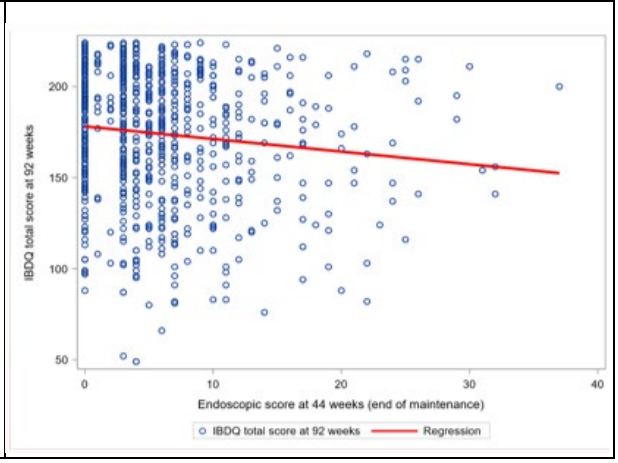
[18] Baert F, Moortgat L, Van Assche G, Caenepeel P, Vergauwe P, De Vos M, Stokkers P, Hommes D, Rutgeerts P, Vermeire S, D'Haens G; Belgian Inflammatory Bowel Disease Research Group; North-Holland Gut Club. Mucosal healing predicts sustained clinical remission in patients with early-stage Crohn's disease. Gastroenterology. 2010. 138(2):463-8; quiz e10-1.

[19] Ungaro RC, Yzet C, Bossuyt P, Baert FJ, Vanasek T, D'Haens GR, Joustra VW, Panaccione R, Novacek G, Reinisch W, Armuzzi A, Golovchenko O, Prymak O, Goldis A, Travis SP, Hébuterne X, Ferrante M, Rogler G, Fumery M, Danese S, Rydzewska G, Pariente B, Hertervig E, Stanciu C, Serrero M, Diculescu M, Peyrin-Biroulet L, Laharie D, Wright JP, Gomollón F, Gubonina I, Schreiber S, Motoya S, Hellström PM, Halfvarson J, Butler JW, Petersson J, Petralia F, Colombel JF. Deep Remission at 1 Year Prevents Progression of Early Crohn's Disease. Gastroenterology. 2020. 159(1):139-147.

[20] Frøslie KF, Jahnsen J, Moum BA, Vatn MH; IBSEN Group. Mucosal healing in inflammatory bowel disease: results from a Norwegian population-based cohort. Gastroenterology. 2007. 133(2):412-22.

GALAXI 1 and IM-UNITI, a multivariate mixed logistic regression model controlling for treatment arm and clinical remission at the end of maintenance found that patients with endoscopic response at the end of maintenance were more likely to have IBDQ remission (not defined in the submission) at Week 92/96 (OR=1.99, 95%CI: 1.16, 3.41). Evidence from published literature reported mixed findings on the possible association between endoscopic remission and patient-reported quality of life. Some evidence indicated that improved endoscopic outcomes were associated with improved quality of life (Panes 2025[21], Taxonera 2019[22], Svedborn 2024[23]), whereas others found no or limited correlation (Taleban 2016, Casellas 2012[24]). Similar to the GALAXI trials, an analysis of VIVID-1 trial data also showed no difference in the mean EQ-5D utility estimates for patients with clinical remission (EQ-5D: 0.866, 95% CI: 0.854–0.878) versus endoscopic remission (EQ-5D: 0.847, 95%CI: 0.826-0.868) at Week 52 (Svedborn 2024).

Figure 3: Scatterplot of endoscopic activity (SES-CD) and health-related quality of life (IBDQ)[a] at Week 92 (IM-UNITI, GALAXI 1, GALAXI 2 and GALAXI 3)

GALAXI 1 and IM-UNITI	GALAXI 2 and GALAXI 3
	

Source: Figures 3.16 and 3.17, pp134-135 of the submission.

[21] Panés J, Louis E, Bossuyt P, Joshi N, Lee WJ, Lacerda AP, Kligys K, Xuan S, Shukla N, Loftus EV Jr. Induction of Endoscopic Response, Remission, and Ulcer-Free Endoscopy With Upadacitinib Is Associated With Improved Clinical Outcomes and Quality of Life in Patients With Crohn's Disease. Inflamm Bowel Dis. 2025. 31(2):394-403.
[22] Taxonera C, López-Sanromán A, Vera-Mendoza I, Domènech E, Ruiz VV, Marín-Jiménez I, Guardiola J, Castro L, Esteve M, Iglesias E, Ceballos D, Martínez-Montiel P, Gisbert JP, Mínguez M, Echarri A, Calvet X, Barrio J, Hinojosa J, Martín-Arranz MD, Márquez-Mosquera L, Bermejo F, Rimola J, Alba C, Pons V, Nos P; Spanish GETECCU group (APPRECIA study). Quality of life during one year of postoperative prophylactic drug therapy after intestinal resection in Crohn's patients: Results of the APPRECIA trial. Dig Liver Dis. 2019. 51(4):529-535.
[23] Svedbom A, Wang X, Hartz S, Essakky S, Panni T. PCR316 Utility Values for Endoscopy and Symptoms-Based Health States in Crohn's Disease: Analysis of Data From a Phase 3 Randomized Controlled Clinical Trial. Value in Health. 2024. 27(12 supplement):S569.
[24] Casellas F, Barreiro de Acosta M, Iglesias M, Robles V, Nos P, Aguas M, Riestra S, de Francisco R, Papo M, Borruel N. Mucosal healing restores normal health and quality of life in patients with inflammatory bowel disease. European journal of gastroenterology & hepatology. 2012. 24(7):762-769.

CD=Crohn's disease; CDAI=Crohn's disease Activity Index; GUS=guselkumab; IBDQ=Inflammatory Bowel disease Questionnaire; SES-CD=simplified endoscopic activity score for CD;

[a] Linear mixed-effects model with a normal distribution was adjusted on treatment arm, clinical remission at end of maintenance and endoscopic score at end of maintenance with a random trial effect.

6.18 The submission concluded that the discordance between clinical remission and endoscopic remission has serious implications, as patients can appear well while still experiencing active inflammation. The submission stated the evidence presented shows that persistent mucosal inflammation despite symptom resolution is associated with worse longer-term outcomes. Conversely, patients with endoscopic response/remission experience fewer symptomatic relapses, lower rates of hospitalisation and surgery and improved quality of life. Hence, from a health economics perspective, including both clinical and endoscopic outcomes ensure a more patient-relevant assessment of treatment value.

- Overall, the ESC considered the new evidence presented in the submission provided mixed support for an independent causal effect of endoscopic remission on longer-term outcomes beyond clinical remission. While there was some indication that endoscopic response may be independently associated with reduced rates of hospitalisation and surgery, these findings are not entirely consistent across analyses, and the magnitude of any effect would likely be modest in absolute terms, given the low underlying risk. The ESC considered there was also some indication that improved endoscopic status may reduce clinical relapse, but the findings were not consistent across the literature. However, the evidence does not support an independent quality of life benefit for endoscopic remission beyond clinical remission, indicating that quality of life is primarily driven by symptoms. The ESC noted the uncertainty associated with the relationship between endoscopic outcomes and longer-term outcomes but considered it was likely that, for some patients, achieving endoscopic remission at 48 weeks could provide a meaningful improvement in long-term outcomes.

Comparative harms

6.19 Table 8 summarises the adverse events (AEs) reported in the GALAXI trials for induction and maintenance treatment, comparing safety outcomes with GUS and UST.

Table 8: Summary of AEs in the pooled GALAXI 1, GALAXI 2 and GALAXI 3 trials for induction and maintenance treatment with GUS and UST

AEs, n/N (%)	Induction (Week 12)			Maintenance (Week 48)		
	GUS IV	UST	PBO	GUS 100	GUS 200[a]	UST
Any AE	306/655 (46.7)	171/362 (47.2)	113/218 (51.8)	271/359 (75.5)	340/442 (76.9)	289/362 (79.8)
Grade ≥3 AEs	21/655 (3.2)	13/362 (3.6)	9/218 (4.1)	23/359 (6.4)	33/442 (7.5)	32/362 (8.8)
Serious AEs	19/655 (2.9)	20/362 (5.5)	13/218 (6.0)	36/359 (10.0)	31/442 (7.0)	43/362 (11.9)
Discontinuation due to AEs	12/655 (1.8)	8/362 (2.2)	9/218 (4.1)	25/359 (7.0)	27/442 (6.1)	28/362 (7.7)
Serious infection	1/655 (0.2)	6/362 (1.7)	0	3/359 (0.8)	5/442 (1.1)	13/362 (3.6)
Death	0	0	0	0	0	0

Blue shading indicates information previously seen by the PBAC...

Source: Table 2.20, p85, Tables 2.24 and 2.25 pp94-962 of the submission, Attachment 2.9 GALAXI GUS vs UST – meta-analyses.xlsx.

AE=adverse event; GUS=guselkumab; IV=intravenous; PBO=placebo; UST=ustekinumab; QxW=every x week;

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a The submission pooled patients from GALAXI 1, where patients on GUS 200 mg Q4W maintenance received either GUS 600 mg IV or GUS 1200 mg IV as induction, which was inconsistent with the TGA PI and induction doses in GALAXI 2 and GALAXI 3 (GUS 200 mg IV).

6.20 Overall, the incidence of AEs was generally similar between GUS, UST and PBO for induction and maintenance therapy across GALAXI 1, GALAXI 2 and GALAXI 3, with few patients experiencing serious or severe AEs. More patients treated with PBO experienced serious AEs or discontinuation due to AEs (mostly attributed to worsening CD) during induction and maintenance. The most commonly reported AEs were infections and gastrointestinal disorders. Safety data reported in the GALAXI trials were consistent with the safety profile of GUS in its approved indications. Based on the direct evidence, the submission maintained that GUS was non-inferior to UST in safety.

Benefits/harms

6.21 A benefits and harms comparison was not presented as direct evidence from the GALAXI trials showed no difference between GUS and UST for induction treatment for any outcome. For maintenance treatment, there were generally no differences between GUS and UST in terms of clinical outcomes, including the proportion of patients with clinical remission at 48 weeks who also achieved clinical remission at Week 12. Further, the incidence of AEs was generally similar between GUS and UST for induction and maintenance.

6.22 However, based on the direct evidence, for every 100 patients treated with GUS 100 mg compared to UST over 48 weeks, regardless of clinical remission at induction, approximately 9 additional patients would achieve endoscopic remission, and approximately 11 additional patients would achieve endoscopic response. For every 100 patients treated with GUS 200 mg compared to UST over 48 weeks, regardless of clinical remission at induction, approximately 12 to 14 patients would achieve endoscopic remission, and 15 to 16 patients would achieve endoscopic response.

Clinical claim

6.23 The submission described GUS as superior compared to UST in terms of effectiveness based on maintenance outcomes of clinical remission, endoscopic remission and endoscopic response at Week 48. In terms of safety, the submission described GUS as non-inferior compared to UST based on the incidence of AEs.

6.24 At the July 2025 PBAC meeting, the PBAC considered that, based on direct evidence, while GUS was non-inferior in terms of effectiveness compared to UST for the outcomes of clinical remission and response, it was likely superior in terms of endoscopic outcomes in the maintenance treatment setting (paragraph 7.1, guselkumab PSD July 2025 PBAC meeting). However, the PBAC also considered that the clinical relevance of endoscopic outcomes was uncertain given there was no difference between GUS and UST for the patient relevant outcome of clinical remission at Week 48 in patients with clinical remission at Week 12 (paragraph 7.5, guselkumab PSD July 2025 PBAC meeting). In terms of safety, the PBAC previously

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considered that the claim of non-inferior comparative safety versus all other b/tsDMARDs (including UST) was reasonable (paragraph 6.49, guselkumab PSD July 2025 PBAC meeting).

6.25 As the primary clinical evidence presented in the submission was unchanged from the July 2025 submission, the assessment of the clinical claim remains unchanged. For induction treatment, the head-to-head evidence showed no difference between GUS and UST across any outcome. For maintenance treatment, there were generally no differences between GUS and UST in terms of clinical remission, including the proportion of patients with clinical remission at Week 48 who also achieved clinical remission at Week 12, noting that patients can only access maintenance treatment on the PBS after achieving clinical remission following induction treatment. In contrast, GUS (100 mg Q8W and 200 mg Q4W) was generally more effective than UST in terms of endoscopic remission and endoscopic response at Week 48. However, as described above, the submission provided mixed evidence on the independent causal effect of endoscopic remission for longer-term outcomes beyond clinical remission. While some analyses suggest endoscopic remission was associated with modest reductions in hospitalisation, surgery, and possibly clinical relapse, there was no evidence of an independent quality of life benefit.

6.26 The ESC noted that, in practice, there may not be any expected differences in terms of endoscopic outcomes, given that maintenance treatment on the PBS is conditional on achieving clinical remission following induction treatment. The ESC noted the submission did not report the proportion of patients with endoscopic response at Week 48 conditional on clinical remission at Week 12, but considered a lower incremental benefit is likely after controlling for induction response.

6.27 The PBAC considered that the claim of superior comparative effectiveness (as measured by endoscopic outcomes at 48 weeks) was reasonable.

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

Economic analysis

6.29 The submission presented an updated modelled economic evaluation comparing GUS 100 mg and 200 mg to UST. At the July 2025 PBAC meeting, the PBAC found the model uninformative, and in the absence of an appropriate model comparing GUS and UST based on endoscopic outcomes, the PBAC was unable to determine the magnitude of price premium for GUS over UST that would be cost-effective (paragraphs 7.8 and 7.9, guselkumab PSD, July 2025 PBAC meeting). The PBAC's concerns and how the submission addressed them are summarised below:

- **The model included a link between endoscopic remission and long-term clinical remission and quality of life that were not supported by the evidence presented (**paragraphs 7.1, guselkumab PSD, July 2025 PBAC meeting)**.** No change was made to the model; the submission argued that the new evidence on the link between endoscopic outcomes, clinical outcomes and quality of life justified the decision

to assign a higher utility to patients in long-term clinical remission with endoscopic response (0.820) compared to patients in long-term clinical remission without endoscopic response (0.748).

- **Cost effectiveness is sensitive to treatment sequencing after GUS or UST** (paragraphs 6.53 and 6.58, guselkumab PSD, July 2025 PBAC meeting)**.** Subsequent treatments were modelled using a weighted 'basket' approach, which was informed by (i) comparative efficacy of GUS versus all PBS-listed b/tsDMARDs estimated from the Australian NMA presented in the July 2025 submission, and (ii) their respective market shares estimated from the 10% PBS data (Dec. 2024 to Nov. 2025);
- **The model included non-significant differences between GUS (100 mg and 200 mg) and UST for clinical remission at week 12 (induction) and Week 48 (maintenance)** (paragraphs 6.62 and 7.5, guselkumab PSD, July 2025 PBAC meeting)**.** The clinical evidence was updated including the removal of non-significant differences between GUS and UST at Week 12 and 48 (assumed equal to UST).
- **Utilities were uncertain and moderately favoured GUS** (paragraphs 6.52 and 6.58, guselkumab PSD, July 2025 PBAC meeting)**.** The utility value for the active disease state was changed from 0.450 to 0.513, which was a more conservative approach. The new estimate was derived from the same study (Gibson 2007[25]), by weighting the utility estimates reported by the CDAI score using the observed CDAI distribution of patients without clinical remission at Week 12 in the GALAXI trials. Other health state utilities for clinical remission remained unchanged (derived from Danese 2019[26]).

6.30 The updated economic evaluation presented in the submission also reported a weighted ICER for GUS versus UST (separate ICERs for GUS 100 and 200 were reported previously), assuming an [redacted]%:[redacted]% split for GUS 200:100 based on expert advice and real-world data, and a number of other changes that were poorly documented in some instances. These changes included: (i) small changes to the evidence base (e.g. inclusion of GALAXI 1 data) and the reference used to estimate the relative treatment effects for subsequent treatments (GUS 200 was used, compared to GUS 100 previously), which together resulted in changes to the estimated induction response probabilities and loss of response probabilities for all therapies; (ii) the proportion of patients transitioning to conventional therapy was updated using more recent data; (iii) the probability of mortality was updated with more recent data; (iv) costs were updated and cost assumptions were changed, including the proportion of patients

[25] Gibson, P. R., et al. 2007. Relationship between disease severity, quality of life and health-care resource use in a cross-section of Australian patients with Crohn's disease. Journal of gastroenterology and hepatology, 22(8), 1306–1312.

[26] Danese, S. et al. 2019. P376 Effects of IV vedolizumab on health-related quality of life and work productivity in patients with Crohn's disease: results from the Phase 3b VERSIFY trial. Journal of Crohn's and Colitis, 13(Supplement_1), S293–S294.

using GUS IV:SC for induction therapy (from 50%:50% to 90%:10%); (v) the discounting formula was corrected. The ESC noted the updated model assumed 50% of patients would receive two UST 45 mg SC injections to achieve a dose of 90 mg at a higher cost than one UST 90 mg SC injection. Assuming 100% of patients received one UST 90 mg SC injection increased the ICER by [redacted]%.

6.31 Table 9 summarises the stepped impact of each change to the modelled economic evaluation presented in the submission compared to the 'corrected' base case presented in the July 2025 submission. Overall, the ICER decreased by approximately [redacted]%, from an estimated weighted ICER of $55,000 to < $75,000 per QALY gained in the July 2025 submission to $45,000 to < $55,000 per QALY gained in the submission, assuming the same weighting across submissions ([redacted]% GUS 100 mg: [redacted]% GUS 200 mg). The main drivers of ICER change were removing the non-statistically significant differences between GUS vs UST (increasing the ICER), more conservative utility for active disease (increasing the ICER), and the new basket approach for modelling subsequent treatments (reducing the ICER).

Table 9: Stepped changes on the ICERs (GUS vs UST, July 2025 submission to July 2026 submission)

	GUS 100 vs UST				GUS 200 vs UST			
Model change	**Inc cost ($)**	**Inc QALY**	**ICER ($)**	**% Δ**	**Inc cost ($)**	**Inc QALY**	**ICER ($)**	**% Δ**
Corrected July 2025 submission base case [a]	[redacted]	**0.150**	[redacted]	**[base]**	[redacted]	**0.21**	[redacted]	**[base]**
(1) Utility value of AD (from 0.450 to 0.513)	[redacted]	0.124	[redacted]3	[redacted]%	[redacted]	0.17	[redacted]2	[redacted]%
(2) (1) + Remission probability at Wk48 [b]	[redacted]	0.018	[redacted]6	[redacted]%	[redacted]	0.12	[redacted]4	[redacted]%
(3) (2) + Remission probability at Wk12 [c]	[redacted]	0.010	[redacted]7	[redacted]%	[redacted]	0.11	[redacted]4	[redacted]%
(4) (3) + Proportion moving to BSC (all)	[redacted]	0.006	[redacted]7	[redacted]%	[redacted]	0.11	[redacted]5	[redacted]%
(5) (4) + Public/Private prescription shares (IFX IV, UST, VDZ IV)	[redacted]	0.006	[redacted]7	[redacted]%	[redacted]	0.11	[redacted]5	[redacted]%
(6) (5) + Mortality (updated ABS)	[redacted]	0.006	[redacted]7	[redacted]%	[redacted]	0.11	[redacted]5	[redacted]%
(7) (6) + Healthcare costs (2026)	[redacted]	0.006	[redacted]7	[redacted]%	[redacted]	0.11	[redacted]5	[redacted]%
(8) (7) + Treatment costs (updated prices & IV/SC shares)	[redacted]	0.006	[redacted]7	[redacted]%	[redacted]	0.11	[redacted]4	[redacted]%
(9) (8) + Subsequent treatment (Basket)	[redacted]	0.109	[redacted]2	-[redacted]%	[redacted]	0.21	[redacted]1	-[redacted]%
(10) (9) + Correcting discounting formula [d]	[redacted]	0.112	[redacted]2	-[redacted]%	[redacted]	0.22	[redacted]1	-[redacted]%
July 2026 submission base case	[redacted]	**0.112**	[redacted]2	**-[redacted]%**	[redacted]	**0.22**	[redacted]1	**-[redacted]%**

Italics indicate results calculated during the evaluation.

Source: Compiled during the evaluation.

AD=active disease; ADA=adalimumab; BSC=best supportive care; CD=Crohn's disease; CDAI=CD activity index; GUS=guselkumab; ICER=incremental cost-effectiveness ratio; IFX=infliximab; Inc=incremental; IV=intravascular; SC=subcutaneous; UST=ustekinumab; UPA=upadacitinib; VDZ=vedolizumab; Wk=week.

Note: The July 2026 submission used a [redacted]%:[redacted]% split for GUS100:GUS200 and reported a weighted ICER ($45,000 to < $55,000/QALY), which was [redacted]% lower than the July 2025 submission weighted ICER ($55,000 to < $75,000/QALY, error corrected), assuming the same split.

[a] The July 2025 submission made a programming error, which incorrectly summed QALYs on subsequent therapy. This error was identified and corrected in the July 2025 Commentary. ICERs vs UST before error correction were: $75,000 to < $95,000/QALY and $55,000 to < $75,000/QALY for GUS 100 mg and GUS 200 mg, respectively (weighted ICER: $55,000 to < $75,000 /QALY).

[b] Remission, W48: GUS 100 mg from 85.7% to 80.7%, GUS 200mg from 87.9% to 86.8%, and UST from 81.8% to 80.7%, plus using ORs from NMA based on GUS 200mg (previously 100 mg), resulting change in all others. The submission did not report or justify this change.

[c] Remission, W12: Rates for GUS 100 mg and 200 mg increased from 48.1% and 40.2% to 48.5% and 41.9%, respectively. The submission did not report or justify this change. However, these values were not used in the model; instead, the UST clinical remission probability was applied to both (46.9%). Additionally, the clinical remission rate for ADA was updated from 40.2% to 42.0%. The submission did not report or justify this change.

[d] The discount formula was revised in the submission (the previous model used EXCEL ROUND function and the current model more appropriately used the FLOOR.MATH function). The submission's report did not state this change .

The redacted values correspond to the following ranges:

[1] *$35,000 to < $45,000*
[2] *$75,000 to < $95,000*
[3] *$95,000 to < $115,000*
[4] *$115,000 to < $135,000*
[5] *$135,000 to < $155,000*
[6] *$755,000 to < $855,000*
[7] *> $1,055,000*

6.32 A summary of the key components of the July 2026 submission's economic evaluation, in comparison with the July 2025 submission, is presented in Table 10.

Table 10: Key components of the economic evaluation

Component	July 2025 submission	July 2026 submission	Justification/comments
Type of analysis	Cost-utility analysis		Unchanged. Reasonable.
Comparator(s)	Adalimumab, infliximab, upadacitinib, ustekinumab, vedolizumab	Ustekinumab	Reasonable simplification, though other treatments remain relevant
Outcomes	Life years (LYs) gained; quality-adjusted life years (QALYs) gained		Unchanged. Reasonable.
Time horizon	10 years vs 48 weeks in GALAXI trials		Unchanged. Reasonable.
Methods used to generate results	Induction period: decision-tree, Maintenance (post-induction) period: Markov model		Unchanged. Reasonable.
Health states	Clinical remission (CDAI <150), Clinical remission with endoscopic response (CDAI <150 and ≥ 50% improvement from baseline in the SES-CD or SES-CD score ≤ 2), Clinical remission without endoscopic response, Active Crohn's disease (CDAI ≥ 150), and Death		Unchanged. Reasonable.
Cycle length	2 weeks		Unchanged. Reasonable.

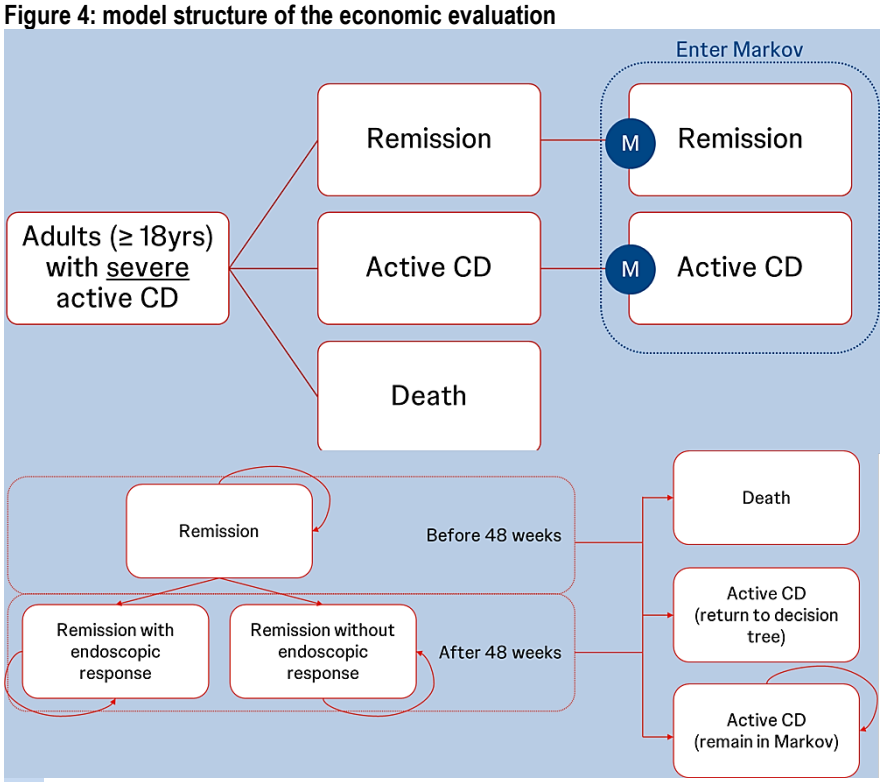
Component	July 2025 submission	July 2026 submission	Justification/comments
Transition probabilities	- **Clinical remission at the end of induction treatment:** naïve comparison. - **Loss of clinical remission after induction period:** calculated assuming an exponential discontinuation rate based on the proportion of patients who maintain clinical remission between the end of induction and Week 48/60. - **Clinical remission at Week 48/60 at the end of induction:** proportion of patients with sustained clinical remission in the GALAXI trials and results of the trial-design-adjusted NMA in terms of clinical remission at Week 48-60. - **Clinical remission from Week 48, with and without endoscopic response**: *post-hoc* analysis from GALAXI 2 and GALAXI 3. - **Loss of clinical remission to subsequent or conventional therapy:** 10% PBS data (Jan10-Aug24). **All-cause mortality:** life tables	- **Clinical remission at the end of induction treatment:** naïve comparison and GALAXI trials. Non-significant differences between GUS vs UST were removed. - **Loss of clinical remission after induction period:** calculated assuming an exponential discontinuation rate based on the proportion of patients who maintain clinical remission between the end of induction and W48/60. - **Clinical remission at Week 48/60 at the end of induction:** proportion of patients with sustained clinical remission in the GALAXI trials and results of the trial-design-adjusted NMA in terms of clinical remission at W48-60. Non-significant difference between GUS 100 and UST was removed. Remission rate for GUS 200 was updated. - **Clinical remission from Week 48, with and without endoscopic response**: *post-hoc* analysis from GALAXI 2 and GALAXI 3. - **Loss of clinical remission to conventional therapy:** 10% PBS (Dec24-Nov25). **All-cause mortality:** life tables (updated ABS list, 2022-2024)	(i) Some non-significant differences between GUS and UST were modelled by assuming the rates observed for UST, in-line with ESC/PBAC advice [a]. The model, however, maintained a large treatment benefit favouring GUS versus UST in terms of loss of clinical response following induction response. (ii) The submission updated clinical remission probability for GUS at Week 12, by including GALAXI 1 for GUS 200 in estimation. It also updated clinical remission probability for ADA without providing any rationale. (iii) The submission updated the clinical remission probability at Week 48 for GUS. For all other treatments, probabilities were derived from the NMA using GUS 200 as the reference (previously GUS 100). As a result, loss of clinical remission after Week 48 was updated across all treatments. (iii) Transitioning to conventional therapy was updated using the updated 10% PBS data (Dec24-Nov25). For GUS, it was appropriately set to be equal to UST. However, the probability of receiving the second subsequent treatment was still dependent on the active treatment.
Software	Excel 2016		Unchanged. Reasonable.

Blue shading represents information previously considered by the PBAC.
Source: Compiled during the evaluation from Table 3-1, p106 of the submission.
CD=Crohn's disease; CDAI=CD activity index; ED=emergency department; GUS=guselkumab; NMA=network meta-analysis; SC=subcutaneous; UST=ustekinumab.
[a] This included the clinical remission rate for GUS 100 and 200 vs UST at induction (Week 12), and GUS 100 vs UST at maintenance (Week 48).

6.33 The model structure was unchanged from the July 2025 submission. All patients entered the model with active CD and received induction treatment with GUS or UST. Patients who achieve clinical remission following induction treatment transition to the

remission health state and remain on maintenance treatment until loss of clinical remission or death. Following 48 weeks of sustained clinical remission, the model partitions those in remission into those with or without endoscopic response. Patients who do not achieve clinical remission following induction treatment and patients who stop responding to maintenance treatment remain in or transition to the active CD health state and receive up to two further lines of subsequent b/tsDMARD treatment or conventional therapy. Patients treated with conventional therapy remain on treatment in active CD for the remainder of the model or until dead. Figure 4 presents the model structure.

Figure 4: model structure of the economic evaluation



Blue shading represents information previously considered by the PBAC.
Source: Figure 3-2, p112 of the submission.
CD=Crohn's disease.

6.34 Table 11 summarises the key transition probabilities applied in the model, including: (i) the probability of clinical remission at the end of induction; (ii) the probability of loss of clinical remission post induction; (iii) the probability of clinical remission with/without endoscopic response post 48 weeks of maintenance; and (iv) the probability of initiating subsequent treatment.

Table 11: Summary of transition probabilities applied in the model

Treatment	Induction period	Maintenance - Jul25 submission			Maintenance - Jul26 submission		
		At Wk 12 (of all patients)	From Wk 48, with endo remission	Loss of remission (per cycle) [a]	At Wk 12 (of all patients)	From Wk 48, with endo remission	Loss of remission (per cycle) [a]
Comparators							
GUS 100	12 Wks	48.1%	67.5%	0.85%	46.9% [b]	67.5%	1.18% [c]
GUS 200	12 Wks	48.1%	66.1%	0.71%	46.9% [b]	66.1%	0.79% [c]
UST	16 Wks	46.9%	56.3%	1.25%	46.9%	56.3%	1.33% [c]
Subsequent b/tsDMARD therapy [d]							
ADA (OR=0.45)	16 Wks	40.2%	56.3% [e]	2.18%	41.9%	56.3% [e]	3.34% [f]
IFX (OR=0.20)	14 Wks	48.1%		6.63%	48.1%		7.59% [f]
UPA (OR=0.38)	12 Wks	44.4%		3.12%	44.4%		3.96% [f]
UST (OR=N/A)	16 Wks	46.9%		1.25%	46.9%		1.33% [f]
VDZ (OR=0.17)	18 Wks	15.2%		1.10%	15.2%		2.31% [f]
Weighted subsequent b/tsDMARD therapy [d]							
GUS 100	16 Wks	*NR*	*NR*	*NR*	41.8%	56.3% [e]	3.23%
GUS 200	16 Wks				41.8%		3.23%
UST	15 Wks				38.8%		4.96%
Subsequent BSC		**Probability BSC (versus b/tsDMARD)**			**Probability BSC (versus b/tsDMARD)**		
Post 1L							
GUS 100		19.4%			10.9%		
GUS 200		19.4%			10.9%		
UST		20.7%			10.9%		
Post 2L							
GUS 100		12.6%			10.2%		
GUS 200		12.6%			10.2%		
UST		8.3%			11.9%		

Blue shading represents information previously considered by the PBAC. *Italics* indicate results estimated/compiled during the evaluation. **Bold** represents information used in the economic model.

Source: Compiled during the evaluation using Table 3-15, p144, Table 3-17, p146, Table 3-19, p148 of the submission and Attachment 3.2 Guselkumab CD Economic Model.xlsx.

1L=first line; 2L=second line; ADA=adalimumab; BSC=best supportive care (conventional therapy); Endo=endoscopic response; GUS=guselkumab; IFX=infliximab; N/A=not applicable; NR=not reported; OR=odds ratio; UPA=upadacitinib; UST=ustekinumab; VDZ=vedolizumab; wk=week.

[a] Two weeks post induction period. Loss of remission was the same for pre-, post-with, and post-without endoscopic response.

[b] The submission assumed that the clinical remission probabilities of GUS in the induction phase was equal to that of UST.

[c] The submission excluded GALAXI 1 in the estimation of clinical remission probabilities in the maintenance phase (W48 remission, all patients), which was used to estimate loss of remission. For GUS 100, although the overall remission rate at Week 12 and 48 were assumed to be equal to UST (due to non-significant differences), the per cycle loss of remission probability [=1-(clinical remission at Week 12 / clinical remission at Week 48 from all patients) ^ (cycle length / follow-up duration)], differed because the cycle transition lengths (i.e., duration of follow-up) were not the same between arms (36 weeks in GUS vs 32 weeks in UST).

[d] The July 2025 submission used IFX as the first subsequent treatment, and VDZ as the second subsequent treatment. The submission used a basket approach to estimate clinical remission or loss of clinical remission in the weighted proportions of subsequent therapies.

[e] Proportions of patients on subsequent treatments with endoscopic response at W48 were assumed to be equal to UST.

[f] The submission excluded GALAXI 1 in the estimation of clinical remission probabilities in the maintenance phase (W48 remission in all patients); therefore, although odds ratios remained the same, but probabilities were different between submissions.

6.35 The model removed non-significant differences between GUS and UST at Weeks 12 and 48, including between GUS 100 and 200 vs UST for clinical remission at Week 12,

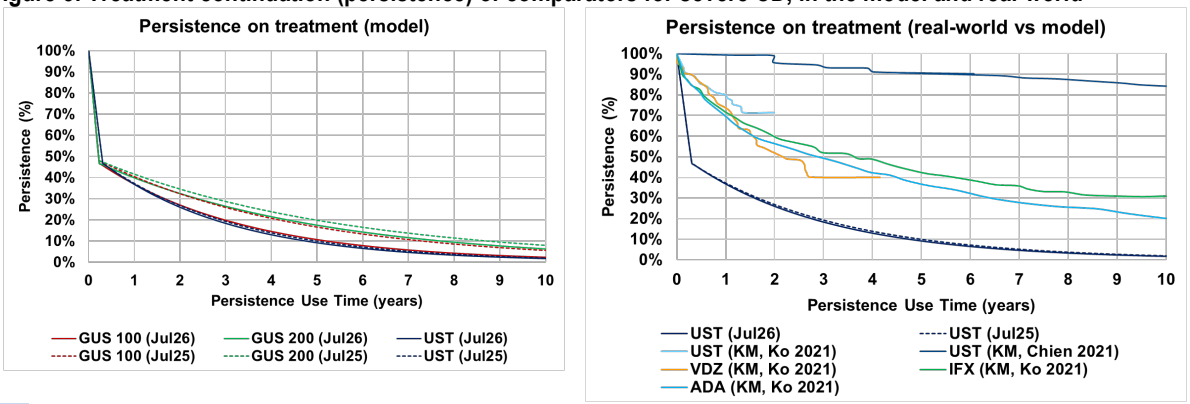
and GUS 100 vs UST for clinical remission at Week 48. Despite this, it maintained the following treatment benefits favouring GUS versus UST:

- The model maintained a large treatment benefit favouring GUS 200 versus UST in terms of loss of clinical response following induction treatment, despite the clinical evidence finding no difference in clinical remission at Week 48 in patients who achieved clinical remission at Week 12. The (weighted) ICER was extremely sensitive to this modelled benefit.
- The model maintained a smaller treatment benefit favouring GUS 100 vs UST due to a modelling artifact in terms of loss of clinical remission, despite assuming no difference in clinical remission rates at Week 12 and 48, due to GUS having a slightly shorter induction period and therefore cycle transition length (follow-up time point minus induction length) between arms, which was not reasonable. The (weighted) ICER was moderately sensitive to this modelled benefit.
- The model maintained the treatment benefit for GUS 100 in terms of the proportion achieving endoscopic response despite the clinical evidence showing no difference between GUS 100 versus UST in the proportion with endoscopic remission at Week 48, conditional on achieving clinical remission at induction. The (weighted) ICER was sensitive to this modelled benefit.
- Aside from minor changes to the loss of remission estimates of individual subsequent treatments (due to small changes to the evidence base), the submission changed the overall approach to modelling subsequent b/tsDMARD treatment. In the July 2025 submission, it was assumed that patients treated with GUS or UST would receive the same subsequent b/tsDMARD in both arms (i.e., IFX as second-line treatment, and VDZ as third-line treatment). In contrast, the submission assumed that patients treated with GUS would receive 'Basket A' (UST, ADA, IFX, UPA and VDZ) and that patients treated with UST would receive 'Basket B' (ADA, IFX, UPA and VDZ) for both first and second subsequent b/tsDMARD treatment. Each basket reflected a composite treatment, comprising all other PBS-listed b/tsDMARDs weighted by their current market shares, but Basket B excluded UST as it would not be available to patients who use UST as a first-line treatment. Adopting this approach, together with the assumed numerical differences in response between current PBS-listed b/tsDMARDs, implies that patients treated with GUS as first-line treatment receive more effective subsequent treatment (Basket A) than those treated with UST as first line treatment (Basket B), favouring GUS. This basket approach to subsequent therapies, which assumed different weighted efficacy depending on the composition of the basket, was inconsistent with the submission's argument that all current PBS treatments are equivalent in terms of efficacy. The ICER was highly sensitive to assumptions about subsequent treatments.

6.36 Other concerns with the derivation of the transition identified in the July 2025 submission remained:

- First, the submission's approach for estimating the loss of clinical remission parameter was considered highly uncertain and was not externally valid, with a much higher proportion of patients remaining on treatment with b/tsDMARDs in practice than assumed in the model (Figure 5). The submission converted the estimated clinical remission at Weeks 48-60 to loss of remission, irrespective of induction response.
- Second, the proportion of patients who maintained clinical remission with endoscopic response assumed throughout the model was based on a post-hoc analysis at one timepoint in the GALAXI trials between GUS and UST. This was done for the purposes of assigning higher utility to patients in sustained clinical remission with endoscopic response, but in the absence of a valid, independent, evidence-based link between endoscopic response and long-term quality of life benefits.
- Third, the submission provided no clinical rationale for why there would be a difference in the probability of receiving subsequent treatment with a third b/tsDMARD depending on the second b/tsDMARD (Table 11). The model, however, was not particularly sensitive to this difference.

Figure 5: Treatment continuation (persistence) of comparators for severe CD, in the model and real-world



Blue shading represents information previously considered by the PBAC.
Source: generated during the evaluation from Attachment 3.2 Guselkumab CD Economic Model.xlsx, Ko 2021 and Chien 2021.
ADA=adalimumab; CD=Crohn's disease; GUS=guselkumab; IFX=infliximab; UST=ustekinumab; VDZ=vedolizumab.

6.37 The utility values for patients in the three clinical remission health states remained unchanged, including the quality-of-life benefit assumed for patients in sustained clinical remission with endoscopic response (0.82) compared to patients in sustained clinical remission without endoscopic response (0.748). These estimates were derived from Danese 2019. The study reported the quality of life (EQ-5D) of patients with moderate to severe CD from an open-label, Phase 3b, single-arm VERSIFY study of IV VDZ over 52 weeks, reporting utility values for those with endoscopic remission (n=16, EQ-5D= 0.91) and without endoscopic remission (n=40, EQ-5D= 0.83) irrespective of clinical remission. Endoscopic remission was defined as a simple endoscopic score for CD of ≤4 at any ileocolonoscopy visit and was used as a proxy for the utility of the clinical remission with endoscopic response health state. Overall, the study was unlikely to provide a reliable estimate for any independent quality of life benefit

associated with endoscopic response, given (i) the very small sample size, (ii) results were not reported by 'endoscopic response', and (iii) results did not control for clinical remission status. A much larger study by Svedborn 2024[27] found no difference in EQ-5D-5L utilities for health states defined by endoscopic remission (0.847) or clinical remission (0.866). As discussed above, the new supportive evidence presented in the submission did not support an independent quality of life benefit for endoscopic outcomes beyond clinical remission (see Comparative effectiveness). The ICER remained moderately sensitive to the assumed quality of life benefit for endoscopic response.

6.38 Compared with the July 2025 model, the submission showed a higher proportion of patients remaining in the clinical remission health state on both first and second subsequent therapies. This reflected a change in the subsequent treatment modelling approach, whereby first and second subsequent therapies were revised from IFX and VDZ in the July 2025 submission to a basket of therapies in the current submission. This change was the primary driver of the increased accumulated QALYs in both arms, with a greater increase observed in the GUS arms, as Basket A used after GUS was more effective than Basket B used after UST.

6.39 Despite excluding some of the non-significant difference between GUS and UST in terms of clinical remission, the model maintained a large treatment benefit in terms of clinical remission (even without endoscopic remission) favouring GUS 100 and GUS 200. Patients treated with GUS (weighted) spent on average 0.84 life years (discounted) longer with clinical remission compared to patients treated with UST over the 10 year-time horizon.

6.40 The key drivers are summarised in the table below.

[27] Svedbom, A., et al., 2024. PCR316 Utility Values for Endoscopy and Symptoms-Based Health States in Crohn's Disease: Analysis of Data From a Phase 3 Randomized Controlled Clinical Trial. Value in Health, 27(12), S569.

Table 12: Key drivers of the model

Description	Method/Value	Impact
Loss of remission (after induction)	Loss of clinical remission after induction was based on the proportion of patients estimated to maintain clinical remission between Weeks 12 and 48 from the GALAXI trials. The model maintained a large treatment benefit in terms of clinical remission favouring GUS 100 and GUS 200 vs UST, despite non-significant differences: • For GUS 200, the model continued to apply a non-statistically significant difference in the proportion of patients with clinical remission at Week 48 conditional on clinical remission at Week 12, leading to a large benefit. • For GUS 100, despite assuming no difference in the proportion of patients with clinical remission at Week 12 and 48, the model still applied a small benefit in terms of loss of clinical remission favouring GUS 100 due to a modelling artifact.	High, favoured GUS
Subsequent treatment	- 1L GUS, 2L/3L: Basket A (ADA, IFX, UPA, VDZ, UST) - 1L UST, 2L/3L: Basket B (ADA, IFX, UPA, VDZ)	High, favoured GUS
Utilities	EQ-5D-5L utility values from remission with (0.820) and without (0.748) endoscopic response (Danese 2019), 'adjusted' to AQoL utilities for remission from Gibson 2007 (post Week 48). The utility values for patients in the three clinical remission health states remained unchanged, including the quality-of-life benefit assumed for patients in sustained clinical remission with endoscopic response and without endoscopic response. The evidence presented by the submission did not support an independent quality of life benefit for endoscopic outcomes beyond clinical remission.	Moderate, favoured GUS

Source: compiled during the evaluation.
ADA=adalimumab; AQoL=Assessment of Quality of Life; GUS=guselkumab; IFX=infliximab; QALY=Quality Adjusted Life Year; 1L=first-line (index) treatment; 2L=second-line treatment; 3L=third-line treatment; UST=ustekinumab; UPA=upadacitinib; VDZ=vedolizumab.

6.41 Table 13 summarises the results of the economic evaluation based on the proposed effective prices for GUS and published price for UST in the July 2026 submission.

Table 13: Results of the economic evaluation (discounted 5%)

Arm	GUS 100 vs UST			GUS 200 vs UST			GUS weighted [a] vs UST		
	GUS 100	UST	Inc.	GUS 200	UST	Inc.	GUS weighted	UST	Inc.
July 2025 submission (base case, corrected)									
Costs	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
QALYs	4.25	4.10	0.15	4.31	4.10	0.21	4.30	4.10	0.20
ICER	$[redacted] [5]			$[redacted] [3]			$[redacted] [3]		
July 2026 submission (base case)									
Costs	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
QALYs	4.69	4.58	0.11	4.80	4.58	0.22	4.78	4.58	0.20
ICER	$[redacted] [4]			$[redacted] [1]			$[redacted] [2]		

Blue shading represents information previously considered by the PBAC.
Source: Table 3-34, p165 of the submission and Attachment 3.1 Guselkumab CD Economic Model.xlsx.
GUS=guselkumab; ICER=incremental cost-effectiveness ratio; Inc=incremental; QALY=Quality Adjusted Life Year; UST=ustekinumab.
a [redacted]% GUS 100 mg and [redacted]% GUS 200 mg.
The redacted values correspond to the following ranges:
[1] *$35,000 to < $45,000*
[2] *$45,000 to < $55,000*
[3] *$55,000 to < $75,000*
[4] *$75,000 to < $95,000*

6.42 For the weighted comparison (assuming [redacted]% GUS 100 and [redacted]% GUS 200), the submission's base case ICER was [redacted]% lower than the corrected base case ICER in the July 2025 submission versus UST ($45,000 to < $55,000/QALY compared to $55,000 to < $75,000/QALY previously). For the individual comparisons, there was a [redacted]% reduction in the ICER for GUS 100 ($75,000 to < $95,000/QALY compared to $75,000 to < $95,000/QALY previously) and a [redacted]% reduction in the ICER for GUS 200 ($45,000 to <

$55,000/QALY compared to $55,000 to < $75,000 per QALY previously). The reduction in the ICER was mostly due to the weighted basket approach for modelling the subsequent treatments. This change increased the incremental benefits as patients in the GUS arms received a more effective basket compared to the UST arm, whilst also reducing the incremental costs due to less active disease. The ESC noted the assumed difference in efficacy for subsequent treatments was inconsistent with previous PBAC recommendations. Further, the ESC considered it was inappropriate for the assumed increased efficacy with UST as a subsequent treatment to translate to a lower ICER, and hence increased price, for GUS. The ESC considered the base case ICERs presented in the submission to be substantially underestimated due to the inclusion of benefits not supported by the clinical evidence.

6.43 Table 14 presents the results of key sensitivity analyses conducted during the evaluation, illustrating the incremental effect on the ICER of the modelled treatment effects. The multivariate analysis illustrates that the ICER was mostly driven by the assumed large treatment benefits favouring GUS versus UST in terms of loss of clinical response following induction treatment, differences in subsequent treatment basket composition, and the assumed utility benefit for endoscopic response. The ESC noted applying plausible and reasonable changes to the economic model resulted in an incremental cost per QALY of > $1,055,000 (multivariate sensitivity analysis 4 in Table 14).

Table 14: Results of sensitivity analyses on corrected base case – GUS 100, and GUS 200, and GUS weighted vs UST

	GUS 100 vs UST				GUS 200 vs UST				GUS weighted vs UST			
Analyses	**Inc. cost**	**Inc. QALY**	**ICER**	**% Δ v Jul26**	**Inc. cost**	**Inc. QALY**	**ICER**	**% Δ v Jul26**	**Inc. cost**	**Inc. QALY**	**ICER**	**% Δ v Jul26**
Base case (July26 submission)	**$[redacted]**	**0.11**	**$[redacted][4]**	**-**	**$[redacted]**	**0.22**	**$[redacted][1]**	**-**	**$[redacted]**	**0.20**	**$[redacted][2]**	**-**
Discount rate (base case: 5%)												
(1) Discount rate=0%	$[redacted]	0.13	$[redacted][4]	-[redacted]%	$[redacted]	0.27	$[redacted][1]	-[redacted]%	$[redacted]	0.24	$[redacted][1]	-[redacted]%
(2) Discount rate=3.5%	$[redacted]	0.12	$[redacted][4]	-[redacted]%	$[redacted]	0.24	$[redacted][1]	-[redacted]%	$[redacted]	0.21	$[redacted][2]	-[redacted]%
Time horizon (base case: 10 years)												
(3) 5 years	$[redacted]	0.08	$[redacted][5]	[redacted]%	$[redacted]	0.13	$[redacted][3]	[redacted]%	$[redacted]	0.12	$[redacted][4]	[redacted]%
(4) 20 years	$[redacted]	0.12	$[redacted][4]	-[redacted]%	$[redacted]	0.26	$[redacted][1]	-[redacted]%	$[redacted]	0.23	$[redacted][1]	-[redacted]%
Utility values (base case: remission=0.766, remission w/wo endoscopic response=0.820/0.748, active disease=0.513)												
(5) No difference in remission w/wo endo (0.766 for all)	$[redacted]	0.10	$[redacted][5]	[redacted]%	$[redacted]	0.19	$[redacted][2]	[redacted]%	$[redacted]	0.17	$[redacted][3]	[redacted]%
(6) Svedborn 2024 CDAI utility for remission (0.866) and AD (0.649)	$[redacted]	0.08	$[redacted][6]	[redacted]%	$[redacted]	0.17	$[redacted][3]	[redacted]%	$[redacted]	0.15	$[redacted][3]	[redacted]%
Subsequent treatment (base case: Basket A after treatment with GUS, Basket B [no UST] after treatment with UST)												
(7) Basket B (w/o UST) for all comparator arms	$[redacted]	0.04	$[redacted][8]	[redacted]%	$[redacted]	0.15	$[redacted][4]	[redacted]%	$[redacted]	0.13	$[redacted][4]	[redacted]%
(8) Basket A (w UST) for all comparator arms	$[redacted]	0.04	$[redacted][8]	[redacted]%	$[redacted]	0.15	$[redacted][4]	[redacted]%	$[redacted]	0.12	$[redacted][5]	[redacted]%
(9) No subsequent therapy, all patients to BSC	$[redacted]	0.04	$[redacted][8]	[redacted]%	$[redacted]	0.16	$[redacted][3]	[redacted]%	$[redacted]	0.14	$[redacted][4]	[redacted]%
Loss of clinical remission after W48 (base case, GUS 100=1.18%, UST=1.33%, due to differences in induction length)												
(10) Both set to 1.18%	$[redacted]	0.08	$[redacted][6]	[redacted]%	$[redacted]	0.19	$[redacted][3]	[redacted]%	$[redacted]	0.17	$[redacted][3]	[redacted]%
(11) Both set to 1.33%	$[redacted]	0.08	$[redacted][6]	[redacted]%	$[redacted]	0.22	$[redacted][1]	[redacted]%	$[redacted]	0.19	$[redacted][2]	[redacted]%
Clinical remission at Week 48 (base case, GUS200=86.8%, UST=80.7%) and loss of clinical remission after Week 48 (base case, GUS200=0.79%, UST=1.33%)												
(12) set GUS200 to UST	$[redacted]	0.11	$[redacted][4]	[redacted]%	$[redacted]	0.08	$[redacted][6]	[redacted]%	$[redacted]	0.09	$[redacted][6]	[redacted]%
UST 45 mg and 90 mg split (base case: 50%:50%)												
(13) 100% 90 mg	$[redacted]	0.11	$[redacted][5]	[redacted]%	$[redacted]	0.22	$[redacted][2]	[redacted]%	$[redacted]	0.20	$[redacted][3]	[redacted]%
Multivariate sensitivity analysis (MVSA)												
MVSA1: (5) + (7)	$[redacted]	0.029	$[redacted][9]	[redacted]%	$[redacted]	0.130	$[redacted][4]	[redacted]%	$[redacted]	0.110	$[redacted][5]	[redacted]%
MVSA2: MVSA1 + (11)	$[redacted]	0.002 [a]	$[redacted][10]	[redacted]%	$[redacted]	0.130	$[redacted][4]	[redacted]%	$[redacted]	0.105	$[redacted][6]	[redacted]%
MVSA3: MVSA2 + (12)	$[redacted]	0.002 [a]	$[redacted][10]	[redacted]%	$[redacted]	0.002 [a]	$[redacted][10]	[redacted]%	$[redacted]	0.002 [a]	$[redacted][10]	[redacted]%
MVSA4: (7) + (11) + (12) [b]	$[redacted]	0.008	$[redacted][10]	[redacted]%	$[redacted]	0.007	$[redacted][10]	[redacted]%	$[redacted]	0.008	$[redacted][10]	[redacted]%

Blue shading represents information previously considered by the PBAC. Italics indicate results calculated during the evaluation.

Source: conducted during the evaluation from Attachment 3.2 Guselkumab CD Economic Model.xls.

BSC=best supportive care; GUS=guselkumab; QALY=Quality Adjusted Life Year; UST=ustekinumab; w=with; w/o=without.

[a] The source of the marginal benefit, after the removal of advantages in the clinical remission and endoscopic outcomes, as well as assuming the same subsequent treatment basket, is unclear.

[b] This MVSA (MVSA4) shows that removing the clinical remission benefits and assuming same subsequent treatment basket across all arms, while maintaining the utility advantage for endoscopic response in GUS arms, results in about 0.008 incremental QALYs in GUS weighted vs UST.

The redacted values correspond to the following ranges:

[1] *$35,000 to < $45,000*

[2] *$45,000 to < $55,000*

[3] *$55,000 to < $75,000*

[4] *$75,000 to < $95,000*

[5] *$95,000 to < $115,000*

[6] *$115,000 to < $135,000*

[8] *$255,000 to < $355,000*

[9] *$355,000 to < $455,000*

[10] *> $1,055,000*

6.44 The PBAC noted the economic model resulted in a small QALY gain (0.02, see MVSA3) even when all clinical benefit was removed from the model which indicates the model is highly favourable to guselkumab.

6.45 At their July 2025 meeting, the PBAC considered GUS was highly unlikely to be cost effective at the price requested in the submission as the cost per patient over 2 years was more than twice that of UST and the benefit in endoscopic remission observed in the trial was limited to a risk difference of 9% to 14% at 48 weeks. The ESC noted that the same price has been requested for GUS in the current submission and that the economic model demonstrated that GUS was not cost-effective at this price.

Drug cost/patient/year

6.46 Table 15 presents the cost per patient per year based on the effective AEMPs.

Table 15: Drug cost/patient/year based on proposed effective AEMP for GUS

	July 2025 submission		July 2026 submission	
GUS Dosing	**Cost/patient/year**	**Cost/patient/year (incl. administration[a])**	**Cost/patient/year**	**Cost/patient/year (incl. administration[a])**
200 mg IV wk 0, 4, 8 induction -> 200 mg SC Q4W maintenance	$[redacted]	$[redacted]	$[redacted]	$[redacted]
200 mg IV wk 0, 4, 8 induction -> 100 mg SC Q8W maintenance	$[redacted]	$[redacted]	$[redacted]	$[redacted]
400 mg SC wk 0, 4, 8 induction -> 200 mg SC Q4W maintenance	$[redacted]	$[redacted]	$[redacted]	$[redacted]
400 mg SC wk 0, 4, 8 induction -> 100 mg SC Q8W maintenance	$[redacted]	$[redacted]	$[redacted]	$[redacted]

Blue shading represents information previously considered by the PBAC. Italics indicate results calculated during the evaluation.
Source: compiled during the evaluation.
GUS=guselkumab; Incl=including; IV=intravenous; SC=subcutaneous; QxW=every x week; wk=week
a Drug cost plus administration cost (MBS item 14245, July 2025 submission: $94.90, July 2026 submission: $114.30 fee).

Estimated PBS usage & financial implications

6.47 This submission was not considered by DUSC.

6.48 At the July 2025 meeting, the PBAC considered that the utilisation estimates provided were reasonable; however, the PBAC noted that the utilisation estimates applied incorrect script equivalence for some medicines (paragraph 7.11, guselkumab PSD, July 2025 PBAC meeting). The submission applied the same market share approach to the financial estimates for the PBS listing of GUS for severe CD, but updated the following parameters:

- Revised the script equivalence for IFX and VDZ;
- Corrected a programming error that doubled the unit price for GUS 100 mg SC for initial treatment;
- Shifted the market by one year (start year from 2026 to 2027), assuming normal background growth in the biologics market;
- Corrected the public/private split for ADA;

- Updated the patient co-payments and MBS fees in line with the latest schedule;
- Updated b/tsDMARD costs and cost assumptions, including the proportion of patients using GUS IV:SC for induction therapy (from 50%:50% to 90%:10%) and GUS200:GUS100 for maintenance therapy (from [redacted]%:[redacted]% to [redacted]%:[redacted]%).

6.49 Table 16 summarises the inputs used for the financial estimates.

Table 16: Data sources and parameter values applied in the utilisation and financial estimates (Y0=2026)

	July 2025 submission	July 2026 submission	Comment
Market share			
Current market (absence of	**Projected number of patient-weeks & scripts** **Projected share of patient-weeks on treatment** ADA [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% IFX [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% UST [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% UPA [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% VDZ [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% **Projected number of patient-weeks on treatment** ADA [redacted] IFX [redacted] UST [redacted] UPA [redacted] VDZ [redacted]	Projected trend and share of patient-weeks on treatment remained unchanged. The conversion of scripts to patient-weeks on treatment for IFX SC, VDZ SC & ADA (initial) were appropriately updated for the new time horizon. Total estimated number of scripts over the first six years of listing increased by 11.5% from 1,460,256 scripts in July 2025 submission to 1,650,524 scripts in July 2026 submission due to relatively high estimated background market growth (+12%).	The general approach was considered reasonable, but the estimated background market growth was uncertain.
Uptake rate	**Uptake (substitution) of GUS** ADA [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% IFX [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% UST [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% UPA [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% VDZ [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% **Market** [redacted]% [redacted]% [redacted]% [redacted]% [redacted]% [redacted]%	Uptake rates were unchanged, but the script equivalence parameters were corrected in the submission. The PBAC considered that the assumed uptake rates were appropriate but noted that the utilisation estimates applied incorrect script equivalence for some medicines (para 7.1, GUS PSD, Jul25). The submission also revised the assumed proportional use GUS IV:SC for induction therapy from 50:50 to 90:10, and the proportion use of GUS 200:100 for maintenance therapy from [redacted]:[redacted] to [redacted]:[redacted]%.	The revised parameters appeared correct and reasonable, and were consistent with assumptions made in the economic model.
Cost of medicines (AEMP)			
GUS	GUS 200 mg IV – initial $3,452.89 $[redacted] GUS 200 mg SC – initial $3,452.89 $[redacted] GUS 100 mg SC - continuing $3,452.89 $[redacted] GUS 200 mg SC – continuing (one injection) $3,452.89 $[redacted]	The proposed AEMPs were unchanged, but a programming error was corrected which doubled the unit cost of GUS 200 SC for induction therapy.	Appropriate.
Comparator b/tsDMARDs	ADA 40 mg SC - initial $505.95 ADA 80 mg SC - initial $618.90 ADA 40 mg SC - continuing $444.17 IFX 100 mg IV $186.16 IFX 120 mg SC (pen) - continuing $226.30 IFX 120 mg SC (pre-filled syringe)- continuing $252.40 UPA 15 mg $1,149.97 UPA 30 mg $1,916.62 UPA 45 mg $2,554.85 UST130 mg IV- initial $3,000.00 UST 45mgSC - continuing $3,809.08 VDZ 300 mg IV $2,949.93 VDZ 108 mg SC $1,602.35	ADA 40 mg SC - initial $392.16 [a] $[redacted] ADA 80 mg SC - initial $546.43 [a] $[redacted] ADA 40 mg SC - continuing $392.16 [a] $[redacted] IFX 100 mg IV $186.16 $[redacted] IFX 120 mg SC (pen)- continuing $252.40 $[redacted] IFX 120 mg SC (pre-filled syringe)- continuing $332.80 $[redacted] UPA 15 mg $1,092.47 $[redacted] UPA 30 mg $1,820.79 $[redacted] [b] UPA 45 mg $2,427.11 $[redacted] [b] UST130 mg IV- initial $560.73 [c] $[redacted] [c] UST 45mgSC - continuing $716.69 [c] $[redacted] [c] VDZ 300 mg IV $2,802.43 $[redacted] [b] VDZ 108 mg SC $1,522.23 $[redacted] [b]	The submission updated the prices of substituted b/tsDMARDs, but the price reduction for ADA was no longer in effect. The price of ADA had minimal impact on the results (see CIC).
CoP	PBS: $41.30, RPBS: $6.60, Based on PBS/RPBS script volume for comparator biologics in 2024.	PBS: $25.00, RPBS: $7.70, Based on PBS/RPBS script volume for biologics in 2025.	Appropriate.

	July 2025 submission	July 2026 submission	Comment
MBS	$116.60 (MBS item 14245, IV administration)	$114.30 (same MBS item number)	Appropriate.

Source: Compiled during the evaluation from Tables 4.4 to 4.15, pp186-200 of the submission, and Attachment 4.1 USM Tremfya CD Mar-26 Base (1 of 3).xlsx.

ADA=adalimumab; Avg=average; b/tsDMARD=biologic/targeted synthetic disease-modifying anti-rheumatic drug; CDAI=Crohn's disease; CoP=copayment; GUS=guselkumab; IFX=infliximab; IV=intravenous; pt=patient; pt-W=patient-week; QxW=every x week; Rx=scripts; SC=subcutaneous; SPD= simplified price disclosure; SPR= statutory price reduction; Tx=treatment; UPA=upadacitinib; UST=ustekinumab; VDZ=vedolizumab; Yr=year.

[a] The July 2026 submission incorrectly assumed an 11.71% simplified price disclosure (SPD) for ADA's published prices ($546.43 for 80 mg, and $392.16 for 40 mg). The actual published prices were: $618.90 for 80 mg, and $444.17 for 40 mg.

[b] The July 2026 submission assumed a 5% anniversary statutory price reduction (SPR) for UPA and VDZ, applied on the effective AEMPs, in the financial analysis.

[c] The July 2026 submission included a price reduction for UST published AEMPs, due to transition to F2 formulary.

6.50 Table 17 presents the estimated net financial implications for the PBS/RPBS and health budget of the proposed PBS listing of GUS for the treatment of severe CD over the first six years.

Table 17: Estimated net cost of GUS to the PBS/RPBS and health budget (effective prices, Year0=2026)

	Year 0	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimation of the use and financial impact of GUS [a]							
GUS scripts	[redacted]4	[redacted]6	[redacted]7	[redacted]8	[redacted]11	[redacted]12	[redacted]1
	[redacted]1	[redacted]5	[redacted]6	[redacted]8	[redacted]10	[redacted]12	[redacted]13
Initial	[redacted]1	[redacted]3	[redacted]3	[redacted]4	[redacted]4	[redacted]4	[redacted]5
Continuing	[redacted]1	[redacted]4	[redacted]5	[redacted]7	[redacted]8	[redacted]10	[redacted]12
GUS, net cost to PBS/RPBS ($)	[redacted]18	[redacted]20	[redacted]23	[redacted]25	[redacted]25	[redacted]25	[redacted]1
	[redacted]14	[redacted]18	[redacted]20	[redacted]23	[redacted]25	[redacted]25	[redacted]25
Estimation of changes in use and financial impact of other medicines [b]							
Comparator scripts	-[redacted]4	-[redacted]5	-[redacted]6	-[redacted]7	-[redacted]10	-[redacted]11	[redacted]1
	[redacted]1	-[redacted]4	-[redacted]5	-[redacted]7	-[redacted]8	-[redacted]10	-[redacted]12
ADA	[redacted]1	-[redacted]3	-[redacted]4	-[redacted]4	-[redacted]5	-[redacted]5	-[redacted]6
IFX	[redacted]1	-[redacted]2	-[redacted]2	-[redacted]2	-[redacted]3	-[redacted]3	-[redacted]3
UPA	[redacted]1	-[redacted]2	-[redacted]3	-[redacted]3	-[redacted]4	-[redacted]4	-[redacted]5
UST	[redacted]1	-[redacted]2	-[redacted]3	-[redacted]3	-[redacted]4	-[redacted]4	-[redacted]4
VDZ	[redacted]1	-[redacted]2	-[redacted]2	-[redacted]2	-[redacted]2	-[redacted]2	-[redacted]3
Comparators, net cost to PBS/RPBS ($)	-$[redacted]16	-$[redacted]16	-$[redacted]17	-$[redacted]18	-$[redacted]19	-$[redacted]19	[redacted]15
	[redacted]15	-$[redacted]16	-$[redacted]17	-$[redacted]5	-$[redacted]18	-$[redacted]19	-$[redacted]20
ADA	[redacted]15	-$[redacted]15	-$[redacted]15	-$[redacted]15	-$[redacted]15	-$[redacted]15	-$[redacted]16
IFX	[redacted]15	-$[redacted]15	-$[redacted]15	-$[redacted]15	-$[redacted]15	-$[redacted]15	-$[redacted]15
UPA	[redacted]15	-$[redacted]15	-$[redacted]15	-$[redacted]15	-$[redacted]15	-$[redacted]16	-$[redacted]16
UST	[redacted]15	-$[redacted]15	-$[redacted]15	-$[redacted]16	-$[redacted]16	-$[redacted]5	-$[redacted]17
VDZ	[redacted]15	-$[redacted]15	-$[redacted]15	-$[redacted]15	-$[redacted]15	-$[redacted]15	-$[redacted]15
Estimated financial implications for the PBS/RPBS and the health budget [a]							
Net cost to PBS/ RPBS ($)	[redacted]17	[redacted]19	[redacted]20	[redacted]22	[redacted]24	[redacted]25	-
	[redacted]15	[redacted]17	[redacted]18	[redacted]20	[redacted]21	[redacted]23	[redacted]25
Net cost to MBS ($)	[redacted]15	[redacted]15	[redacted]15	[redacted]15	[redacted]15	[redacted]15	-
	[redacted]15	-[redacted]15	-[redacted]15	-[redacted]15	-[redacted]15	-[redacted]15	-[redacted]15
Net cost to health budget ($)	[redacted]17	[redacted]19	[redacted]20		[redacted]24	[redacted]25	-
	[redacted]15	[redacted]17	[redacted]18	[redacted]20	[redacted]21	[redacted]23	[redacted]25

Blue shading represents information previously considered by the PBAC.

Source: Compiled during the evaluation, from Table 4.13, p197, Tables 4.15, p200, Table 4.18, p203, Table 4.20, p206, Table 4.22, p208, Table 4.27, p214, and Table 4.28, p214 of the submission, Attachment 4.1 USM Tremfya CD Mar-26 Base (1 of 3).xlsx, Attachment 4.2 USM Tremfya CD Mar-26 Base (2 of 3).xlsx and Attachment 4.3 USM Tremfya CD Mar-26 Base (3 of 3).xlsx.

ADA=adalimumab; GUS=guselkumab; IFX=infliximab; UPA=upadacitinib; UST=ustekinumab; VDZ=vedolizumab; Yrs=years.

[a] Calculated by adding across all three EXCEL files.

[b] Derived only from file 1 of 3, which includes all affected scripts.

The redacted values correspond to the following ranges:

[1] < 500
[2] 500 to < 5,000
[3] 5,000 to < 10,000
[4] 10,000 to < 20,000
[5] 20,000 to < 30,000
[6] 30,000 to < 40,000
[7] 40,000 to < 50,000
[8] 50,000 to < 60,000
[10] 60,000 to < 70,000
[11] 70,000 to < 80,000
[12] 80,000 to < 90,000
[13] 100,000 to < 200,000
[14] net cost saving
[15] $0 to < $10 million
[16] $10 million to < $20 million[17] $20 million to < $30 million
[18] $30 million to < $40 million
[19] $40 million to < $50 million
[20] $50 million to < $60 million

[21] *$60 million to < $70 million*
[22] *$70 million to < $80 million*[23] *$80 million to < $90 million*
[24] *$90 million to < $100 million*
[25] *$100 million to < $200 million*

6.51 The total estimated net cost to the PBS/RPBS over the first six years of listing decreased by [redacted]%, from $400 million to < $500 million in the July 2025 submission to $300 million to < $400 million in the July 2026 submission. The reduction in the net cost was driven by a programming error that doubled the unit cost of GUS SC in the induction phase, which was partly offset by a larger eligible population from the one-year delay to listing and high background market growth. The ESC noted the estimated net cost was substantial given the marginal clinical benefit of GUS.

6.52 Consistent with the July 2025 submission, the net cost to the PBS/RPBS and the health budget was driven by the relatively higher proposed cost per patient with GUS compared to the alternative b/tsDMARDs, the assumed uptake/substitution rates assumed for each comparator (given the average cost per patient differs by treatment), and the estimated rate of market growth. The assumption that the proposed listing would not grow the market beyond the current background rate was inconsistent with the claim that patients would remain on treatment longer (in clinical remission) with GUS compared to the alternative b/tsDMARDs.

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

7 PBAC Outcome

7.1 The PBAC recommended the Section 100 (Highly Specialised Drugs Program) Public/Private Hospital and General Schedule Pharmaceutical Benefits Scheme (PBS) listings of guselkumab for the treatment of adults with severe Crohn's disease (CD). As for the July 2025 submission, the PBAC noted while guselkumab was non-inferior in terms of effectiveness compared to ustekinumab for the outcomes of clinical remission and response, it was likely superior in terms of endoscopic outcomes in the maintenance treatment setting. However, the PBAC noted the difference in the proportion of patients achieving an endoscopic response after 48 weeks of treatment was modest (9-15%) and the impact of this difference on longer term outcomes was uncertain and unable to be reliably quantified. The PBAC considered the economic model included benefits which were not supported by the available data, and it did not enable a reliable estimate of the incremental cost effectiveness ratio (ICER) to be determined. In the context of the potential increase in the proportion of patients achieving endoscopic outcomes, and the clinical need for additional treatment options, the PBAC considered guselkumab would be cost effective with a cost per patient over two years approximately [redacted]% higher than for ustekinumab. Noting the higher cost per patient compared to all other b/tsDMARDs, the PBAC considered it would be appropriate for guselkumab use to be restricted to patients who have had inadequate response, loss of response or intolerance to at least one other PBS listed b/tsDMARD for severe Crohn's disease. The PBAC advised the restriction criteria should be finalised in consultation with the relevant professional bodies. For the

financial estimates, the PBAC considered the utilisation of guselkumab should be reduced to account for the more restricted patient population.

7.2 The PBAC welcomed input from individuals, health professionals and organisations. The PBAC noted the significant quality of life impact severe CD has on patients and the importance of having additional treatment options available, particularly medicines with different mechanisms of action.

7.3 As for the July 2025 submission, the PBAC considered ustekinumab was a reasonable comparator.

7.4 The PBAC noted no new clinical data were presented in the submission. The submission was based on three head-to-head randomised trials comparing guselkumab to ustekinumab and placebo for induction and maintenance treatment: GALAXI 1 (n=309), GALAXI 2 (n=508) and GALAXI 3 (n=513). All trials were multicentre, randomised, placebo-controlled, double-blind trials where patients with moderate to severe CD were randomised to guselkumab (100 mg every 8 weeks or 200 mg every 4 weeks), ustekinumab or placebo for 48 weeks. Each trial used a treat-through design where patients randomised to guselkumab or ustekinumab remained on the same treatment for induction (Weeks 0-12) and maintenance therapy (Weeks 12-48) irrespective of induction response. For induction treatment (i.e. Week 12), there was no difference between guselkumab and ustekinumab in terms of clinical remission or clinical response. For maintenance treatment (i.e. Week 48), there were generally no difference between guselkumab 100 mg, guselkumab 200 mg and ustekinumab in terms of clinical remission and clinical response outcomes, with the exception of a few comparisons that favoured guselkumab 200 mg over ustekinumab on maintenance of clinical remission and durable clinical remission. The PBAC again noted guselkumab 100 mg and guselkumab 200 mg were generally more effective than ustekinumab in terms of endoscopic remission and endoscopic response outcomes. The PBAC noted an additional 9% (100 mg dose) to 14% (200 mg dose) of patients achieved endoscopic remission, and an additional 11% (100 mg dose) to 15% (200 mg dose) achieved an endoscopic response at 48 weeks. The PBAC agreed with the ESC that the benefit in clinical practice may be lower as only patients who achieve a response after induction therapy are eligible to continue with maintenance treatment on the PBS (see paragraph 6.26).

7.5 The PBAC previously considered that it was unclear if achieving endoscopic remission would lead to better longer-term outcomes for patients (see paragraph 6.15). To address this, the submission presented evidence to link endoscopic outcomes and longer-term health outcomes, including clinical remission, the need for surgery/ hospitalisation and health-related qualify of life. The PBAC considered the evidence suggested there was a small potential reduction in surgery/ hospitalisation for patients who achieve endoscopic outcomes, a weak signal for a link with clinical remission and inconsistent evidence for a correlation with health-related quality of life. On balance, the PBAC agreed with the ESC that, for some patients, achieving endoscopic remission at 48 weeks could provide a meaningful improvement in long-

term outcomes. However, the PBAC noted the magnitude of this benefit over the longer-term was uncertain and unable to be reliably quantified.

7.6 The PBAC noted the submission requested the same price as in July 2025 and recalled it had previously considered guselkumab was highly unlikely to be cost effective at that price as the cost per patient over 2 years was more than twice that of ustekinumab (see paragraph 6.45). Additionally, the PBAC previously considered that, in the absence of an appropriate economic model comparing guselkumab and ustekinumab based on endoscopic outcomes, it was unable to determine the magnitude of price premium for guselkumab over ustekinumab that would be cost effective (paragraph 6.29).

7.7 The PBAC noted the submission presented an updated cost utility analysis, based on endoscopic outcomes, comparing guselkumab to ustekinumab (see paragraph 6.30 for a description of changes), with an incremental cost effectiveness ratio (ICER) of $45,000 to < $55,000 per quality adjusted life year (QALY) (weighted across the two guselkumab dosage regimens). The PBAC agreed with the ESC that the ICER was substantially underestimated and noted applying plausible and reasonable changes to the economic model resulted in an incremental cost per QALY of > $1,055,000. Overall, the PBAC considered the model did not provide a reliable estimate of the ICER, however the PBAC considered it did demonstrate that guselkumab was not cost effective at the price requested in the submission.

7.8 The PBAC noted the clinical need for additional treatment options, particularly in those who have not responded to other b/tsDMARDs. In this context, and acknowledging the modest incremental benefit in the proportion of patients achieving endoscopic outcomes at 48 weeks, the PBAC considered guselkumab would be cost effective with a cost per patient over two years approximately 10% higher than that for ustekinumab.

7.9 The PBAC advised the following equi-effective doses remained appropriate to calculate the cost per patient over two years:

Guselkumab 200 mg intravenously at week 0, 4, and 8, or guselkumab 400 mg subcutaneously (SC) at week 0, 4, and 8 followed by guselkumab 200 mg SC at week 12, and then every 4 weeks, or guselkumab 100 mg SC at week 16 and then every 8 weeks is equi-effective to ustekinumab 390 mg IV at week 0 and 90 mg SC at week 8 followed by 90 mg SC every 8 weeks or every 12 weeks.

The PBAC considered a split of dosage regimens, as applied in the financial estimates (see Table 16), was reasonable.

7.10 Noting the higher cost per patient compared to all other b/tsDMARDs, the PBAC considered it would be appropriate for guselkumab to be available for patients who have inadequate response, loss of response or intolerance to at least one other b/tsDMARD. This would ensure guselkumab was available for patients with a high clinical need but would not be the first choice for treatment naïve patients where alternative less expensive treatments may be effective.

7.11 The PBAC considered it would be appropriate for guselkumab to be listed with a higher level of restriction than other b/tsDMARDs i.e., as an 'Authority Required – In Writing (full assessment)' item. The PBAC advised the restriction criteria should be finalised in consultation with the relevant professional bodies prior to listing.

7.12 The PBAC considered the methodology for estimating the utilisation of guselkumab was appropriate but uptake should be changed (informed by PBS utilisation data) to account for the more restricted patient population. The PBAC advised that utilisation should be reviewed 2 years after listing.

7.13 The PBAC recalled it had previously advised that the pre-filled pen and pre-filled syringe forms of guselkumab could be considered equivalent for the purposes of substitution (paragraph 7.12, guselkumab PSD, July 2025 PBAC meeting).

7.14 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met. Specifically, the PBAC found that in the circumstances of its recommendation for guselkumab:

a) The treatment is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over alternative therapies;

b) The treatment is not expected to address a high and urgent unmet clinical need as there are alternative therapies available;

c) It was not necessary to make a finding in relation to whether it would be in the public interest for the subsequent pricing application to be progressed under Pricing Pathway A because one or more of the preceding tests had failed

7.15 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:
Recommended

8 Recommended listing

The restriction will be finalised pending consultation (as per paragraph 7.11).

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 had no comment.