Medicinrådet

# Bilag til direkte indplacering af guselkumab i Medicinrådets evidensgennemgang vedrørende biologiske og målrettede syntetiske lægemidler til colitis ulcerosa

*Vers. 1.0*

# Bilagsoversigt

1. Forhandlingsnotat fra Amgros vedr. guselkumab
2. Ansøgers endelige ansøgning vedr. guselkumab

Amgros I/S
Dampfærgevej 22
2100 København Ø
Danmark

T +45 88713000
F +45 88713008

Medicin@amgros.dk
www.amgros.dk

08.08.2025

DBS/LSC

# Forhandlingsnotat

| | |
|---|---|
| Dato for behandling i Medicinrådet | 03.09.2025 |
| Leverandør | Johnson & Johnson |
| Lægemiddel | Tremfya (guselkumab) |
| Ansøgt indikation | Behandling af voksne patienter med moderat til svært aktiv colitis ulcerosa, som ikke har responderet tilstrækkeligt på, ikke længere responderer på eller er intolerante over for enten konventionel behandling eller en biologisk behandling |
| Nyt lægemiddel / indikationsudvidelse | Indikationsudvidelse – direkte indplacering i behandlingsvejledning |

## Prisinformation

Amgros har forhandlet pris på nye styrker af Tremfya (guselkumab).

[redacted]

*Tabel 1: Forhandlingsresultat*

| Lægemiddel | Styrke (pakningsstørrelse) | AIP (DKK) | Nuværende SAIP, (DKK) | Rabat ift. AIP |
|---|---|---|---|---|
| Tremfya | 200 mg, 1 stk. hætteglas | 14.188,17 | [redacted] | [redacted] |
| Tremfya | 200 mg, 1 stk. pen | 14.188,17 | [redacted] | [redacted] |

Prisen er betinget af Medicinrådets anbefaling. Det betyder, at hvis Medicinrådet ikke anbefaler Tremfya, indkøbes lægemidlet til AIP.

Amgros har følgende aftalepriser på Tremfya 100 mg pen og sprøjte:

*Tabel 2: Aftalepriser*

| Lægemiddel | Styrke (pakkings-størrelse) | AIP (DKK) | Nuværende SAIP, (DKK) | Rabat ift. AIP |
|---|---|---|---|---|
| Tremfya | 100 mg, 1 stk. pen/sprøjte | 14.188,17 | [redacted] | [redacted] |

## Aftaleforhold

[redacted]

## Konkurrencesituationen

[redacted]

Tabel 2 viser lægemiddeludgifter på udvalgte sammenlignelige lægemidler. Lægemiddeludgiften pr. patient er beregnet på 78 uger (18 måneders behandling) jf. det kliniske sammenligningsgrundlag i Medicinrådets opsummering af evidensgennemgang vedrørende biologiske og målrettede syntetiske lægemidler til colitis ulcerosa.

*Tabel 3: Sammenligning af lægemiddeludgifter pr. patient*

| Lægemiddel | Styrke (pakningsstørrelse) | Dosering | Pris pr. pakning (SAIP, DKK) | Lægemiddeludgift pr. behandling på 78 uger (SAIP, DKK)* |
|---|---|---|---|---|
| Amgevita (biosimilær, adalimumab) | 40 mg, 2 stk. pen/sprøjte | **Induktion (s.c.):** 160 mg uge 0, 80 mg uge 2. **Vedligeholdelse (s.c.):** 40 mg (SC) hver 2. uge. | [redacted] | [redacted] |
| Simponi (golimumab) | 100 mg, 1 stk. pen<br>50 mg, 1 stk. pen | **Induktion (s.c.):** 200 mg uge 0, 100 mg uge 2. **Vedligeholdelse (s.c.):** 50 mg (< 80 kg) hver 4. uge. | [redacted] | [redacted] |
| Tremfya (guselkumab) | 200 mg, 1 stk. hætteglas **NY**<br>100 mg, 1 stk. pen/sprøjte | **Induktion (i.v.):** 200 mg uge 0, 4 og 8. **Vedligeholdelse (s.c.):** 100 mg hver 8. uge | [redacted] | [redacted] |
| Tremfya (guselkumab) | 200 mg, 1 stk. hætteglas **NY**<br>200 mg, 1 stk. pen/sprøjte **NY** | **Induktion (i.v.):** 200 mg uge 0, 4 og 8. **Vedligeholdelse (s.c.):** 200 mg hver 4. uge | [redacted] | [redacted] |
| Zessly (infliximab) | 100 mg, 3 stk. hætteglas | **Induktion (i.v.):** 5 mg/kg mg uge 0, 4 og 6. **Vedligeholdelse (i.v.):** 5 mg/kg mg hver 8. uge | [redacted] | [redacted] |
| Omvoh (mirikizumab) | 300 mg, 1 stk. hætteglas<br>100 mg, 2 stk. pen | **Induktion (i.v.):** 300 mg uge 0, 4 og 8. **Vedligeholdelse (s.c.):** 200 mg hver 4. uge. | [redacted] | [redacted] |
| Entyvio (vedolizumab) | 300 mg, 1 stk. hætteglas | **Induktion (i.v.):** | [redacted] | [redacted] |

| | | | | |
|---|---|---|---|---|
| | 108 mg, 1 stk. pen/sprøjte | 300 mg uge 0 og 2<br>**Vedligeholdelse (s.c.):**<br>108 mg uge 6, og herefter 108 mg hver 2. uge. | [redacted] | |
| Entyvio (vedolizumab) | 300 mg, 1 stk. hætteglas | **Induktion (i.v.):**<br>300 mg uge 0, 2 og 6.<br>**Vedligeholdelse (i.v.):**<br>300 mg hver 8. uge. | [redacted] | [redacted] |
| Stelara (ustekinumab) | 130 mg, 1 stk. hætteglas<br><br>90 mg, 1 stk. sprøjte | **Induktion (i.v.):**<br>390 mg (55-85 kg) uge 0.<br>**Vedligeholdelse (s.c.):**<br>90 mg i uge 8 og herefter hver 12. uge. | [redacted] | [redacted] |

*jf. det kliniske sammenligningsgrundlag i Medicinrådets opsummering af evidensgennemgang vedrørende biologiske og målrettede syntetiske lægemidler til colitis ulcerosa
Note: Gennemsnitsvægt for en patient er estimeret til 75 kg
[redacted]

## Status fra andre lande

*Tabel 4: Status fra andre lande*

| Land | Status | Link |
|---|---|---|
| **Norge** | Under vurdering | Link til status |
| **England** | Under vurdering | Link til status |

## Opsummering

[redacted]

# Application for the assessment of guselkumab (Tremfya®) by updating the Danish Medicines Council's guideline regarding biological and targeted synthetic drugs for the treatment of ulcerative colitis

# Contact information

| Contact information | |
|---|---|
| **Name** | **Asbjørn Lydert Hansen Kvist** |
| Title | Country HEMAR Manager |
| Phone number | +45 29998267 |
| E-mail | ahanse13@its.jnj.com |
| **Name** | **Kari Stougaard Chu** |
| Title | Field Medical Advisor, Immunology |
| Phone number | +45 29998276 |
| E-mail | kjacobse@its.jnj.com |

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# Abbreviations

| Abbreviations | Definition |
|---|---|
| AE | Adverse event |
| BMSL | Biological and targeted synthetic medicine |
| CD64 | Fc-gamma receptor 1 |
| CI | Confidence interval |
| COVID-19 | Coronavirus disease-19 |
| DMC | Danish Medicines Council |
| EIM | Extra-intestinal manifestations |
| EMA | European Medicines Agency |
| I-# | Week number in induction |
| IBD | Inflammatory Bowel Disease |
| IBDQ | Inflammatory Bowel Disease Questionnaire |
| ICE | Intercurrent event |
| IL | Interleukin |
| IS-1 | Induction Study 1 |
| IS-2 | Induction Study 2 |
| IV | Intravenous |
| M | Maintenance |
| MS | Maintenance study |
| N/A | Not applicable |
| q4w | Every 4 weeks |
| q8w | Every 8 weeks |

| | |
|---|---|
| SC | Subcutaneous |
| TNF-α | Tumour necrosis factor α |
| UC | Ulcerative colitis |

# 1. Regulatory information on the pharmaceutical

**Table 1 Overview of the pharmaceutical**

| Overview of the pharmaceutical | |
|---|---|
| **Proprietary name** | Tremfya® |
| **Generic name** | Guselkumab |
| **Therapeutic indication as defined by EMA** | Guselkumab for the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, lost response, or were intolerant to either conventional therapy, or a biological treatment (1). |
| **Marketing authorization holder in Denmark** | Johnson & Johnson |
| **ATC code** | L04AC16 |
| **Combination therapy and/or co-medication** | Immunomodulators and/or corticosteroids may be continued during treatment with guselkumab. In patients who have responded to treatment with guselkumab, corticosteroids may be reduced or discontinued in accordance with standard of care (1). |
| **(Expected) Date of EC approval** | April 25th 2025 |
| **Has the pharmaceutical received a conditional marketing authorization?** | No |
| **Accelerated assessment in the European Medicines Agency (EMA)** | No |
| **Orphan drug designation (include date)** | No |
| **Other therapeutic indications approved by EMA** | Guselkumab is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy (2).<br><br>Guselkumab, alone or in combination with methotrexate, is indicated for the treatment of active psoriatic arthritis in adult patients who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug therapy (2). |

| Overview of the pharmaceutical | |
|---|---|
| **Other indications that have been evaluated by the Danish Medicines Council (DMC) (yes/no)** | Yes. Guselkumab is indicated for psoriatic arthritis (3) and for plaque psoriasis (4, 5) and have previously been evaluated by the DMC. |
| **Dispensing group** | NBS |
| **Packaging – types, sizes/number of units and concentrations** | Guselkumab (Tremfya®) 100 mg solution for injection in pre-filled pen<br>Guselkumab (Tremfya®) 100 mg solution for injection in pre-filled syringe<br>Guselkumab (Tremfya®) 200 mg solution for injection in pre-filled pen<br>Guselkumab (Tremfya®) 200 mg solution for intravenous (IV) |

Abbreviations: DMC = Danish Medicines Council; EMA = European Medicines Agency; IV = intravenous; UC = ulcerative colitis.
Source: Johnson & Johnson (1); European Medicines Agency, 2024 (2); Danish Medicines Agency, 2024 (6).

# 2. Summary table

**Table 2 Summary table**

| Summary | |
|---|---|
| **Therapeutic indication relevant for the assessment** | Guselkumab for the treatment of adult patients with moderately to severely active UC who have had an inadequate response, lost response, or were intolerant to either conventional therapy, or a biological treatment. |
| **Dosage regiment and administration:** | The recommended induction dose is 200 mg guselkumab IV infusion at Week 0, Week 4, and Week 8.<br>The recommended and standard maintenance dose is 100 mg guselkumab subcutaneous (SC) injection starting at Week 16 and every 8 weeks (q8w). Alternatively, for patients who do not show adequate therapeutic benefit to induction treatment according to clinical judgement, a maintenance dose of 200 mg SC injection starting at Week 12 and every 4 weeks (q4w) thereafter, may be considered. As evident from section 5.2 and 6.2, the two maintenance regimens show comparable efficacy. |
| **Choice of comparator [if any]** | Placebo is the chosen comparator, as placebo is the comparator in the key QUASAR trial. Furthermore, using placebo as comparator is in line with the study setup for mirikuzumab (Omvoh), which an interleukin (IL)-23 already included in the existing treatment guideline (7). |

| Summary | |
|---|---|
| **Most important efficacy endpoints (Difference/gain compared to comparator)** | **Clinical remission at Week 12**<br>• Biological and targeted synthetic medicine (BMSL)-naïve, placebo IV: n=16/137 (11.6%)<br>• BMSL-naïve, guselkumab 200 mg IV: n=64/202 (31.7%)<br>• BMSL-experienced subgroup, placebo IV: n=5/136 (3.7%)<br>• BMSL- experienced subgroup, guselkumab 200 mg IV: n=26/208 (12.5%)<br>**Corticosteroid-free clinical remission at maintenance Week 44**<br>• BMSL-naïve, placebo SC: n=28/108 (25.9%)<br>• BMSL-naïve, guselkumab 100 mg SC q8w: n=53/105 (50.5%)<br>• BMSL-naïve, guselkumab 200 mg SC q4w: n=54/96 (56.3%)<br>• BMSL- experienced subgroup, placebo SC: n=5/75 (6.7%)<br>• BMSL- experienced subgroup, guselkumab 100 mg SC q8w: n=31/77 (40.3%)<br>• BMSL- experienced subgroup, guselkumab 200 mg SC q4w: n=35/88 (39.8%)<br>**Endoscopic mucosal healing at maintenance Week 44**<br>• BMSL-naïve, placebo SC: n=28/108 (25.9%)<br>• BMSL-naïve, guselkumab 100 mg SC q8w: n=56/105 (53.3%)<br>• BMSL-naïve, guselkumab 200 mg SC q4w: n=57/96 (59.4%)<br>• BMSL- experienced subgroup, placebo SC: n=6/75 (8.0%)<br>• BMSL- experienced subgroup, guselkumab 100 mg SC q8w: n=35/77 (45.5%)<br>• BMSL- experienced subgroup, guselkumab 200 mg SC q4w: n=37/88 (42.0%)<br>**Inflammatory Bowel Disease Questionnaire (IBDQ) remission at maintenance Week 44**<br>• BMSL-naïve, placebo SC: n=53/108 (49.1%)<br>• BMSL-naïve, guselkumab 100 mg SC q8w: n=71/105 (67.6%) |

| Summary | |
|---|---|
| | • BMSL-naïve, guselkumab 200 mg SC q4w: n=71/96 (74.0%)<br>• BMSL- experienced subgroup, placebo SC: n=14/75 (18.7%)<br>• BMSL- experienced subgroup, guselkumab 100 mg SC q8w: n=45/77 (58.4%)<br>• BMSL- experienced subgroup, guselkumab 200 mg SC q4w: n=47/88 (53.4%) |
| **Most important serious adverse events for the intervention and comparator** | Generally, serious AEs were not frequent. The only serious AE that occurred among ≥5% were worsening of UC which occurred in 5.1% in the placebo IV q4w arm among the BMSL-naïve subgroup in the Induction Study 2 (IS-2) (worsening of UC occurred in 1.0% in the guselkumab 200 mg IV q4w arm). In the BMSL- experienced subgroup, 4.4% experienced worsening of UC in the placebo IV q4w arm and 1.9% in the guselkumab 200 mg IV q4w arm in the IS-2. |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; IBDQ = Inflammatory Bowel Disease Questionnaire; IL = interleukin; IS-2 = Induction Study 2; IV = intravenous; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.
Source: Janssen Cilag, 2025 (1); Janssen Research & Development, 2024 (8) (9).

# 3. The patient population, intervention and relevant outcomes

## 3.1 The medical condition, patient population, current treatment options and choice of comparator(s)

### 3.1.1 Introduction to ulcerative colitis

Inflammatory bowel disease (IBD) is a chronic inflammatory condition of the gastrointestinal (GI) tract. The two most common forms of IBD are Crohn's disease (CD) and UC, which are heterogenous conditions with overlapping clinical presentation (10-12). Whereas CD is characterised by patchy, transmural inflammation across any part of the GI tract, UC is characterised by continuous, more superficial inflammation of the mucosal layers in the colon and rectum that begins distally and extends proximally as the disease progresses (i.e., begins at the rectum and moves upward toward through the colon) (10, 13-15). Ulcerative colitis is a progressive condition that follows a relapsing -remitting disease course, in which patients have periods of no/minimal symptoms followed by flares of more active disease (16, 17). The most common symptoms of UC are blood in the stool and diarrhoea (14, 18); patients may also experience bowel urgency, increased frequency of bowel

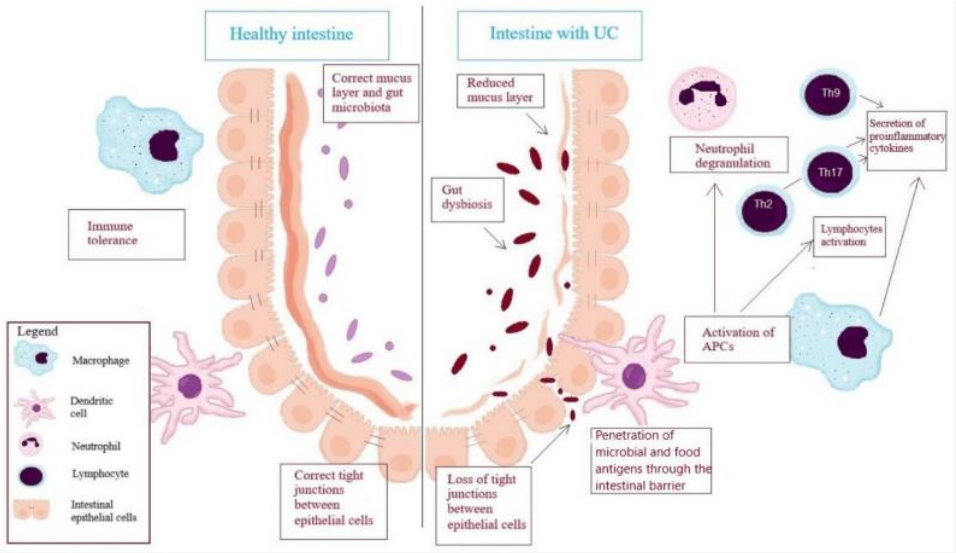
movements, incontinence, fatigue, abdominal pain, tenesmus, mucus discharge, and/or nocturnal defecations/diarrhoea, particularly among those with more severe activity (10, 14, 18).

Although UC-related inflammation primarily manifests in the colon, it is a systemic condition that may extend to other organs (19). Inflammatory pathologies that occur outside of the GI tract are typically referred to as extraintestinal manifestations (EIMs), and they can be either dependent or independent of GI inflammation (19). The most common EIM are arthropathies, with other EIMs affecting the skin, eyes, and liver (14). In a recent meta-analysis, 27% of patients with UC had at least one joint, ocular, or skin EIM (20).

### 3.1.2 Pathobiology

The pathogenesis of UC involves genetic and environmental factors that contribute to dysbiosis, a disrupted intestinal epithelium, and dysregulated innate and adaptive immune system responses (21, 22). In UC, the epithelial barrier (i.e., the mucus layer and epithelium) is damaged, allowing for increased permeability of luminal antigens than can induce an immune reaction and resulting inflammation. Additionally, commensal bacteria, which help to support normal gut homeostasis in healthy individuals, enter the dysfunctional epithelium and produces an immune response and intestinal inflammation (23). Dysbiosis is also present in UC, though it is unclear if it causes or results from inflammation (24). Immune activation causes an inflammatory cascade that contributes to further epithelial barrier dysfunction and inflammation, which contributes to more severe and chronic disease (24). Figure 1 displays intestinal function in healthy and UC states.

**Figure 1 Pathogenesis of UC**

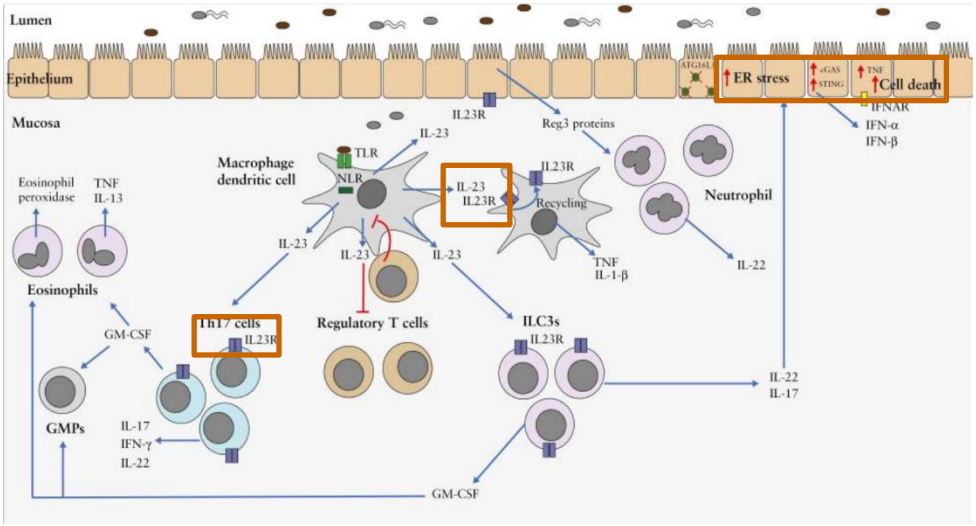



Abbreviations: APC = antigen-presenting cells; Th2 = T helper 2; Th9 = T helper 9; Th17 = T helper 17; UC = ulcerative colitis.
Source: Kałużna, Olczyk (25).

Interleukin (IL)-23 plays an important role in the inflammatory processes involved in UC, as it mediates both innate and adaptive immune responses, and also plays an important role in mucosal barrier function (26, 27). In individuals with UC, microbial penetration of

the epithelial barrier stimulates dendritic cells, macrophages, and neutrophils, resulting in increased IL-23 expression. Notably, samples of inflamed mucosa from patients with UC show increased IL-23 expression, and in patients with CD, IL-23 expression is positively correlated with the severity of lesions identified in endoscopy. This increased expression of IL-23 ultimately contributes to the production of a gamut of proinflammatory cytokines, while concurrently limiting regulatory T cell (Treg) activation, driving inflammation and tissue damage in the intestine (26). Figure 2 provides a detailed overview of the role of IL-23 in intestinal inflammation in IBD.

**Figure 2 Role of IL-23 in intestinal inflammation in IBD**




The above figure depicts the diverse downstream immunological effects of IL-23 produced by macrophages and dendritic cells in response to microbial stimulation. IL-23 enhances the induction and survival of Th17 cells, releasing the IL-17, interferon gamma (IFNγ), IL-22 and GM-CSF cytokines, the last of these promoting accumulation of granulocyte-monocyte progenitor cells and activated eosinophils in the intestine. IL-23 inhibits the induction of regulatory T cells and orchestrates the production of cytokines such as IL-17, IL-22, and GM-CSF from group 3 innate lymphoid cells. Autocrine effects of IL-23 on macrophages including pro-inflammatory cytokine production and IL-23R recycling have also been reported. IL-23 additionally induces the production of neutrophil chemoattractant Reg proteins by intestinal epithelial cells, in turn serving as an additional source of IL-22. IL-22 exerts dichotomous effects in intestinal inflammation, including induction of ER stress in the intestinal epithelium, leading to cell death.

Abbreviations: ER = endoplasmic reticulum; GM-CSF = granulocyte-macrophage colony-stimulating factor; IBD = inflammatory bowel disease; IFNγ = interferon gamma; IL-17 = interleukin 17; IL-22 = interleukin 22; IL-23 = interleukin 23; IL-23R = interleukin 23 receptor; Th17 = T helper 17.
Source: Sewell and Kaser (27).

Recent evidence underscores the importance of T helper 17 (Th17) cells and more-broadly the significant role that the IL-23/Th17 axis plays in chronic intestinal inflammation (21, 26, 28). Indeed, when antigen-presenting cells bind to Th17 cells, IL-23 plays a direct role in Th17 activation, which triggers the release of several proinflammatory cytokines, including tumour necrosis factor alpha (tumour necrosis factor-α [TNF-α]), INFγ, IL-6, IL-17A, IL-17F, and IL-22, leading to downstream proinflammatory responses. For example, IL-17 activates additional proinflammatory cytokines independently or in combination with TNF-α, leading to further inflammation and intestinal mucosa damage, which can in turn result in fibrosis over time in some patients (28). Of interest, a recent *in vitro* study found that the ability of guselkumab to also bind to CD64 on IL-23—producing cells through guselkumab's native Fc region may contribute to its enhanced functional potency with respect to

the inhibition of IL-23 signalling compared with risankizumab, which has a mutated Fc region (29). This suggests that guselkumab may be more effective at neutralising IL-23 by targeting IL-23 at its source of production.

Ulcerative colitis is marked by tissue damage, which impairs function and contributes to symptoms characteristic of UC, including blood in the stool and diarrhoea. Features of endoscopic assessment in UC typically include erythema (redness), mucosal granularity and friability (i.e., rough appearance and bleeding from light touch, respectively), and loss of vascular markings, but may also include erosions, ulcers, and spontaneous bleeding with more severe inflammation (18, 30). Known, but rare, long-term complications in UC may include fibrosis and strictures that worsen with more severe and chronic inflammation, impairing colonic function (31, 32).

Separate guidelines on surgical treatment of UC were published by ECCO in 2022 (33). Typically, surgery is an option for acute severe ulcerative colitis and patients with medically refractory UC (i.e., steroid dependency, immunomodulator or biologic-refractory disease). Up to a quarter of patients with UC require a surgical intervention, and the decision to pursue surgery considers symptoms, medical care and immunosuppressive therapies, malignancy risk, functional outcomes, perioperative complications.

## 3.2 The intervention

**Table 3 Overview of guselkumab**

| Overview of guselkumab | |
|---|---|
| **Therapeutic indication relevant for the assessment** | Guselkumab for the treatment of adult patients with moderately to severely active UC who have had an inadequate response, lost response, or were intolerant to either conventional therapy, or a biological treatment. |
| **Method of administration** | Induction: IV infusion*<br><br>Maintenance: SC injection |
| **Dosing** | The recommended induction dose is 200 mg guselkumab at Week 0, Week 4, and Week 8.<br><br>The recommended and standard maintenance dose is 100 mg guselkumab SC starting at Week 16 and q8w. Alternatively, for patients not showing adequate therapeutic benefit to induction treatment according to clinical judgement, a maintenance dose of 200 mg SC starting at Week 12 and q4w thereafter, may be considered. As evident from section 5.2 and 6.2, the two maintenance regimens show comparable efficacy. |
| **Should the pharmaceutical be administered with other medicines?** | No, however, immunomodulators and/or corticosteroids may be continued during treatment with guselkumab. In patients who have responded to treatment with guselkumab, corticosteroids may be reduced or discontinued in accordance with standard of care. |

| Overview of guselkumab | |
|---|---|
| **Treatment duration / criteria for end of treatment** | Consideration should be given to discontinuing treatment in patients who have shown no evidence of therapeutic benefit after 24 weeks of treatment.<br><br>If a patient develops a clinically important or serious infection or is not responding to standard therapy, the patient should be monitored closely and treatment should be discontinued until the infection resolves. If a serious hypersensitivity reaction occurs, administration of guselkumab should be discontinued immediately. |
| **Necessary monitoring, both during administration and during the treatment period** | After proper training in SC injection technique, patients may inject guselkumab if a physician determines that this is appropriate. However, the physician should ensure appropriate medical follow-up of patients.<br><br>Patients receiving guselkumab should be monitored for signs and symptoms of active tuberculosis during and after treatment. |
| **Need for diagnostics or other tests (e.g. companion diagnostics). How are these included in the model?** | No diagnostic tests are required for patients.<br><br>No model has been developed for this this application. |
| **Package size(s)** | Guselkumab (Tremfya®) 100 mg solution for injection in pre-filled pen<br><br>Guselkumab (Tremfya®) 100 mg solution for injection in pre-filled syringe<br><br>Guselkumab (Tremfya®) 200 mg solution for injection in pre-filled pen ¤<br><br>Guselkumab (Tremfya®) 200 mg solution for IV ¤ |

Abbreviations: IV = intravenous; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.
Notes: *Currently, data on the SC induction from the ASTRO study is pending. Therefore, SC induction is not included in this application. ¤ Not available from Medicinpriser.dk until June 2025.
Source: Johnson & Johnson (1); Danish Medicines Agency, 2024 (6).

### 3.2.1 Treatment with guselkumab

Guselkumab is the only dual-acting IL-23 inhibitor (i.e., to Fc-gamma receptor 1 [CD64] and IL-23) and neutralises inflammation locally at the source of IL-23 production (29, 34). Specifically, guselkumab is a human IgG1λ monoclonal antibody that binds selectively to the IL-23 protein with high specificity and affinity through the antigen binding site. IL-23 is a cytokine that is involved in inflammatory and immune responses. By blocking IL-23 from binding to its receptor, guselkumab inhibits IL-23-dependent cell signalling and release of proinflammatory cytokines (1).

In patients with UC, levels of IL-23 are elevated in the colon tissue. In *in vitro* models, guselkumab was shown to inhibit the bioactivity of IL-23 by blocking its interaction with cell surface IL-23 receptor, disrupting IL-23 mediated signalling, activation, and cytokine cascades. Guselkumab exerts clinical effects in plaque psoriasis, and psoriatic arthritis, CD, and UC through blockade of the IL 23 cytokine pathway (1).

Myeloid cells expressing Fc-gamma receptor 1 have been shown to be a predominant source of IL-23 in inflamed tissue in psoriasis and UC. Guselkumab has demonstrated *in vitro* blocking of IL-23 and binding to Fc-gamma receptor 1. These results indicate that guselkumab is able to neutralise IL-23 at the cellular source of inflammation (1, 29).

### 3.2.2 The intervention in relation to Danish clinical practice

The intervention is expected to be placed in the "use" category for BMSL-naïve patients and "use" category for BMSL-experienced patients in v2.3 of the DMC ulcerative colitis treatment guideline (35).

Placebo is considered a relevant comparator, as placebo is the comparator in the key QUASAR trial. Furthermore, using placebo as comparator is in line with the study setup for mirikuzumab (Omvoh), which is an interleukin (IL)-23 already included in the existing treatment guideline (7).

# 4. Overview of literature

Table 4 presents the relevant literature included in this application. In agreement with the DMC and as the treatment guideline includes a network meta-analysis, a systematic literature search has not been conducted for this application. In Table 4, only QUASAR is presented and not ASTRO (36), as ASTRO is still ongoing and full data from an early data cut-off is not available (Week 12 data was presented (37) and Week 24 data was presented in May 6$^{th}$, 2025 (38)). In contrary to QUASAR, guselkumab is administered subcutaneously in the induction phase in ASTRO.

**Table 4 Relevant literature included in the assessment of efficacy and safety**

| Trial name, NCT identifier and reference (Full citation incl. reference number)* | Study design | Study duration | Dates of study (Start and expected completion date, data cut-off and expected data cut-offs) | Patient population (specify if a subpopulation in the relevant study) | Intervention | Comparator | Relevant for PICO nr. in treatment guideline | Outcomes and follow-up period |
|---|---|---|---|---|---|---|---|---|
| QUASAR, NCT04033445<br><br>Peyrin-Biroulet et al. (2023). Guselkumab in Patients With Moderately to Severely Active Ulcerative Colitis: QUASAR Phase 2b Induction Study. (39)<br><br>Rubin et al. (2025). Guselkumab in patients with moderately to severely active ulcerative colitis (QUASAR): phase 3 double- | Randomised, phase 2b/3, double-blinded, placebo-controlled study. QUASAR comprises three separate studies conducted under a single protocol: Induction Study 1 (IS-1) (a phase 2b induction dose ranging study)Ω, IS-2 (a phase 3 induction study), and a phase 3 re-randomised | IS-2: 12 weeks.<br><br>Participants from IS-1 and IS-2 entered the MS at the earliest at Week 12. The MS comprised Week maintenance (M)-0 to M-44. | Start: 26/09/19<br><br>Primary completion: 19/09/23<br><br>Estimated study completion: 27/10/27<br><br>Data cut-off IS-2: 12/01/23<br><br>Data cut-off MS: 19/09/23<br><br>Future data cut-offs: No future data cut-offs for the randomised phase. Future data cut-offs are | Patients with moderate to severely active UC who had demonstrated an inadequate response or failure to tolerate conventional or advanced therapy.<br><br>Both the advanced therapy naïve and advanced therapy failure subpopulations are relevant. | IS-2: guselkumab 200 mg IV at Week number in induction (I-#)-0, I-4, and I-8.<br><br>Standard maintenance dose: guselkumab 100 mg SC q8w (Week M-0 through M-44)<br><br>Alternative maintenance dose: guselkumab 200 mg SC q4w (Week M-0 through M-44) | IS-2: Placebo IV at Weeks I-0, I-4, and I-8.<br><br>MS: Placebo SC q4w (Week M-0 through M-44). | 1 and 2 | Aligning with the DMC's template, primary and secondary outcomes in the study that are also included in the treatment guideline are listed here.<br><br>**IS-2**<br><br>The primary endpoint was clinical remission (Week I-12). Secondary endpoints included were IBDQ remission at Week I-12. Safety data were included as well.<br><br>**MS**<br><br>Secondary endpoints included corticosteroid-free (i.e., not requiring any treatment with corticosteroids for at least 8 weeks prior) clinical remission at Week M-44, endoscopic mucosal healing at Week M-44, and IBDQ remission at Week M-44. Safety data through Week M-44 were also included. |

| Trial name, NCT identifier and reference (Full citation incl. reference number)* | Study design | Study duration | Dates of study (Start and expected completion date, data cut-off and expected data cut-offs) | Patient population (specify if a subpopulation in the relevant study) | Intervention | Comparator | Relevant for PICO nr. in treatment guideline | Outcomes and follow-up period |
|---|---|---|---|---|---|---|---|---|
| blind, randomised, placebo-controlled induction and maintenance studies (40) | maintenance study (MS). | | expected for the long-term extension study (NCT04033445) based on QUASAR. | | | | | |

Abbreviations: I-# = week number in induction; IS-1 = Induction Study 1; IS-2 = Induction Study 2; IBDQ = Inflammatory Bowel Disease Questionnaire; IV = intraveneous; M = Maintenance; MS = maintenance study; N/A = not applicable; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.
Notes: * If there are several publications connected to a trial, include all publications used. Ω IS-1 will not be described any further, as it is a phase 2b induction dose ranging study, and as the efficacy and safety of the approved induction dose is assessed in IS-2.
Source: ClinicalTrials.gov, 2019 (41); Johnson & Johnsons (42) (43) (8).

# 5. Clinical question(s) 1

## 5.1 Efficacy of guselkumab compared to placebo for BMSL-naïve patients with moderate to severe UC

### 5.1.1 Relevant studies

The relevant studies are listed in Table 4. The application includes the pre-defined sub-population of advanced therapy naïve patients. I.e., patients who are naïve to treatment with TNF-α antagonists, integrin antagonist (vedolizumab), or JAK inhibitor (tofacitinib). Since the definition of advanced therapy in QUASAR aligns with the DMC's definition of BMSL, patients who are naïve to advanced therapy will henceforth be referred to as BMSL-naïve patients.

### 5.1.2 Comparability of studies

The Danish treatment guidelines for moderate to severe UC in BMSL-naïve patients are informed by 21 unique studies. The studies include randomised controlled, double-blinded and single-blinded studies, which are primarily phase 2 and 3 studies (44). The QUASAR study, which informs this submission, is a randomised controlled, double-blinded, phase 2b/3 trial, making it comparable to the studies informing the treatment guideline. The latest data cut-off for the QUASAR study was in 2023, and thus it is more recent than the studies informing the treatment guidelines, which are published from 2003-2019 (8, 44).

In QUASAR, clinical remission was measured at Week I-12 (i.e., Week 12). The treatment guideline currently includes data from Week 6-10; however, the expert committee has assessed that data at Week 12 can be used to evaluate this efficacy endpoint. In addition, upon request from the DMC, clinical remission at Week M-44 is included in this application. The DMC defines clinical remission as the proportion of patients achieving a total Mayo score of ≤2, no subscore >1, and a rectal bleeding score of 0 (44, 45), aligning with the definition applied in QUASAR. Both corticosteroid-free clinical remission as well as endoscopic mucosal healing were measured at Week M-44 in QUASAR (i.e., Week 56 or Week 68 when adding the induction period, as participants entered the MS at Week I-12 or I-24 [see Appendix A for further details]). In the treatment guideline, it is stated that data from Week 44 to 60 is relevant for both of these endpoints (44). The DMC defines systemic steroid-free remission as not receiving systemic corticosteroid treatment and have a total Mayo score of ≤2, no subscore >1, and a rectal bleeding score of 0 (44, 45), aligning with the definition applied in QUASAR . According to the DMC treatment guideline, AEs should be assessed quantitatively by number and percentage experiencing at least one serious AE and qualitatively (44, 45). Both a quantitative and qualitative description of AEs is reported in this application for QUASAR. According to the treatment guideline, quality of life should be measured as proportion of patients achieving a score ≥ 170 on the IBDQ and as change from baseline in IBDQ. This should be assessed at the longest follow-up (44, 45). In the treatment guideline, it is also stated that IBDQ is relevant to

assess after induction treatment, i.e., at Week 6-8. However, the expert committee found the available data to be too difficult to compare, and therefore IBDQ has not been assessed in the treatment guideline (44). In this application, both the proportion of patients achieving a score ≥ 170 on the IBDQ as well as change from baseline in IBDQ score at Week M-44 are included.

### 5.1.3 Comparability of patients across studies and with Danish patients eligible for treatment

Table 5 presents the baseline characteristics of BMSL-naïve patients from QUASAR IS-2 (Induction phase) as this best represents the patients who will initiate treatment in Denmark.

The DMC's expert committee estimate that BMSL-naïve patients with moderate to severe UC have an average weight of approximately 75 kg (44), aligning with the participants include in QUASAR with (mean weight of 70.94-73.19) (Table 5).

According to the DMC's treatment guideline for moderate to severe UC, the patient populations in the 21 included studies are generally comparable across the included studies and align with the Danish patient population (44). Since the baseline characteristics of the QUASAR BMSL-naïve patient population closely match those of these 21 studies informing the guideline, it is expected that the QUASAR patient population is also comparable to the Danish patient population.

**Table 5 Baseline characteristics of BMSL-naïve patients in studies included for the comparative analysis of efficacy and safety**

| | QUASAR IS-2 | |
|---|---|---|
| | Placebo IV<br>N = 137 | Guselkumab 200 mg IV<br>N = 202 |
| **Age in years, mean (SD)** | 37.18 (12.49) | 41.32 (13.70) |
| **Sex, n (%)** | | |
| **Females** | 60 (43.8) | 85 (42.1) |
| **Males** | 77 (56.2) | 117 (57.9) |
| **Race, n (%)** | | |
| **Asian** | 30 (21.9) | 46 (22.9) |
| **White** | 107 (78.1) | 152 (75.6) |
| **Black or African American** | 0 (0) | 1 (0.5) |
| **Multiple** | 0 (0) | 0 (0) |

| | QUASAR IS-2 | |
|---|---|---|
| | Placebo IV<br>N = 137 | Guselkumab 200 mg IV<br>N = 202 |
| Not reported | 0 (0) | 2 (1) |
| Height in cm, mean (SD) | 170.32 (9.57) | 170.45 (9.77) |
| Weight in kg, mean (SD) | 70.94 (15.80) | 73.19 (17.15) |
| Extent of disease, n (%) | | |
| Limited to left side of colon | 56 (40.9) | 114 (56.4) |
| Extensive | 81 (59.1) | 88 (43.6) |
| Severity of UC disease, n (%) | | |
| Moderate (6 ≤ Mayo score ≤ 10) | 115 (83.9) | 170 (84.2) |
| Mayo score < 6 | 22 (16.1) | 32 (15.8) |
| Severity of endoscopy subscore, n (%) | | |
| Moderate (endoscopy subscore = 2) | 62 (45.3) | 83 (41.1) |
| Moderate (endoscopy subscore = 3) | 75 (54.7) | 119 (58.9) |
| Extraintestinal manifestations, n (%) | | |
| Present | 11 (8) | 13 (6.4) |
| Absent | 126 (92) | 189 (93.6) |
| Fecal calprotectin, mg/kg | | |
| N | 122 | 177 |
| Mean (SD) | 3 088 (4861.69) | 2 932.64 (4915.27) |
| Abnormal fecal calprotectin (>250 mg/kg) , n (%) | 106 (86.9) | 153 (86.4) |
| <250 mg/kg, n (%) | 16 (13.1) | 24 (13.6) |

| | QUASAR IS-2 | |
|---|---|---|
| | **Placebo IV**<br>**N = 137** | **Guselkumab 200 mg IV**<br>**N = 202** |
| **CRP, mg/L** | | |
| **N** | 136 | 201 |
| **Mean (SD)** | 7.45 (12.44) | 8.07 (12.48) |
| **Abnormal CRP (> 3 mg/L )** | 70 (51.5) | 111 (55.2) |
| **≤ 3 mg/L** | 66 (48.5) | 90 (44.8) |
| **Albumin, g/L** | | |
| **Mean (SD)** | 43.51 (4.34) | 43.35 (4.33) |
| **Abnormal albumin (< 33 g/L)** | 137 (100) | 202 (100) |
| **UC disease duration in years, mean (SD)** | 5.37 (5.36) | 6.41 (7.40) |
| **Mayo score, mean (SD)** | 8.95 (1.41) | 9 (1.41) |
| **Partial Mayo score, mean (SD)** | 6.4 (1.24) | 6.41 (1.25) |
| **Modified Mayo score, mean (SD)** | 6.72 (1.12) | 6.8 (1.17) |

Abbreviations: BMSL = biological and targeted synthetic medicine; CRP = C-reactive protein IV = intravenous; IS-2 = Induction Study 2; SD = standard deviation; UC = ulcerative colitis.

Source: Johnson & Johnson (9)

## 5.2 Comparative analyses of efficacy and safety

### 5.2.1 Efficacy and safety – results per study

In this section, results for the BMSL-naïve subgroup from the randomised full analysis set in QUASAR IS-2 are presented. The randomised full analysis set include participants with a modified Mayo score of 5 to 9 who were randomised and treated in the IS-2. The modified Mayo score is a 3-component (stool frequency, rectal bleeding, and endoscopy subscores) Mayo score without the physician's global assessment. A score 5 to 6 points indicates moderately active disease, a score of 7 to 9 points indicates severely active disease (43). The proportion of BMSL-naïve patients that discontinued the QUASAR IS-2 study and the reason for discontinuation is presented by treatment arm in Table 6.

Results for the BMSL-naïve subgroup from the randomised full analysis set in QUASAR MS are presented as well. The randomised full analysis set include participants with a modified Mayo score of 5 to 9 who were randomised and treated in the MS (8). The proportion of BMSL-naïve patients that discontinued the QUASAR MS study and the reason for discontinuation is presented by treatment arm in Table 7.

**Table 6 Discontinuation in QUASAR IS-2 (BMSL-naïve subgroup)**

| | Placebo IV<br>N = 137 | Guselkumab 200 mg IV<br>N = 202 |
|---|---|---|
| **Subjects who discontinued study treatment prior to Week I-12, n (%)** | 10 (7.3) | 5 (2.5) |
| **Reason for discontinuation, n (%)** | | |
| **Adverse event** | 3 (2.2) | 1 (0.5) |
| **Lack of efficacy** | 0 (0.0) | 1 (0.5) |
| **Pregnancy** | 0 | 1 (0.5) |
| **Withdrawal by subject** | 6 (4.4) | 2 (1.0) |
| **Other** | 1 (0.7) | 0 (0.0) |

Abbreviations: BMSL = biological and targeted synthetic medicine; I-# = week number in induction; IS-2 = induction study 2; IV = intravenous.

Source: Johnson & Johnson (9)

**Table 7 Discontinuation in QUASAR MS (BMSL-naïve subgroup)**

| | Placebo SC<br>N = 109 | Guselkumab 100 mg SC | Guselkumab 200 mg SC |
|---|---|---|---|

| | | N = 104 | N = 96 |
|---|---|---|---|
| **Subjects who discontinued study treatment prior to Week M-44, n (%)** | 11 (10.1) | 9 (8.7) | 9 (9.4) |
| **Reason for discontinuation, n (%)** | | | |
| **Adverse event** | 5 (4.6) | 1 (1.0) | 4 (4.2) |
| **Lack of efficacy** | 2 (1.8) | 1 (1.0) | 0 (0.0) |
| **Lost to follow-up** | 0 (0.0) | 1 (1.0) | 1 (1.0) |
| **Physician decision** | 0 (0.0) | 1 (1.0) | 0 (0.0) |
| **Withdrawal by subject** | 3 (2.8) | 4 (3.8) | 3 (3.1) |
| **Other** | 1 (0.9) | 1 (1.0) | 1 (1.0) |

Abbreviations: BMSL = biological and targeted synthetic medicine; M = maintenance; MS = maintenance study; SC = subcutaneous.

Source: Johnson & Johnson (9)

#### 5.2.1.1 Clinical remission at Week I-12

Table 8 presents clinical remission at Week I-12, defined as meeting the criteria for clinical remission at Week I-12. Clinical remission is defined as a Mayo stool frequency subscore of 0 or 1 and not increased from induction baseline, a Mayo rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1 with no friability present on the endoscopy (43). A statistically significantly higher proportion of patients in the guselkumab group was in clinical remission at Week I-12 compared with the placebo group (31.7% vs. 11.7%, p < 0.001).

**Table 8 Clinical remission at Week I-12 (BMSL-naïve subgroup)**

| Clinical remission at Week I-12 | Placebo IV<br>N = 137 | Guselkumab 200 mg IV<br>N = 202 |
|---|---|---|
| n (%) (95% confidence interval [CI]) [a, b, c] | 16 (11.7) (6.3, 17.1) | 64 (31.7) (25.3, 38.1) |
| Adjusted treatment difference (95% CI), p-value [d, e] | Reference | 20.0% (11.6, 28.3), < 0.001 |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; CI = confidence interval; COVID-19 = Coronavirus disease-19; I-# = week number in induction; ICE = intercurrent event; IV = intravenous; UC = ulcerative colitis.

Notes: a ICE strategies: Subjects who had an ostomy or colectomy (ICE 1), a prohibited change in UC medications (ICE 2), or discontinued study agent due to lack of efficacy or an AE of worsening of UC (ICE 3) prior to the designated timepoint were considered not to have achieved any of the key efficacy endpoints shown at the designated timepoint. For subjects who discontinued study agent due to Coronavirus disease-19 (COVID-19) related reasons

(excluding COVID-19 infection) or regional crisis in Russia and Ukraine (ICE 4) prior to the designated timepoint, their observed values were used, if available. Subjects who experienced ICE 5 (discontinued study agent due to reasons other than those in ICEs 3 and 4) prior to the designated timepoint were considered not to have achieved any of the key efficacy endpoints shown at the designated timepoint. b Nonresponder imputation for missing data: After accounting for ICEs, subjects who were missing one or more of the components pertaining to an endpoint at the designated timepoint were considered not to have achieved the endpoint. c The CIs for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. d The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. e The p-values were based on the Cochran-Mantel-Haenszel chi-square test, stratified by concomitant use of corticosteroids at baseline (Yes/No).

Source: Janssen Research & Development, 2024, attachment TEFKEY501B (43).

#### 5.2.1.2 Clinical remission at week M-44

Table 9 presents clinical remission at Week M-44. Statistically significantly higher proportions of participants in the guselkumab 100 mg (50.9%) and 200 mg (57.7%) groups were in clinical remission at Week M-44 compared with the placebo group (25.9%; p<0.001 highly significant for both) (Table 9). 50.5% of patients in the guselkumab 100 mg group and 58.3% of patients in the guselkumab 200 mg group achieved clinical remission at week M-44. As the CIs overlap, the efficacy of guselkumab 100 mg q8w and guselkumab 200 mg q4w is considered equivalent.

**Table 9 Clinical remission at Week M-44 (BMSL-naïve subgroup)**

| Clinical remission at Week M-44 | Placebo SC<br>N = 108 | Guselkumab 100 mg SC q8w<br>N = 105 | Guselkumab 200 mg SC q4w<br>N = 96 |
|---|---|---|---|
| n (%) (95% CI) [a, b, c] | 28 (25.9) (17.7, 34.2) | 53 (50.5) (40.9, 60.0) | 56 (58.3) (48.5, 68.2) |
| Adjusted treatment difference (95% CI), p-value [d, e] | Reference | 24.3 (12.0, 36.5), < 0.001 | 28.8 (16.5, 41.1), < 0.001 |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; CI = confidence interval; COVID-19 = coronavirus disease-19; ICE = intercurrent event; IV = intravenous; M = maintenance; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.

Notes: a Intercurrent event (ICE) strategies: Subjects who had an ostomy or colectomy (ICE 1), a dose adjustment (including a sham dose adjustment) (ICE 2), a prohibited change in UC medications (ICE 3), or discontinued study agent due to lack of efficacy or an AE of worsening of UC (ICE 4) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44. For subjects who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine (ICE 5) prior to Week M-44, their observed values (if available) were used. Subjects who experienced ICE 6 (discontinued study agent due to reasons other than those in ICEs 4 and 5) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44.b Nonresponder imputation for missing data: Subjects who were missing one or more of the components pertaining to this endpoint at Week M-44 were considered not to have achieved this endpoint. c The CIs for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. d The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. e The p-values were based on the Cochran-Mantel-Haenszel test, stratified by clinical remission status at maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, placebo IV crossover to guselkumab 200 mg IV).

Source: Janssen Research & Development, 2024, attachment TEFKEY610A (8).

### 5.2.1.3 Corticosteroid-free clinical remission at week M-44

Table 10 presents corticosteroid-free clinical remission at Week M-44 defined as not requiring any treatment with corticosteroids for at least 8 weeks prior to Week M-44 and also meeting the criteria for clinical remission at Week M-44. Statistically significantly higher proportions of participants in the guselkumab 100 mg (50.9%) and 200 mg (55.7%) groups were in corticosteroid-free clinical remission at Week M-44 compared with the placebo group (25.9%; p<0.001 highly significant for both). 50.5% of patients in the guselkumab 100 mg group and 56.3% of patients in the guselkumab 200 mg group achieved corticosteroid-free clinical remission at week M-44. As the CIs overlap, the efficacy of guselkumab 100 mg q8w and guselkumab 200 mg q4w is considered equivalent (Table 10).

**Table 10 Corticosteroid-free clinical remission at week M-44 (BMSL-naïve subgroup)**

| Corticosteroid-free clinical remission at week M-44 | Placebo SC<br>N = 108 | Guselkumab 100 mg SC q8w<br>N = 105 | Guselkumab 200 mg SC q4w<br>N = 96 |
|---|---|---|---|
| n (%) (95% CI) [a, b, c] | 28 (25.9) (17.7, 34.2) | 53 (50.5) (40.9, 60.0) | 54 (56.3) (46.3, 66.2) |
| Adjusted treatment difference (95% CI), p-value [d, e] | Reference | 24.3 (12.0, 36.5), < 0.001 | 26.5 (14.2, 38.9), < 0.001 |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; CI = confidence interval; COVID-19 = coronavirus disease-19; ICE = intercurrent event; IV = intravenous; M = maintenance; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.

Notes: a Intercurrent event (ICE) strategies: Subjects who had an ostomy or colectomy (ICE 1), a dose adjustment (including a sham dose adjustment) (ICE 2), a prohibited change in UC medications (ICE 3), or discontinued study agent due to lack of efficacy or an AE of worsening of UC (ICE 4) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44. For subjects who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine (ICE 5) prior to Week M-44, their observed values (if available) were used. Subjects who experienced ICE 6 (discontinued study agent due to reasons other than those in ICEs 4 and 5) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44.b Nonresponder imputation for missing data: Subjects who were missing one or more of the components pertaining to this endpoint at Week M-44 were considered not to have achieved this endpoint. c The CIs for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. d The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. e The p-values were based on the Cochran-Mantel-Haenszel test, stratified by clinical remission status at maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, placebo IV crossover to guselkumab 200 mg IV).

Source: Janssen Research & Development, 2024, attachment TEFKEY610A (8).

### 5.2.1.4 Endoscopic mucosal healing at week M-44

Table 11 presents endoscopic mucosal healing (improvement) at Week M-44 is defined as an endoscopy subscore of 0 or 1 with no friability present on the endoscopy (8). A higher proportion of participants in the guselkumab 100 mg (53.3%) and 200 mg (59.4%) groups achieved endoscopic mucosal healing at Week M-44 compared with the placebo group (25.9%). As the CIs overlap, the efficacy of guselkumab 100 mg q8w and guselkumab 200 mg q4w is considered equivalent (Table 11).

**Table 11 Endoscopic mucosal healing at week M-44 (BMSL-naïve subgroup)**

| Endoscopic mucosal healing at week M-44 | Placebo SC<br>N = 108 | Guselkumab 100 mg SC q8w<br>N = 105 | Guselkumab 200 mg SC q4w<br>N = 96 |
|---|---|---|---|
| n (%) (95% CI) [a, b, c] | 28 (25.9) (17.7, 34.2) | 56 (53.3) (43.8, 62.9) | 57 (59.4) (49.6, 69.2) |
| Adjusted treatment difference (95% CI), p-value [d, e] | Reference | 27.2 (15.0, 39.5), < 0.001 | 30.0 (17.6, 42.4), < 0.001 |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; CI = confidence interval; COVID-19 = coronavirus disease-19; ICE = intercurrent event; IV = intravenous; M = maintenance; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.

Notes: a ICE strategies: Subjects who had an ostomy or colectomy (ICE 1), a dose adjustment (including a sham dose adjustment) (ICE 2), a prohibited change in UC medications (ICE 3), or discontinued study agent due to lack of efficacy or an AE of worsening of UC (ICE 4) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44. For subjects who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine (ICE 5) prior to Week M-44, their observed values (if available) were used. Subjects who experienced ICE 6 (discontinued study agent due to reasons other than those in ICEs 4 and 5) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44. b Nonresponder imputation for missing data: Subjects who were missing one or more of the components pertaining to this endpoint at Week M-44 were considered not to have achieved this endpoint. Subjects who had an unevaluable biopsy (i.e., a biopsy that was collected, but could not be assessed due to sample preparation or technical errors) were considered not to have achieved the histology endpoint. c The CIs for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. d The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. e The p-values were based on the Cochran-Mantel-Haenszel test, stratified by clinical remission status at maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, placebo IV crossover to guselkumab 200 mg IV).

Source: Janssen Research & Development, 2024, attachment TEFKEY610A (8).

#### 5.2.1.5 IBDQ remission at week I-12

Table 12 presents IBDQ remission at Week I-12 defined as a total IBDQ score ≥ 170 at Week I-12. A statistically significantly higher proportion of patients in the guselkumab group was in IBDQ remission at Week I-12 compared with the placebo group (62.4% vs. 34.3%, p < 0.001).

**Table 12 IBDQ remission at week I-12 (BMSL-naïve subgroup)**

| IBDQ remission at week I-12 | Placebo IV<br>N = 137 | Guselkumab 200 mg IV<br>N = 202 |
|---|---|---|
| n (%)[a, b] | 47 (34.3) | 126 (62.4) |
| Adjusted treatment difference (95% CI), p-value [d, e] | Reference | 28.1 (17.7, 38.5), < 0.001 |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; CI = confidence interval; COVID-19 = Coronavirus disease-19; I-# = week number in induction; ICE = intercurrent event; IV = intravenous; UC = ulcerative colitis.

Notes: a ICE strategies: Subjects who had an ostomy or colectomy (ICE 1), a dose adjustment (including a sham dose adjustment) (ICE 2), a prohibited change in UC medications (ICE 3), or discontinued study agent due to lack

of efficacy or an AE of worsening of UC (ICE 4) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44. For subjects who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine (ICE 5) prior to Week M-44, their observed values (if available) were used. Subjects who experienced ICE 6 (discontinued study agent due to reasons other than those in ICEs 4 and 5) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44. b Nonresponder imputation for missing data: After accounting for ICEs, subjects who were missing one or more of the components pertaining to an endpoint at the designated timepoint were considered not to have achieved the endpoint. d The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. e The p-values were based on the Cochran-Mantel-Haenszel chi-square test, stratified by concomitant use of corticosteroids at baseline (Yes/No).

Source: Johnson & Johnson (9)

#### 5.2.1.6 IBDQ remission at week M-44

Table 13 presents IBDQ remission at week M-44 defined as a total IBDQ score ≥ 170 at week M-44. A statistically significantly higher proportions of participants in the guselkumab 100 mg (67.9%) and 200 mg (74.2%) groups were in IBDQ remission at Week M-44 compared with the placebo group (49.1%; p=0.005 and p<0.001 for the guselkumab 100 mg and 200 mg group, respectively). 67.6% of patients in the guselkumab 100 mg group and 74.0% of patients in the guselkumab 200 mg group achieved IBDQ remission at week M-44. As the CIs overlap, the efficacy of guselkumab 100 mg q8w and guselkumab 200 mg q4w is considered equivalent (Table 13).

**Table 13 IBDQ remission at week M-44 (BMSL-naïve subgroup)**

| IBDQ remission at week M-44 | Placebo SC<br>N = 108 | Guselkumab 100 mg SC q8w<br>N = 105 | Guselkumab 200 mg SC q4w<br>N = 96 |
|---|---|---|---|
| n (%) (95% CI) [a, b, c] | 53 (49.1) (39.6, 58.5) | 71 (67.6) (58.7, 76.6) | 71 (74.0) (65.2, 82.7) |
| Adjusted treatment difference (95% CI), p-value [d, e] | Reference | 18.9 (6.1, 31.7), 0.006 | 23.9 (11.3, 36.5), < 0.001 |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; CI = confidence interval; COVID-19 = coronavirus disease-19; ICE = intercurrent event; IBDQ = Inflammatory Bowel Disease Questionnaire; IV = intravenous; M = maintenance; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.

Notes: a ICE strategies: Subjects who had an ostomy or colectomy (ICE 1), a dose adjustment (including a sham dose adjustment) (ICE 2), a prohibited change in UC medications (ICE 3), or discontinued study agent due to lack of efficacy or an AE of worsening of UC (ICE 4) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44. For subjects who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine (ICE 5) prior to Week M-44, their observed values (if available) were used. Subjects who experienced ICE 6 (discontinued study agent due to reasons other than those in ICEs 4 and 5) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44.b Nonresponder imputation for missing data: Subjects who were missing one or more of the components pertaining to this endpoint at Week M-44 were considered not to have achieved this endpoint. c The CIs for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. d The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. e The p-values were based on the Cochran-Mantel-Haenszel test, stratified by clinical remission status at maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, placebo IV crossover to guselkumab 200 mg IV).

Source: Janssen Research & Development, 2024, attachment TEFKEY610A (8).

#### 5.2.1.7 CFB in IBDQ total score through week M-44

Table 14 presents change from baseline in IBDQ total score through week M-44. Participants in the guselkumab 100 mg (LS mean CFB = -2.199) and 200 mg (LS mean CFB = -0.863) dose had a statistically significant change from baseline compared at Week M-44 compared with the placebo group (difference in LS mean = 19.944 and 20.714 respectively, p<0.0001).

**Table 14 Change from baseline in IBDQ total score through week M-44 (BMSL-naïve subgroup)**

| Study | Treatment arm | N [a] | LS Mean CFB (SE) [b] | Difference in LS mean CFB | 95% CI | p-value |
|---|---|---|---|---|---|---|
| **QUASAR MS** | Guselkumab 100 mg SC q8w | 103 | -2.199 (3.36) | 19.944 | 10.61, 29.28 | <0.0001 |
| | Guselkumab 200 mg SC q4w | 93 | -0.863 (3.66) | 20.714 | 10.79, 30.64 | <0.0001 |
| | Placebo SC | 105 | Vs. GUS 100: -22.14 (3.34) | Reference | | |
| | | | Vs. GUS 200: -21.58 (3.46) | Reference | | |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; CI = confidence interval; COVID-19 = coronavirus disease-19; ICE = intercurrent event; IBDQ = Inflammatory Bowel Disease Questionnaire; IV = intravenous; M = maintenance; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.

Note: [a] N is number of subjects with IBDQ measurements at baseline and at Week 44. [b] Least squares means are derived based on a pairwise comparison Mixed-effects Model for Repeated Measures (MMRM) with N number of subjects with IBDQ measurements at baseline and at Week 44. Analyses were performed without stratification to avoid numerical issues.

Source: Johnson & Johnson (9)

### 5.2.2 Please provide a qualitative description of safety data. Differences in definitions of outcomes between studies

During the IS-2, 9 (6.6%) of 137 patients in the placebo IV q4w arm and 3 (1.5%) of 202 patients in the guselkumab 200 mg IV q4w experienced at least one serious AE. An overview of all SAEs experienced by any patient during the IS-2 is presented in Table 15.

**Table 15 Serious adverse events (IS-2 BMSL-naïve subgroup)**

| | Placebo IV q4w N = 137 | Guselkumab 200 mg IV q4w N = 202 |
|---|---|---|

| | | |
|---|---|---|
| **Subjects with one or more SAEs, n (%)** | 9 (6.6) | 3 (1.5) |
| **Gastrointestinal disorders** | 8 (5.8) | 3 (1.5) |
| **Worsening of UC** | 7 (5.1) | 2 (1.0) |

Abbreviations: BMSL = biological and targeted synthetic medicine; IS-2 = induction study 2; IV = intravenous; qw4 = every 4 weeks; SAE = serious adverse event; UC = ulcerative colitis.

Source: Johnson & Johnson (9)

54 (39.4%) patients in the placebo IV q4w arm and 92 (45.5%) in the guselkumab 200 mg IV arm experienced any AE. An overview of all AEs experienced by at least 5% of the BMSL-naïve IS-2 patient population is presented in Table 16.

**Table 16 Adverse events occurring in ≥5% in any treatment arm (BMSL-naïve subgroup)**

| | Placebo IV q4w N = 137 | Guselkumab 200 mg IV q4w N = 202 |
|---|---|---|
| **Subjects with one or more AEs, n (%)** | 54 (39.4) | 92 (45.5) |
| **Blood and lymphatic system disorders** | 13 (9.5) | 18 (8.9) |
| **Anaemia** | 8 (5.8) | 12 (5.9) |
| **Gastrointestinal disorders** | 18 (13.1) | 19 (9.4) |
| **Colitis ulcerative** | 9 (6.6) | 2 (1.0) |
| **Infections and infestations** | 18 (13.1) | 28 (13.9) |
| **COVID-19** | 7 (5.1) | 6 (3.0) |

Abbreviations: BMSL = biological and targeted synthetic medicine; COVID-19 = coronavirus disease-19; AE = adverse event; IV = intravenous; q4w = every 4 weeks.

Source: Johnson & Johnson (9)

In the following, Week M-44 safety data are presented for the BMSL-naïve patients from the randomised safety analysis set. One of 109 (0.9%) participants in the placebo group, 3 of 104 (2.9%) in the guselkumab 100 mg SC q8w group, and 5 of 96 (5.2%) participants in the guselkumab 200 mg q4w group experienced at least one serious AE. No deaths occurred in any of the treatment arms. 64.2% experienced an AE in the placebo group, 59.6% in the guselkumab 100 mg SC q8w, and 64.6% in the guselkumab group 200 mg q4w. An overview of all SAEs experienced by any patient as well as all AEs experienced by at least 5% of the patient population during the MS is provided in Table 17 and Table 18, respectively.

**Table 17 Serious adverse events (MS BMSL-naïve subgroup)**

| | Placebo SC q4w<br>N = 109 | Guselkumab 100 mg SC q8w<br>N = 104 | Guselkumab 200 mg SC q4w<br>N = 96 |
|---|---|---|---|
| **Subjects with one or more SAEs, n (%)** | 1 (0.9) | 3 (2.9) | 5 (5.2) |
| **Eye disorders** | (0.0) | (0.0) | 1 (1.0) |
| **Cataract** | (0.0) | (0.0) | 1 (1.0) |
| **Gastrointestinal disorders** | 1 (0.9) | 1 (1.0) | 1 (1.0) |
| **Abdominal pain** | (0.0) | (0.0) | 1 (1.0) |
| **Infections and infestations** | (0.0) | (0.0) | 1 (1.0) |
| **Complicated appendicitis** | (0.0) | (0.0) | 1 (1.0) |
| **Neoplasms benign, malignant and unspecified (including cysts and polyps)** | (0.0) | (0.0) | 1 (1.0) |
| **Adenocarcinoma** | (0.0) | (0.0) | 1 (1.0) |
| **Psychiatric disorders** | (0.0) | 1 (1.0) | 1 (1.0) |
| **Anxiety** | (0.0) | (0.0) | 1 (1.0) |
| **Reproductive system and breast disorders** | (0.0) | (0.0) | 1 (1.0) |
| **Gynaecomastia** | (0.0) | (0.0) | 1 (1.0) |

Abbreviations: BMSL = biological and targeted synthetic medicine; MS = maintenance study; q4w = every 4 weeks; q8w = every 8 weeks; SAE = serious adverse event; SC = subcutaneous.

Source: Johnson & Johnson (9)

**Table 18 Adverse events occurring in ≥5% in any treatment arm (MS BMSL-naïve subgroup)**

| | Placebo SC q4w<br>N = 78 | Guselkumab 100 mg SC q8w<br>N = 75 | Guselkumab 200 mg SC q4w<br>N = 87 |
|---|---|---|---|

| | | | |
|---|---|---|---|
| **Subjects with one or more AEs, n (%)** | 70 (64.2) | 62 (59.6) | 62 (64.6) |
| **Gastrointestinal disorders** | 34 (31.2) | 16 (15.4) | 27 (28.1) |
| **Worsening of UC** | 26 (23.9) | 3 (2.9) | 10 (10.4) |
| **General disorders and administration site conditions** | 6 (5.5) | 6 (5.8) | 13 (13.5) |
| **Pyrexia** | 2 (1.8) | 3 (2.9) | 6 (6.3) |
| **Infections and infestations** | 36 (33.0) | 30 (28.8) | 26 (27.1) |
| **COVID-19** | 12 (11.0) | 14 (13.5) | 9 (9.4) |
| **Nasopharyngitis** | 5 (4.6) | 6 (5.8) | 4 (4.2) |
| **Upper respiratory tract infection** | 5 (4.6) | 3 (2.9) | 6 (6.3) |
| **Musculoskeletal and connective tissue disorders** | 9 (8.3) | 8 (7.7) | 14 (14.6) |
| **Arthralgia** | 4 (3.7) | 4 (3.8) | 6 (6.3) |
| **Nervous system disorders** | 10 (9.2) | 9 (8.7) | 6 (6.3) |
| **Headache** | 7 (6.4) | 4 (3.8) | 4 (4.2) |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; COVID-19 = coronavirus disease-19; MS = maintenance study; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.

Source: Johnson & Johnson (9)

### 5.2.3 Method of synthesis

N/A

### 5.2.4 Results from the comparative analysis

N/A

**Table 19 Results from the comparative analysis of [intervention] vs. [comparator] for [patient population]**

| Outcome measure | [Intervention] (N=x) | [Comparator] (N=x) | Result |
|---|---|---|---|
| N/A | N/A | N/A | N/A |

# 6. Clinical question(s) 2

## 6.1 Efficacy of guselkumab compared to placebo for BMSL-experienced patients with moderate to severe UC

### 6.1.1 Relevant studies

The relevant studies are listed in Table 4. The application includes the pre-defined sub-population of advanced therapy failure patients. I.e., patients who have failed to treatment with TNF-α antagonists, integrin antagonist (vedolizumab), or JAK inhibitor (tofacitinib). Since the definition of advanced therapy in QUASAR aligns with the DMC's definition of BMSL, patients who have failed advanced therapy will henceforth be referred to as BMSL -experienced patients.

### 6.1.2 Comparability of studies

The Danish treatment guideline for moderate to severe UC in BMSL experienced patients are informed by 12 unique studies. The studies include randomised controlled, double-blinded and single-blinded studies, which are primarily phase 2 and 3 studies (44). The QUASAR study, which informs this submission, is a randomised controlled, double-blinded, phase 2b/3 trial, making it comparable to the studies which inform the guideline. The latest data cut-off for the QUASAR study was in 2023.

In the DMC's treatment guideline, clinical question 2 concerns BMSL-experienced patients, i.e., it is not specified whether the patients should have failed a BMSL treatment. In this application, BMSL-experienced subgroups from QUSAR MS (n=240) and QUASAR IS-2 (n=344) are included. Data from BMSL-experienced without documented failure subgroups are also available in QUASAR MS (n=19) and QUASAR IS-2 (n=18) but not included in this application because of the small sizes in these subgroups.

In QUASAR, clinical remission was measured at Week I-12 (i.e., Week 12). The treatment guideline currently includes data from Week 6-10; however, the expert committee has assessed that data at Week 12 can be used to evaluate this efficacy endpoint. In addition, upon request from the DMC, clinical remission at Week M-44 is included in this application The DMC defines clinical remission as the proportion of patients achieving a total Mayo score of ≤2, no subscore >1, and a rectal bleeding score of 0 (44, 45), aligning with the definition applied in QUASAR. Both corticosteroid-free clinical remission as well as endoscopic mucosal healing were measured at Week M-44 in QUASAR (i.e., Week 56 or Week 68 when adding the induction period, as participants entered the MS at Week I-12 or I-24 [see Appendix A for further details]). In the treatment guideline, it is stated that data from

Week 44 to 60 is relevant for both of these endpoints (44). The DMC defines systemic steroid-free remission as not receiving systemic corticosteroid treatment and have a total Mayo score of ≤2, no subscore >1, and a rectal bleeding score of 0 (44, 45), aligning with the definition applied in QUASAR. According to the DMC treatment guideline, AEs should be assessed quantitatively by number and percentage experiencing at least one serious AE and qualitatively (44, 45). Both a quantitative and qualitative description of AEs is reported in this application for QUASAR. According to the treatment guideline, quality of life should be measured as proportion of patients achieving a score ≥ 170 on the IBDQ and as change from baseline in IBDQ. This should be assessed at the longest follow-up (44, 45). In the treatment guideline it is also stated that IBDQ is relevant to assess after induction treatment, i.e., at Week 6-8. However, the expert committee found the available data to be too difficult to compare, and therefore IBDQ has not been assessed in the treatment guideline (44). In this application, both the proportion of patients achieving a score ≥ 170 on the IBDQ as well as change from baseline in IBDQ score at Week M-44 are included.

### 6.1.3 Comparability of patients across studies and with Danish patients eligible for treatment

Table 20 presents the baseline characteristics of BMSL-naïve patients in QUASAR IS-2 (Induction phase) as this best represents the patients who will initiate treatment in Denmark.

The DMC's expert committee estimate that BMSL-experienced patients with moderate to severe UC have an average weight of approximately 75 kg (44), aligning with the participants include in QUASAR with (mean weight of 72.57 -72.62) (Table 20).

According to the DMC's treatment guideline for moderate to severe UC in BMSL-experienced patients, the patient populations in the 12 included studies are generally comparable across the included studies and align with the Danish patient population (44). Since the baseline characteristics of the QUASAR BMSL-experienced patient population closely match those of these 12 studies informing the guidelines, it is expected that the QUASAR patient population is also comparable to the Danish patient population.

**Table 20 Baseline characteristics of BMSL-experienced patients in studies included for the comparative analysis of efficacy and safety**

| | QUASAR IS-2 | |
|---|---|---|
| | **Placebo IV**<br>**N = 136** | **Guselkumab 200 mg IV**<br>**N = 208** |
| **Age in years, mean (SD)** | 42.64 (13.86) | 40.88 (14.23) |
| **Sex, n (%)** | | |
| **Females** | 150 (43.6) | 93 (44.7) |
| **Males** | 194 (56.4) | 115 (55.3) |

| | QUASAR IS-2 | |
|---|---|---|
| | Placebo IV<br>N = 136 | Guselkumab 200 mg IV<br>N = 208 |
| **Race, n (%)** | | |
| **Asian** | 31 (22.8) | 42 (20.3) |
| **White** | 92 (67.6) | 142 (68.6) |
| **Black or African American** | 3 (2.2) | 3 (1.4) |
| **Multiple** | 0 (0.0) | 1 (0.5) |
| **Not reported** | 10 (7.4) | 19 (9.2) |
| **Height in cm, mean (SD)** | 169.22 (9.80) | 170.03 (9.79) |
| **Weight in kg, mean (SD)** | 72.57 (18.31) | 72.62 (16.52) |
| **Extent of disease, n (%)** | | |
| **Limited to left side of colon** | 72 (52.9) | 112 (53.8) |
| **Extensive** | 64 (47.1) | 96 (46.2) |
| **Severity of UC disease, n (%)** | | |
| **Moderate (6 ≤ Mayo score ≤ 10)** | 109 (80.1) | 166 (79.8) |
| **Mayo score < 6** | 27 (19.9) | 42 (20.2) |
| **Severity of endoscopy sub-score, n (%)** | | |
| **Moderate (endoscopy sub-score = 2)** | 35 (25.7) | 39 (18.8) |
| **Moderate (endoscopy sub-score = 3)** | 101 (74.3) | 169 (81.3) |
| **Extraintestinal manifesta-tions, n (%)** | | |

| | QUASAR IS-2 | |
|---|---|---|
| | Placebo IV<br>N = 136 | Guselkumab 200 mg IV<br>N = 208 |
| **Present** | 19 (14) | 44 (21.2) |
| **Absent** | 117 (86) | 164 (78.8) |
| **Fecal calprotectin, mg/kg** | | |
| **N** | 126 | 184 |
| **Mean (SD)** | 2369.67 (3043.88) | 3953.1 (5477.58) |
| **Abnormal fecal calprotectin (>250 mg/kg), n (%)** | 114 (90.5) | 172 (93.5) |
| **<250 mg/kg, n (%)** | 12 (9.5) | 12 (6.5) |
| **CRP, mg/L** | | |
| **N** | 135 | 205 |
| **Mean (SD)** | 9.22 (10.95) | 9.89 (12.32) |
| **Abnormal CRP (>3 mg/L)** | 87 (64.4) | 131 (63.9) |
| **≤ 3 mg/L** | 48 (35.6) | 74 (36.1) |
| **Albumin, g/L** | | |
| **Mean (SD)** | 42.48 (3.77) | 42.5 (3.72) |
| **Abnormal albumin (< 33 g/L)** | 136 (100) | 208 (100) |
| **UC disease duration in years, mean (SD)** | 8.68 (7.23) | 9.07 (7.96) |
| **Mayo score, mean (SD)** | 9.34 (1.24) | 9.3 (1.30) |
| **Partial Mayo score, mean (SD)** | 6.6 (1.16) | 6.49 (1.19) |

| | QUASAR IS-2 | |
|---|---|---|
| | **Placebo IV**<br>**N = 136** | **Guselkumab 200 mg IV**<br>**N = 208** |
| **Modified Mayo score, mean (SD)** | 7.03 (1.01) | 7 (1.08) |

Abbreviations: BMSL = biological and targeted synthetic medicine; IV = intravenous; SD = standard deviation; UC = ulcerative colitis.

Source: Johnson & Johnson (9)

## 6.2 Comparative analyses of efficacy and safety

### 6.2.1 Efficacy and safety – results per study

In this section, results for the BMSL-experienced subgroup from the randomised full analysis set in QUASAR IS-2 are presented. The randomised full analysis set include participants with a modified Mayo score of 5 to 9 who were randomised and treated in the IS-2 (43). The proportion of BMSL-experienced patients that discontinued the QUASAR IS-2 study and the reason for discontinuation is presented by treatment arm in Table 21.

In this section, results for the BMSL experienced subgroup from the randomised full analysis set in QUASAR MS are included. The randomised full analysis set include participants with a modified Mayo score of 5 to 9 who were randomised and treated in the MS (8). The proportion of BMSL-experienced patients that discontinued the QUASAR MS study and the reason for discontinuation is presented by treatment arm in Table 22.

**Table 21 Discontinuation in QUASAR IS-2 (BMSL-experienced subgroup)**

| | Placebo IV<br>N = 136 | Guselkumab 200 mg IV<br>N = 208 |
|---|---|---|
| **Subjects who discontinued study treatment prior to Week I-12, n (%)** | 13 (9.6) | 13 (6.3) |
| **Reason for discontinuation, n (%)** | | |
| **Adverse event** | 5 (3.7) | 6 (2.9) |
| **Lack of efficacy** | 0 (0.0) | 1 (0.5) |
| **Death** | 1 (0.7) | 1 (0.5) |
| **Physician decision** | 2 (1.5) | 1 (0.5) |
| **Withdrawal by subject** | 5 (3.7) | 4 (1.9) |

Abbreviations: BMSL = biological and targeted synthetic medicine; IV = intravenous; I-# = week number in induction; IS-2 = induction study 2.

Source: Johnson & Johnson (9)

**Table 22 Discontinuation in QUASAR MS (BMSL-experienced subgroup)**

| | Placebo SC<br>N = 78 | Guselkumab 100 mg SC<br>N = 75 | Guselkumab 200 mg SC<br>N = 87 |
|---|---|---|---|
| **Subjects who discontinued study treatment prior to Week M-44, n (%)** | 17 (21.8) | 10 (13.3) | 12 (13.8) |

| | | | |
|---|---|---|---|
| **Reason for discontinuation, n (%)** | | | |
| **Adverse event** | 7 (9.0) | 6 (8.0) | 5 (5.7) |
| **Lack of efficacy** | 4 (5.1) | 1 (1.3) | 1 (1.1) |
| **Physician decision** | 1 (1.3) | 2 (2.7) | 1 (1.1) |
| **Withdrawal by subject** | 5 (6.4) | 1 (1.3) | 4 (4.6) |
| **Other** | 0 (0.0) | 0 (0.0) | 1 (1.1) |

Abbreviations: BMSL = biological and targeted synthetic medicine; M = maintenance; MS = maintenance study; SC = subcutaneous.

Source: Johnson & Johnson (9)

#### 6.2.1.1 Clinical remission at Week I-12

Table 23 presents clinical remission at Week I-12. A statistically significantly higher proportion of patients in the guselkumab group was in clinical remission at Week I-12 compared with the placebo group (11.8% vs. 3.7%, p = 0.009).

**Table 23 Clinical remission at Week I-12 (BMSL-experienced subgroup)**

| Clinical remission at Week I-12 | Placebo IV<br>N = 136 | Guselkumab 200 mg IV<br>N = 208 |
|---|---|---|
| n (%) (95% CI) [a, b, c] | 5 (3.7) (0.5, 6.8) | 26 (12.5) (8.0, 17.0) |
| Adjusted treatment difference (95% CI), p-value [d, e] | Reference | 8.8% (3.4, 14.3), 0.005 |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; CI = confidence interval; COVID-19 = Coronavirus disease-19; I-# = week number in induction; ICE = intercurrent event; IV = intravenous; UC = ulcerative colitis.
Notes: [a] ICE Strategies: Subjects who had an ostomy or colectomy (ICE 1), a prohibited change in UC medications (ICE 2), or discontinued study agent due to lack of efficacy or an AE of worsening of UC (ICE 3) prior to the designated timepoint were considered not to have achieved any of the key efficacy endpoints shown at the designated timepoint. For subjects who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine (ICE 4) prior to the designated timepoint, their observed values were used, if available. Subjects who experienced ICE 5 (discontinued study agent due to reasons other than those in ICEs 3 and 4) prior to the designated timepoint were considered not to have achieved any of the key efficacy endpoints shown at the designated timepoint. [b] Nonresponder imputation for missing data: After accounting for ICEs, subjects who were missing one or more of the components pertaining to an endpoint at the designated timepoint were considered not to have achieved the endpoint. [c] The CI for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. [d] The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. [e] The p-values were based on the Cochran-Mantel-Haenszel chi-square test, stratified by concomitant use of corticosteroids at baseline (Yes/No).
Source: Janssen Research & Development, 2024, attachment TEFKEY501D (43).

### 6.2.1.2 Clinical remission at week M-44

Table 24 presents clinical remission at Week M-44. Statistically significantly higher proportions of participants in the guselkumab 100 mg (39.5%) and 200 mg (39.5%) groups were in clinical remission at Week M-44 compared with the placebo group (8.1%; p<0.001 highly significant for both). 40.3% of patients in the guselkumab 100 mg group and 39.8% of patients in the guselkumab 200 mg group achieved clinical remission at week M-44. As the CIs overlap, the efficacy of guselkumab 100 mg q8w and guselkumab 200 mg q4w is considered equivalent (Table 24).

**Table 24 Clinical remission at Week M-44 (BMSL-experienced subgroup)**

| Clinical remission at Week M-44 | Placebo SC<br>N = 75 | Guselkumab 100 mg SC q8w<br>N = 77 | Guselkumab 200 mg SC q4w<br>N = 88 |
|---|---|---|---|
| n (%) (95% CI) [a, b, c] | 6 (8.0) (1.9, 14.1) | 31 (40.3) (29.3, 51.2) | 35 (39.8) (29.5, 50.0%) |
| Adjusted treatment difference (95% CI), p-value [d, e] | Reference | 30.4 (18.7, 42.1), < 0.001 | 32.4 (21.1, 43.7), < 0.001 |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; CI = confidence interval; COVID-19 = coronavirus disease-19; ICE = intercurrent event; IV = intravenous; M = maintenance; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.
Notes: [a] ICE Strategies: Subjects who had an ostomy or colectomy (ICE 1), a dose adjustment (including a sham dose adjustment) (ICE 2), a prohibited change in UC medications (ICE 3), or discontinued study agent due to lack of efficacy or an AE of worsening of UC (ICE 4) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44. For subjects who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine (ICE 5) prior to Week M-44, their observed values (if available) were used. Subjects who experienced ICE 6 (discontinued study agent due to reasons other than those in ICEs 4 and 5) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44.[b] Nonresponder imputation for missing data: Subjects who were missing one or more of the components pertaining to this endpoint at Week M-44 were considered not to have achieved this endpoint. [c] The CIs for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. [d] The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. [e] The p-values were based on the Cochran-Mantel-Haenszel test, stratified by clinical remission status at maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, placebo IV crossover to guselkumab 200 mg IV).
Source: Janssen Research & Development, 2024, attachment TEFKEY610D (8).

### 6.2.1.3 Corticosteroid-free clinical remission at week M-44

Table 25 presents corticosteroid-free clinical remission at week M-44 (definition is provided in section 5.2.1.3). Statistically significantly higher proportions of participants in the guselkumab 100 mg (39.5%) and 200 mg (39.5%) groups were in corticosteroid-free clinical remission at Week M-44 compared with the placebo group (6.8%; p<0.001 highly significant for both). 40.3% of patients in the guselkumab 100 mg group and 39.8% of patients in the guselkumab 200 mg group achieved corticosteroid-free clinical remission at week M-44. As the CIs overlap, the efficacy of guselkumab 100 mg q8w and guselkumab 200 mg q4w is considered equivalent (Table 25).

**Table 25 Corticosteroid-free clinical remission at week M-44 (BMSL-experienced subgroup)**

| Corticosteroid-free clinical remission at week M-44 | Placebo SC<br>N = 75 | Guselkumab 100 mg SC q8w<br>N = 77 | Guselkumab 200 mg SC q4w<br>N = 88 |
|---|---|---|---|
| n (%) (95% CI) [a, b, c] | 5 (6.7) (1.0, 12.3) | 31 (40.3) (29.3, 51.2) | 35 (39.8) (29.5, 50.0) |
| Adjusted treatment difference (95% CI), p-value [d, e] | Reference | 32.0 (20.6, 43.4), < 0.001 | 33.8 (22.8, 44.9), < 0.001 |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; CI = confidence interval; COVID-19 = coronavirus disease-19; ICE = intercurrent event; IV = intravenous; M = maintenance; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.
Notes: [a] ICE Strategies: Subjects who had an ostomy or colectomy (ICE 1), a dose adjustment (including a sham dose adjustment) (ICE 2), a prohibited change in UC medications (ICE 3), or discontinued study agent due to lack of efficacy or an AE of worsening of UC (ICE 4) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44. For subjects who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine (ICE 5) prior to Week M-44, their observed values (if available) were used. Subjects who experienced ICE 6 (discontinued study agent due to reasons other than those in ICEs 4 and 5) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44.[b] Nonresponder imputation for missing data: Subjects who were missing one or more of the components pertaining to this endpoint at Week M-44 were considered not to have achieved this endpoint. [c] The CIs for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. [d] The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight.[e] The p-values were based on the Cochran-Mantel-Haenszel test, stratified by clinical remission status at maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, placebo IV crossover to guselkumab 200 mg IV).
Source: Janssen Research & Development, 2024, attachment TEFKEY610D (8).

#### 6.2.1.4 Endoscopic mucosal healing at week M-44

Table 26 presents endoscopic mucosal healing (improvement) at week M-44 (definition is provided in section 5.2.1.4). A higher proportion of participants in the guselkumab 100 mg (45.5%) and 200 mg (42.0%) groups achieved endoscopic mucosal healing at Week M-44 compared with the placebo group (8.0%). As the CIs overlap, the efficacy of guselkumab 100 mg q8w and guselkumab 200 mg q4w is considered equivalent (Table 26).

**Table 26 Endoscopic mucosal healing at week M-44 (BMSL-experienced subgroup)**

| Endoscopic mucosal healing at week M-44 | Placebo SC<br>N = 75 | Guselkumab 100 mg SC q8w<br>N = 77 | Guselkumab 200 mg SC q4w<br>N = 88 |
|---|---|---|---|
| n (%) (95% CI) [a, b, c] | 6 (8.0) (1.9, 14.1) | 35 (45.5) (34.3, 56.6) | 37 (42.0) (31.7, 52.4) |
| Adjusted treatment difference (95% CI), p-value [d, e] | Reference | 35.8 (23.8, 47.8), < 0.001 | 34.6 (23.8, 42.5), < 0.001 |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; CI = confidence interval; COVID-19 = coronavirus disease-19; ICE = intercurrent event; IV = intravenous; M = maintenance; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.

Notes: [a] ICE strategies: Subjects who had an ostomy or colectomy (ICE 1), a dose adjustment (including a sham dose adjustment) (ICE 2), a prohibited change in UC medications (ICE 3), or discontinued study agent due to lack of efficacy or an AE of worsening of UC (ICE 4) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44. For subjects who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine (ICE 5) prior to Week M-44, their observed values (if available) were used. Subjects who experienced ICE 6 (discontinued study agent due to reasons other than those in ICEs 4 and 5) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44.[b] Nonresponder Imputation for missing data: Subjects who were missing one or more of the components pertaining to this endpoint at Week M-44 were considered not to have achieved this endpoint. Subjects who had an unevaluable biopsy (i.e., a biopsy that was collected, but could not be assessed due to sample preparation or technical errors) were considered not to have achieved the histology endpoint. [c] The CIs for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. [d] The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. [e] The p-values were based on the Cochran-Mantel-Haenszel test, stratified by clinical remission status at maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, placebo IV crossover to guselkumab 200 mg IV).
Source: Janssen Research & Development, 2024, attachment TEFKEY610D (8).

#### 6.2.1.5 IBDQ remission at week I-12

Table 27 presents IBDQ remission at Week I-12 defined as a total IBDQ score ≥ 170 at Week I-12. A statistically significantly higher proportion of patients in the guselkumab group was in IBDQ remission at Week I-12 compared with the placebo group (39.4% vs. 24.3%, p = 0.0024).

**Table 27 IBDQ remission at week I-12 (BMSL-experienced subgroup)**

| IBDQ remission at week I-12 | Placebo IV<br>N = 136 | Guselkumab 200 mg IV<br>N = 208 |
|---|---|---|
| n (%)[a, b] | 33 (24.3) | 82 (39.4) |
| Adjusted treatment difference (95% CI), p-value [d, e] | Reference | 15.2% (5.4, 25.0), 0.0024 |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; CI = confidence interval; COVID-19 = Coronavirus disease-19; I-# = week number in induction; ICE = intercurrent event; IV = intravenous; UC = ulcerative colitis.
Notes: [a] ICE Strategies: Subjects who had an ostomy or colectomy (ICE 1), a dose adjustment (including a sham dose adjustment) (ICE 2), a prohibited change in UC medications (ICE 3), or discontinued study agent due to lack of efficacy or an AE of worsening of UC (ICE 4) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44. For subjects who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine (ICE 5) prior to Week M-44, their observed values (if available) were used. Subjects who experienced ICE 6 (discontinued study agent due to reasons other than those in ICEs 4 and 5) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44. [b] Nonresponder imputation for missing data: After accounting for ICEs, subjects who were missing one or more of the components pertaining to an endpoint at the designated timepoint were considered not to have achieved the endpoint. [d] The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. [e] The p-values were based on the Cochran-Mantel-Haenszel chi-square test, stratified by concomitant use of corticosteroids at baseline (Yes/No).
Source: Johnson & Johnson (9)

#### 6.2.1.6 IBDQ remission at week M-44

Table 28 presents IBDQ remission at week M-44 (definition is provided in section 0). Statistically significantly higher proportions of participants in the guselkumab 100 mg (57.9%) and 200 mg (52.3%) groups were in IBDQ remission at Week M-44 compared with the

placebo group (17.6%; p<0.001 highly significant for both). 58.4% of patients in the guselkumab 100 mg group and 53.4% of patients in the guselkumab 200 mg group achieved IBDQ remission at week M-44. As the CIs overlap, the efficacy of guselkumab 100 mg q8w and guselkumab 200 mg q4w is considered equivalent (Table 28).

**Table 28 IBDQ remission at week M-44 (BMSL-experienced subgroup)**

| IBDQ remission at week M-44 | Placebo SC<br>N = 75 | Guselkumab 100 mg SC q8w<br>N = 77 | Guselkumab 200 mg SC q4w<br>N = 88 |
|---|---|---|---|
| n (%) (95% CI) [a, b, c] | 14 (18.7) (9.8, 27.5) | 45 (58.4) (47.4, 69.4) | 47 (53.4) (43.0, 63.8) |
| Adjusted treatment difference (95% CI), p-value [d, e] | Reference | 37.9 (25.7, 50.1), < 0.001 | 35.4 (22.7, 48.0), < 0.001 |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; CI = confidence interval; COVID-19 = coronavirus disease-19; IBDQ = Inflammatory Bowel Disease Questionnaire; ICE = intercurrent event; IV = intravenous; M = maintenance; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.
Notes: [a] ICE strategies: Subjects who had an ostomy or colectomy (ICE 1), a dose adjustment (including a sham dose adjustment) (ICE 2), a prohibited change in UC medications (ICE 3), or discontinued study agent due to lack of efficacy or an AE of worsening of UC (ICE 4) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44. For subjects who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine (ICE 5) prior to Week M-44, their observed values (if available) were used. Subjects who experienced ICE 6 (discontinued study agent due to reasons other than those in ICEs 4 and 5) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44. [b] Nonresponder imputation for missing data: Subjects who were missing one or more of the components pertaining to this endpoint at Week M-44 were considered not to have achieved this endpoint. [c] The CIs for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. [d] The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. [e] The p-values were based on the Cochran-Mantel-Haenszel test, stratified by clinical remission status at maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, placebo IV crossover to guselkumab 200 mg IV).
Source: Janssen Research & Development, 2024, attachment TEFKEY610D (8).

### 6.2.1.7 CFB in IBDQ total score through week M-44

Table 29 presents change from baseline in IBDQ total score through week M-44. Participants in the guselkumab 100 mg (LS mean CFB = 0.742) and 200 mg (LS mean CFB = -6.292) dose had a statistically significant change from baseline compared at Week M-44 compared with the placebo group (difference in LS mean = 34.110 and 28.320 respectively, p<0.0001).

**Table 29 Change from baseline in IBDQ total score through week M-44 (BMSL-experienced subgroup)**

| Study | Treatment arm | N [a] | LS Mean CFB (SE) [b] | Difference in LS mean CFB | 95% CI | p-value |
|---|---|---|---|---|---|---|
| **QUASAR MS** | Guselkumab 100 mg SC q8w | 73 | 0.742 (3.640) | 34.110 | 23.91, 44.31 | <0.0001 |

| | | | | | |
|---|---|---|---|---|---|
| Guselkumab 200 mg SC q4w | 105 | -6.292 (3.480) | 28.320 | 18.31, 38.33 | <0.0001 |
| Placebo SC | 74 | Vs. GUS 100: -33.37 (3.647) | Reference | | |
| | | Vs. GUS 200: 34.61 (3.692) | Reference | | |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; CI = confidence interval; COVID-19 = coronavirus disease-19; ICE = intercurrent event; IBDQ = Inflammatory Bowel Disease Questionnaire; IV = intravenous; M = maintenance; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.

Note: [a] N is number of subjects with IBDQ measurements at baseline and at Week 44. [b] Least squares means are derived based on a pairwise comparison Mixed-effects Model for Repeated Measures (MMRM) with N number of subjects with IBDQ measurements at baseline and at Week 44. Analyses were performed without stratification to avoid numerical issues.

Source: Johnson & Johnson (9)

### 6.2.2 Please provide a qualitative description of safety data. Differences in definitions of outcomes between studies

During the IS-2, 10 (7.4%) of 136 patients in the placebo IV q4w arm and 9 (4.3%) of 208 patients in the guselkumab 200 mg IV q4w experienced at least one serious AE. An overview of all SAEs experienced by any patient during the IS-2 is presented in Table 30.

**Table 30 Serious adverse events (IS-2 BMSL-experienced subgroup)**

| | Placebo IV q4w N = 136 | Guselkumab 200 mg IV q4w N = 208 |
|---|---|---|
| **Subjects with one or more SAEs, n (%)** | 10 (7.4) | 9 (4.3) |
| **Gastrointestinal disorders** | 7 (5.1) | 5 (2.4) |
| **Worsening of UC** | 6 (4.4) | 4 (1.9) |
| **Infections and infestations** | 0 (0.0) | 3 (1.4) |

Abbreviations: BMSL = biological and targeted synthetic medicine; IS-2 = induction study 2; IV = intravenous; qw4 = every 4 weeks; SAE = serious adverse event; UC = ulcerative colitis.

Source: Johnson & Johnson (9)

81 (59.6%) patients in the placebo IV q4w arm and 114 (54.8%) in the guselkumab 200 mg IV arm experienced any AE. An overview of all AEs experienced by at least 5% of the BMSL-experienced IS-2 patient population is presented in Table 31.

**Table 31 Adverse events occurring in ≥5% in any treatment arm (IS-2 BMSL-experienced subgroup)**

| | Placebo IV q4w<br>N = 136 | Guselkumab 200 mg IV q4w<br>N = 208 |
|---|---|---|
| **Subjects with one or more AEs, n (%)** | 81 (59.6) | 114 (54.8) |
| **Blood and lymphatic system disorders** | 13 (9.6) | 13 (6.3) |
| **Anaemia** | 10 (7.4) | 8 (3.8) |
| **Gastrointestinal disorders** | 30 (22.1) | 27 (13.0) |
| **Worsening of UC** | 13 (9.6) | 8 (3.8) |
| **Infections and infestations** | 25 (18.4) | 38 (18.3) |
| **COVID-19** | 5 (3.7) | 15 (7.2) |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; COVID-19 = coronavirus disease-19; IS-2 = induction study 2; IV = intravenous; q4w = every 4 weeks; UC = ulcerative colitis.

Source: Johnson & Johnson (9)

In the following, Week M-44 safety data are presented for the BMSL-experienced patients from the randomised safety analysis set. None of 78 participants in the placebo group experienced a serious AE, 2 of 75 (2.7%) of the guselkumab 100 mg SC q8w group, and 6 of 87 (6.9%) in the guselkumab 200 mg SC q4w group experienced a serious AE. No deaths occurred in any of the treatment arms. 74.4% in the placebo group, 72.0% in the guselkumab 100 mg SC q8w, and 74.7% in the guselkumab 200 mg SC q4w group experienced an AE. An overview of all SAEs experienced by any patient as well as all AEs experienced by at least 5% of the patient population during the MS is provided in Table 32 and Table 33, respectively.

**Table 32 Serious adverse events (MS BMSL-experienced subgroup)**

| | Placebo SC q4w<br>N = 78 | Guselkumab 100 mg SC q8w<br>N = 75 | Guselkumab 200 mg SC q4w<br>N = 87 |
|---|---|---|---|
| **Subjects with one or more SAEs, n (%)** | 0 (0.0) | 2 (2.7) | 6 (6.9) |
| **Cardiac disorders** | 0 (0.0) | 0 (0.0) | 1 (1.1) |
| **Atrial fibrillation** | 0 (0.0) | 0 (0.0) | 1 (1.1) |
| **Gastrointestinal disorders** | 0 (0.0) | 1 (1.3) | 1 (1.1) |
| **Worsening of UC** | 0 (0.0) | 1 (1.3) | 1 (1.1) |
| **Infections and infestations** | 0 (0.0) | 1 (1.3) | 1 (1.1) |
| **Abscess** | 0 (0.0) | 1 (1.3) | 0 (0.0) |

| | | | |
|---|---|---|---|
| **Bacterial infection** | 0 (0.0) | 0 (0.0) | 1 (1.1) |
| **Injury, poisoning and procedural complications** | 0 (0.0) | 0 (0.0) | 2 (2.3) |
| **Incarcerated incisional hernia** | 0 (0.0) | 0 (0.0) | 1 (1.1) |
| **Incisional hernia** | 0 (0.0) | 0 (0.0) | 1 (1.1) |
| **Postoperative respiratory failure** | 0 (0.0) | 0 (0.0) | 1 (1.1) |
| **Rib fracture** | 0 (0.0) | 0 (0.0) | 1 (1.1) |
| **Musculoskeletal and connective tissue disorders** | 0 (0.0) | 0 (0.0) | 1 (1.1) |
| **Osteoarthritis** | 0 (0.0) | 0 (0.0) | 1 (1.1) |
| **Neoplasms benign, malignant and unspecified (incl cysts and polyps)** | 0 (0.0) | 0 (0.0) | 1 (1.1) |
| **Fibroadenoma of breast** | 0 (0.0) | 0 (0.0) | 1 (1.1) |
| **Nervous system disorders** | 0 (0.0) | 0 (0.0) | 1 (1.1) |
| **Guillain-Barre syndrome** | 0 (0.0) | 0 (0.0) | 1 (1.1) |
| **Psychiatric disorders** | 0 (0.0) | 0 (0.0) | 1 (1.1) |
| **Anxiety** | 0 (0.0) | 0 (0.0) | 1 (1.1) |

Abbreviations: BMSL = biological and targeted synthetic medicine; MS = maintenance study; q4w = every 4 weeks; q8w = every 8 weeks; SAE = serious adverse event; SC = subcutaneous; UC = ulcerative colitis.

**Table 33 Adverse events occurring in ≥5% in any treatment arm (MS BMSL-experienced subgroup)**

| | Placebo SC q4w<br>N = 78 | Guselkumab 100 mg SC q8w<br>N = 75 | Guselkumab 200 mg SC q4w<br>N = 87 |
|---|---|---|---|
| **Subjects with one or more AEs, n (%)** | 58 (74.4) | 54 (72.0) | 65 (74.7) |
| **Gastrointestinal disorders** | 35 (44.9) | 29 (38.7) | 22 (25.3) |
| **Worsening of UC** | 28 (35.9) | 13 (17.3) | 15 (17.2) |
| **General disorders and administration site conditions** | 9 (11.5) | 7 (9.3) | 18 (20.7) |
| **Injection site reaction** | 0 (0.0) | 0 (0.0) | 5 (5.7) |

| | | | |
|---|---|---|---|
| **Pyrexia** | 3 (3.8) | 4 (5.3) | 3 (3.4) |
| **Infections and infestations** | 26 (33.3) | 27 (36.0) | 31 (35.6) |
| **COVID-19** | 15 (19.2) | 9 (12.0) | 8 (9.2) |
| **Nasopharyngitis** | 4 (5.1) | 2 (2.7) | 3 (3.4) |
| **Upper respiratory tract infection** | 3 (3.8) | 3 (4.0) | 6 (6.9) |
| **Musculoskeletal and connective tissue disorders** | 13 (16.7) | 16 (21.3) | 12 (13.8) |
| **Arthralgia** | 8 (10.3) | 4 (5.3) | 7 (8.0) |
| **Back pain** | 3 (3.8) | 7 (9.3) | 1 (1.1) |
| **Nervous system disorders** | 5 (6.4) | 3 (4.0) | 10 (11.5) |
| **Headache** | 4 (5.1) | 2 (2.7) | 4 (4.6) |
| **Respiratory, thoracic and mediastinal disorders** | 2 (2.6) | 6 (8.0) | 10 (11.5) |
| **Cough** | 2 (2.6) | 4 (5.3) | 3 (3.4) |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; COVID-19 = coronavirus disease-19; MS = maintenance study; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.

### 6.2.3 Method of synthesis

N/A

### 6.2.4 Results from the comparative analysis

N/A

**Table 34 Results from the comparative analysis of [intervention] vs. [comparator] for [patient population]**

| Outcome measure | [Intervention] (N=x) | [Comparator] (N=x) | Result |
|---|---|---|---|
| N/A | N/A | N/A | N/A |

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# Appendix A. Main characteristics of studies included

**Table 35 Main characteristic of studies included**

| Trial name: QUASAR | NCT number: NCT04033445 |
|---|---|
| **Objective** | The purpose of this study is to evaluate the efficacy and safety of guselkumab in participants with moderately to severely active UC. |
| **Publications – title, author, journal, year** | Guselkumab in Patients With Moderately to Severely Active Ulcerative Colitis: QUASAR Phase 2b Induction Study. Peyrin-Biroulet L, Allegretti JR, Rubin DT, Bressler B, Germinaro M, Huang KG, Shipitofsky N, Zhang H, Wilson R, Han C, Feagan BG, Sandborn WJ, Panés J, Hisamatsu T, Lichtenstein GR, Sands BE, Dignass A; QUASAR Study Group. Gastroenterology. 2023 (39)<br><br>Guselkumab in patients with moderately to severely active ulcerative colitis (QUASAR): phase 3 double-blind, randomised, placebo-controlled induction and maintenance studies. Rubin DT, Allegretti JR, Panés J, Shipitofsky N, Yarandi SS, Huang KG, Germinaro M, Wilson R, Zhang H, Johanns J, Feagan BG, Hisamatsu T, Lichtenstein GR, Bressler B, Peyrin-Biroulet L, Sands BE, Dignass A; QUASAR Study Group. Lancet. 2025 (40) |
| **Study type and design** | QUASAR is a double-blinded randomised placebo-controlled parallel-group assignment phase 2b/3 study. The investigators and participants were masked. QUSAR is ongoing.<br><br>Specifically, QUASAR comprises a phase 2b induction study (IS-1), a phase 3 induction study (IS-2), and a phase 3 MS. IS-1 will not be described any further, as it is an induction dose ranging study, and the efficacy and safety of the approved induction dose is assessed in IS-2.<br><br>**QUASAR IS-2**<br><br>Participants were randomised in a 3:2 ratio to guselkumab 200 mg IV or placebo administered at Weeks I-0, I-4, and I-8. Participants were allocated to a treatment group using permuted block randomisation stratified by advanced-failure status (i.e., inadequate response or failure to tolerate tumour necrosis factor α antagonists, vedolizumab, or tofacitinib) (Yes/No), region (Eastern Europe, Asia, or Rest of World), and concomitant use of corticosteroids at baseline (Yes/No).<br><br>In Week I-0 to Week I-12 no crossover was allowed. Participants initially randomised to placebo who were not in clinical response at Week I-12 crossed over to guselkumab. Additionally, participants initially randomised to guselkumab 200 mg IV who were not in clinical response at Week I-12 received guselkumab 200 mg SC. To maintain the blind, both IV and SC administrations were given to all participants who were not in clinical response at Week I-12 and continued in IS-2.<br><br>**QUASAR MS** |

| Trial name: QUASAR | NCT number: NCT04033445 |
|---|---|
| | The following populations from QUASAR IS-1 and IS-2 were re-randomised in a 1:1:1 ratio to guselkumab 200 mg SC q4w, guselkumab 100 mg SC q8w, or placebo SC:<br>• Guselkumab clinical responders at Week I-12<br>• Placebo IV → guselkumab clinical responders at Week I-24 (i.e., participants initially randomised to placebo who were not in clinical response at Week I-12 crossed over to guselkumab. At Week I-24, participants were re-evaluated for clinical response and clinical responders entered the MS).<br>Participants were allocated to an intervention group using permuted block randomisation stratified by clinical remission status at Maintenance baseline (Yes/No), concomitant use of corticosteroids at Maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, and placebo IV → guselkumab 200 mg IV). |
| **Sample size (n)** | **QUASAR IS-2**<br>Of the 736 randomised participants, 702 participants had a baseline modified Mayo Score of 5 to 9. One of these participants was randomised to placebo but was not treated because of inadequate venous access for study intervention administration and protocol-specified laboratory assessments. Therefore, the Full Analysis Set, which is the primary efficacy analysis set, is comprised of 701 treated participants with a baseline modified Mayo Score of 5 to 9.<br>Overall, 49.1% (n=344) of participants had a history of BMSL-experienced and 50.9% (n=357) of participants did not (339 of these 357 participants were BMSL-naïve and 18 were BMSL-experienced without documented failure).<br>**QUASAR MS**<br>Of the 846 participants treated in the MS (267 from IS-1 and 579 from IS-2), 805 (95.2%) participants had a modified Mayo score of 5 to 9 at induction baseline (i.e., the Full Analysis Set) and were treated. Placebo responders at Week I-12 and guselkumab 24-Week responders were not randomised. The primary analysis population for this study consists of 568 participants in the Randomised Full Analysis Set, (i.e., participants with a modified Mayo score of 5 to 9 at induction baseline who were randomised and treated in the MS).<br>311 participants were BMSL-naïve, 236 participants were BMSL-experienced , while 21 were biologic-experienced without documented failure. |
| **Main inclusion criteria** | • Documented diagnosis of UC<br>• Moderately to severely active UC, defined by modified Mayo score<br>• Demonstrated inadequate response or intolerance to medical therapies specified in the protocol |

| Trial name: QUASAR | | NCT number: NCT04033445 |
|---|---|---|
| | • Screening laboratory test results within the parameters specified in the protocol | |
| **Main exclusion criteria** | • Diagnosis of indeterminate colitis, microscopic colitis, ischemic colitis, or Crohn's disease or clinical findings suggestive of Crohn's disease<br>• UC limited to the rectum only or to less than 20 cm of the colon<br>• Presence of a stoma<br>• Presence or history of a fistula<br>• Receiving prohibited medications and/or treatment | |
| **Intervention** | **QUASAR IS-2**<br>• Guselkumab 200 mg IV at Weeks I-0, I-4, and I-8. 202 BMSL-naïve and 208 BMSL-experienced participants were randomised to 200 mg guselkumab IV.<br>Subsequent study treatment will be determined by the participant's clinical response status at Week I-12:<br>• Guselkumab clinical responders at Week I-12 entered the MS.<br>• Participants initially randomised to guselkumab 200 mg IV who were not in clinical response at Week I-12 received three doses of guselkumab 200 mg SC at Weeks I-12, I-16, and I-20.<br>**QUSAR MS**<br>• Standard dose (guselkumab 100 mg SC q8w): Participants received guselkumab 100 mg SC q8w starting at Week M-4 through Week M-44. To maintain the blind, participants received one placebo SC injection + one injection of 100 mg guselkumab or two placebo SC injections at alternate visits. 105 BMSL-naïve and 77 BMSL-experienced participants were randomised to 100 mg guselkumab SC q8w.<br>• Alternative dose (guselkumab 200 mg SC q4w): Participants received guselkumab 200 mg SC q4w starting at Week M-0 through Week M-44. Participants received two injections of 100 mg guselkumab at each visit. 96 BMSL-naïve and 88 BMSL-experienced participants were randomised to 200 mg guselkumab SC q4w.<br>In addition, guselkumab induction 24-week responders from IS-1 or IS-2 entered the MS but were not randomised. Participants remained on their assigned study intervention through Week M-44. | |
| **Comparator(s)** | **QUSAR IS-2**<br>• Placebo at Weeks I-0, I-4, and I-8. 137 BMSL-naïve and 136 BMSL-experienced participants were randomised to placebo IV.<br>Subsequent study treatment will be determined by the participant's clinical response status at Week I-12: | |

| Trial name: QUASAR | NCT number: NCT04033445 |
|---|---|
| | • Placebo clinical responders at Week I-12 entered the MS.<br>• Participants initially randomised to placebo who were not in clinical response at Week I-12 crossed over to guselkumab and received three doses of guselkumab 200 mg IV at Weeks I-12, I-16, and I-20.<br><br>**QUSAR MS**<br><br>• Placebo: Participants received placebo SC q4w starting at Week M-0 through Week M-44. To maintain the blind, participants received 2 placebo injections at each visit. 108 BMSL-naïve and 75 BMSL-experienced participants were randomised to placebo SC.<br><br>In addition, induction placebo responders at Week I-12 from IS-1 or IS-2 entered the MS but were not randomised. Participants remained on their assigned study intervention through Week M-44. |
| **Follow-up time** | **QUSAR IS-2**<br><br>The average duration of follow-up in the safety analysis set was 12.1[a] weeks in the placebo IV group, 12.3[a] weeks in the guselkumab 200 mg IV group, 13.9[a] weeks in the placebo IV → guselkumab 200 mg IV group, and 14.6[b] weeks in the guselkumab 200 mg IV group → guselkumab 200 mg SC group.<br><br>**QUASAR MS**<br><br>The average duration of follow-up (up to dose adjustment) in the randomised safety analysis set was 34.0 weeks in the placebo SC group[c,d], 40.5 weeks in the 100 mg SC q8w group, and 39.2 weeks in the 200 mg SC q4w group.<br><br>The average duration of follow-up in the nonrandomised safety analysis set was 40.3 weeks in the placebo SC group[e] (induction placebo IV responders) and 42.8 in the guselkumab 200 mg SC q4w group (induction guselkumab 24-week responders[f]). |
| **Primary, secondary and exploratory endpoints** | **QUASAR IS-2**<br><br><u>Endpoints included in this application:</u><br><br>The primary endpoint was clinical remission at Week I-12. The secondary endpoint included was IBDQ remission at Week I-12. Safety data were included as well.<br><br><u>Other endpoints:</u><br><br>Secondary endpoints were symptomatic remission at Week I-12, endoscopic healing (i.e., endoscopic improvement) at Week I-12, clinical response at Week I-12, symptomatic remission at Week I-4, endoscopic mucosal healing (i.e., endoscopic mucosal improvement) at Week I-12, fatigue response at Week I-12, symptomatic remission at Week I-2, and endoscopic normalisation at Week I-12. |

| Trial name: QUASAR | NCT number: NCT04033445 |
|---|---|
| | **QUASAR MS**<br><br>Endpoints included in this application:<br><br>Secondary endpoints were corticosteroid-free (i.e., not requiring any treatment with corticosteroids for at least 8 weeks prior) clinical remission at Week M-44, endoscopic mucosal healing at Week M-44, and IBDQ remission at Week M-44. Safety data were included as well.<br><br>Other endpoints:<br><br>The primary endpoint was clinical remission at Week M-44.<br><br>Secondary endpoints were symptomatic remission at Week M-44, endoscopic healing at Week M-44, maintenance of clinical response at Week M-44, fatigue response at Week M-44, clinical remission at Week M-44 among the participants who had achieved clinical remission at maintenance baseline (i.e., maintenance of clinical remission at Week M-44), and endoscopic normalisation at Week M-44. |
| **Method of analysis** | All efficacy analyses were intention-to-treat analyses presented for the BMSL-naïve and BMSL-experienced subgroup.<br><br>All efficacy analyses include the presentation of numbers, percentages, and CIs as well as adjusted treatment difference. The adjusted treatment difference and corresponding CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. Similarly, the p-values were based on Cochran-Mantel-Haenszel tests with stratification. |
| **Subgroup analyses** | **QUASAR IS-2**<br><br>Prespecified subgroup analyses for the primary endpoint were performed (if the number of participants within each level of the subgroup permitted) based on baseline demographic characteristics, baseline UC disease characteristics, baseline UC-related concomitant medication use, and baseline UC-related medication history (including advanced therapy-experienced status).<br><br>Prespecified analyses were conducted to evaluate the efficacy of the following key endpoints based on advanced therapy-failure status, biologic-failure status, baseline Mayo endoscopy subscore (2 vs 3), and baseline colonic molecular prediction signature status:<br><br>• Clinical remission at Week I-12<br>• Clinical response at Week I-12<br>• Symptomatic remission at Week I-2, Week I-4, Week I-8 and Week I-12<br>• IBDQ remission at Week I-12<br>• Fatigue response at Week I-12<br>• Endoscopic healing at Week I-12<br>• Endoscopic normalisation at Week I-12 |

| Trial name: QUASAR | NCT number: NCT04033445 |
|---|---|
| | • Histologic healing at Week I-12<br>• Histologic remission at Week I-12<br>• Histologic-endoscopic mucosal healing at Week I-12<br>• Histologic-endoscopic mucosal healing (Alternative Definition 1) at Week I-12<br>• Deep histologic-endoscopic mucosal healing at Week I-12<br>**QUASAR MS**<br>Prespecified subgroup analyses for the primary endpoint were performed based on demographic and UC disease characteristics, concomitant UC medication use, and history of UC-related medications (including advanced therapy-failure status), all at Week 0 of the induction study, as well as maintenance stratification factors and UC clinical disease characteristics at Week 0 of the MS. Additional subgroup analyses for clinical remission at Week M-44 and other key endpoints were also performed.<br>In addition to the subgroup analyses performed for the primary endpoint, prespecified subgroup analyses were conducted based on advanced therapy-failure status, baseline clinical status, inflammatory biomarker thresholds, and baseline body weight for key efficacy endpoints including primary, major secondary, and other selected histologic and endoscopic efficacy endpoints. |
| **Other relevant information** | **QUASAR IS-2**<br>Participants who were not in clinical response at Week I-24 did not receive further study intervention and completed a safety follow-up visit approximately 12 weeks after their last dose of study intervention.<br>All UC-specific medical therapies were to be maintained at a stable dose through to the end of IS-2 and could only be discontinued or reduced in dose if investigator judgment required it because of toxicity or medical necessity. The initiation or increase in dose of UC-specific medical therapies (or any restricted/prohibited medication or therapy) during IS-2 prohibited a participant from entering the MS.<br>**QUASAR MS**<br>For participants who were receiving oral corticosteroids on entry in the MS, the investigator was to begin tapering the daily dose of corticosteroids at Week M-0. Other UC-specific medical therapies were to be maintained at stable doses through Week M-44 (without initiation or increase in dose) unless investigator judgment required that the therapy be discontinued, or the dose be reduced because of toxicity or medical necessity. Tapering of the daily dose of corticosteroids was allowed to be paused for participants who met clinical flare criteria. |

Abbreviations: BMSL = biological and targeted synthetic medicine; CI = confidence interval; I-# = week number in induction; IBDQ = Inflammatory Bowel Disease Questionnaire; IS-1 = induction study 1; IS-2 = induction study 2; IV = intravenous; M = maintenance; MS = maintenance study; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.

Notes: [a] Includes data up to Week I-12 for subjects who received treatment at Week I-12. Includes all data through final safety visit for subjects who did not receive treatment at Week I-12. [b] Includes data from Week I-12 onward. [c] Participants who were in clinical response to guselkumab IV induction dosing and were randomised to placebo SC on entry into this MS. [d] Includes data from Week M-0 up to the time of dose adjustment for participants who had a dose adjustment or through Week M-44 for those who did not. [e] Participants who were in clinical response to placebo IV induction dosing and received placebo SC on entry into this MS. Includes data from Week M-0 through Week M-44. [f] Participants who were not in clinical response to guselkumab IV at Week I-12 but were in clinical response at Week I-24 after receiving SC administrations of guselkumab from Week I-12. Includes data from Week M-0 through Week M-44.
Source: ClinicalTrials.gov, 2019 (41); Janssen Research & Development, 2023 (43); Janssen Research & Development, 2024 (8).

# Appendix B. Efficacy results per study

**Results per study**

**Table 36 Results per study (QUASAR)**

| Results of QUASAR (NCT04033445) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Estimated absolute difference in effect | | | Estimated relative difference in effect | | | Description of methods used for estimation | References |
| Outcome | Study arm | N | Result (CI) | Difference | 95% CI | *P* value | Difference [a] | 95% CI | *P* value | | |
| Clinical remission, BMSL-naïve subgroup (week 12) [b, c] | Placebo IV | 137 | n = 16 (11.7%) (CI: 6.3%, 17.1%) | Reference | Reference | Reference | Reference | Reference | Reference | The CIs for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. The p-values were based on the Cochran-Mantel-Haenszel chi-square test, stratified by concomitant use of corticosteroids at baseline (Yes/No). | Janssen Research & Development, 2023 (43) |
| | Guselkumab 200 mg IV | 202 | n = 64 (31.7%) (CI: 25.3%, 38.1%) | N/A | N/A | N/A | 20.0% | 11.6%, 28.3% | <0.001 | | |
| | Placebo IV | 136 | n = 5 (3.7%) (CI: 0.5%, 6.8%) | Reference | Reference | Reference | Reference | Reference | Reference | The CIs for the proportion of subjects meeting the endpoint in each treatment | Janssen Research & |

| Results of QUASAR (NCT04033445) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Estimated absolute difference in effect | | | Estimated relative difference in effect | | | Description of methods used for estimation | References |
| Outcome | Study arm | N | Result (CI) | Difference | 95% CI | *P* value | Difference [a] | 95% CI | *P* value | | |
| Clinical remission, BMSL-experienced subgroup (week 12) [b, c] | Guselkumab 200 mg IV | 208 | n = 26 (12.5%) (CI: 8.0%, 17.0%) | N/A | N/A | N/A | 8.8% | 3.4%, 14.3% | 0.005 | group were based on the normal approximation confidence limits. The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. The p-values were based on the Cochran-Mantel-Haenszel chi-square test, stratified by concomitant use of corticosteroids at baseline (Yes/No). | Development, 2023 (43) |
| Clinical remission, BMSL-naïve subgroup (week M-44) [c, d] | Placebo SC | 108 | n = 28 (25.9%) (CI: 17.7%, 34.2%) | N/A | N/A | N/A | Reference | | | The CIs for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. The p-values were based on the Cochran-Mantel-Haenszel test, stratified by clinical remission status at maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, placebo IV crossover to guselkumab 200 mg IV). | Janssen Research & Development, 2024 (8) |
| | Guselkumab 100 mg SC q8w | 105 | n = 53 (50.5%) (CI: 40.9%, 60.0%) | N/A | N/A | N/A | 24.3% | 12.0%, 36.5% | <0.001 | | |
| | Guselkumab 200 mg SC q4w | 96 | n = 56 (58.3%) (CI: 48.5%, 68.2%) | N/A | N/A | N/A | 28.8% | 16.5%, 41.1% | <0.001 | | |

| Results of QUASAR (NCT04033445) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Estimated absolute difference in effect | | | Estimated relative difference in effect | | | Description of methods used for estimation | References |
| **Outcome** | **Study arm** | **N** | **Result (CI)** | **Difference** | **95% CI** | ***P* value** | **Difference [a]** | **95% CI** | ***P* value** | | |
| Clinical remission, BMSL-experienced subgroup (week M-44) [c, d] | Placebo SC | 75 | n = 6 (8.1%) (CI: 1.9%, 14.1%) | N/A | N/A | N/A | Reference | | | The CIs for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. The adjusted treatment difference CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. The p-values were based on the Cochran-Mantel-Haenszel test, stratified by clinical remission status at maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, placebo IV crossover to guselkumab 200 mg IV). | Janssen Research & Development, 2024 (8) |
| | Guselkumab 100 mg SC q8w | 77 | n = 31 (40.3%) (CI: 29.3%, 51.2%) | N/A | N/A | N/A | 30.4% | 18.7%, 42.1% | <0.001 | | |
| | Guselkumab 200 mg SC q4w | 88 | n = 35 (39.8%) (CI: 29.5%, 50.0%) | N/A | N/A | N/A | 32.4% | 21.1%, 43.7% | <0.001 | | |
| Corticosteroid-free clinical remission, BMSL-naïve subgroup (week M-44) [c, d] | Placebo SC | 108 | n = 28 (25.9%) (CI: 17.7%, 34.2%) | N/A | N/A | N/A | Reference | | | The CIs for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. The | Janssen Research & Development, 2024 (8) |
| | Guselkumab 100 mg SC q8w | 105 | n = 53 (50.5%) (CI: 40.9%, 60.0%) | N/A | N/A | N/A | 24.3% | 12.0%, 36.5% | <0.001 | | |

| Results of QUASAR (NCT04033445) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Estimated absolute difference in effect | | | Estimated relative difference in effect | | | Description of methods used for estimation | References |
| **Outcome** | **Study arm** | **N** | **Result (CI)** | **Difference** | **95% CI** | ***P* value** | **Difference [a]** | **95% CI** | ***P* value** | | |
| | Guselkumab 200 mg SC q4w | 96 | n = 54 (56.3%) (CI: 46.3%, 66.2%) | N/A | N/A | N/A | 26.5% | 14.2%, 38.9% | <0.001 | p-values were based on the Cochran-Mantel-Haenszel test, stratified by clinical remission status at maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, placebo IV crossover to guselkumab 200 mg IV). | |
| Corticosteroid-free clinical remission, BMSL-experienced subgroup (week M-44) [c, d] | Placebo SC | 75 | n = 5 (6.7%) (CI: 1.0%, 12.3%) | N/A | N/A | N/A | Reference | | | The CIs for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. The p-values were based on the Cochran-Mantel-Haenszel test, stratified by clinical remission status at maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, placebo IV crossover to guselkumab 200 mg IV). | Janssen Research & Development, 2024 (8) |
| | Guselkumab 100 mg SC q8w | 77 | n = 31 (40.3%) (CI: 29.3%, 51.2%) | N/A | N/A | N/A | 32.0% | 20.6%, 43.4% | <0.001 | | |
| | Guselkumab 200 mg SC q4w | 88 | n = 35 (39.8%) (CI: 29.5%, 50.0%) | N/A | N/A | N/A | 33.8% | 22.8%, 44.9% | <0.001 | | |

| Results of QUASAR (NCT04033445) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Estimated absolute difference in effect | | | Estimated relative difference in effect | | | Description of methods used for estimation | References |
| **Outcome** | **Study arm** | **N** | **Result (CI)** | **Difference** | **95% CI** | ***P* value** | **Difference [a]** | **95% CI** | ***P* value** | | |
| Endoscopic mucosal healing, BMSL-naïve subgroup (week M-44) [c, d] | Placebo SC | 108 | n = 28 (25.9%) (CI: 17.7%, 34.2%) | N/A | N/A | N/A | Reference | | | The CIs for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. The p-values were based on the Cochran-Mantel-Haenszel test, stratified by clinical remission status at maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, placebo IV crossover to guselkumab 200 mg IV). | Janssen Research & Development, 2024 (8) |
| | Guselkumab 100 mg SC q8w | 105 | n = 56 (53.3%) (CI: 43.8%, 62.9%) | N/A | N/A | N/A | 27.2% | 15.0%, 39.5% | <0.001 | | |
| | Guselkumab 200 mg SC q4w | 96 | n = 57 (59.4%) (CI: 49.6%, 69.2%) | N/A | N/A | N/A | 30.0% | 17.6%, 42.4% | <0.001 | | |
| Endoscopic mucosal healing, BMSL-experienced subgroup (week M-44) [c, d] | Placebo SC | 75 | n = 6 (8.0%) (CI: 1.9%, 14.1%) | N/A | N/A | N/A | Reference | | | The CIs for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. The | Janssen Research & Development, 2024 (8) |
| | Guselkumab 100 mg SC q8w | 77 | n = 35 (45.5%) (CI: 34.3%, 56.6%) | N/A | N/A | N/A | 35.8% | 23.8%, 47.8% | <0.001 | | |

| Results of QUASAR (NCT04033445) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Estimated absolute difference in effect | | | Estimated relative difference in effect | | | Description of methods used for estimation | References |
| **Outcome** | **Study arm** | **N** | **Result (CI)** | **Difference** | **95% CI** | ***P* value** | **Difference [a]** | **95% CI** | ***P* value** | | |
| | Guselkumab 200 mg SC q4w | 88 | n = 37 (42.0%) (CI: 31.7%, 52.4%) | N/A | N/A | N/A | 34.6% | 23.8%, 42.5% | <0.001 | p-values were based on the Cochran-Mantel-Haenszel test, stratified by clinical remission status at maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, placebo IV crossover to guselkumab 200 mg IV). | |
| IBDQ remission, BMSL-naïve subgroup (week I-12) b, c | Placebo IV | 137 | n = 47 (34.3%) | N/A | N/A | N/A | Reference | | | The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. The p-values were based on the Cochran-Mantel-Haenszel chi-square test, stratified by concomitant use of corticosteroids at baseline (Yes/No). | Johnson & Johnson (9) |
| | Guselkumab 200 mg IV | 202 | n = 126 (62.4%) | N/A | N/A | N/A | 28.1% | 17.7%, 38.5% | <0.001 | | |
| IBDQ remission, BMSL-experienced subgroup (week I-12) [b, c] | Placebo IV | 136 | n = 33 (24.3%) | N/A | N/A | N/A | Reference | | | The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. The p-values were based on the Cochran-Mantel-Haenszel chi-square test, stratified by concomitant use of corticosteroids at baseline (Yes/No). | Johnson & Johnson (9) |
| | Guselkumab 200 mg IV | 208 | n = 82 (39.4%) | N/A | N/A | N/A | 15.2% | 5.4%, 25.0% | 0.0024 | | |

| Results of QUASAR (NCT04033445) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Estimated absolute difference in effect | | | Estimated relative difference in effect | | | Description of methods used for estimation | References |
| Outcome | Study arm | N | Result (CI) | Difference | 95% CI | *P* value | Difference [a] | 95% CI | *P* value | | |
| IBDQ remission, BMSL-naïve subgroup (week M-44) [c, d] | Placebo SC | 108 | n = 53 (49.1%) (CI: 39.6%, 58.5%) | N/A | N/A | N/A | Reference | | | The CIs for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. The p-values were based on the Cochran-Mantel-Haenszel test, stratified by clinical remission status at maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, placebo IV crossover to guselkumab 200 mg IV). | Janssen Research & Development, 2024 (8) |
| | Guselkumab 100 mg SC q8w | 105 | n = 71 (67.6%) (CI: 58.7%, 76.6%) | N/A | N/A | N/A | 18.9% | 6.1%, 31.7% | 0.006 | | |
| | Guselkumab 200 mg SC q4w | 96 | n = 71 (74.0%) (CI: 65.2%, 82.7%) | N/A | N/A | N/A | 23.9% | 11.3%, 36.5% | <0.001 | | |
| IBDQ remission, BMSL-experienced subgroup (week M-44) [c, d] | Placebo SC | 75 | n = 14 (18.7%) (CI: 9.8%, 27.5%) | N/A | N/A | N/A | Reference | | | The CIs for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. The adjusted treatment difference and CIs were based on the Wald statistic with Cochran-Mantel-Haenszel weight. The | Janssen Research & Development, 2024 (8) |
| | Guselkumab 100 mg SC q8w | 77 | n = 45 (58.4%) (CI: 47.4%, 69.4%) | N/A | N/A | N/A | 37.9% | 25.7%, 50.1% | <0.001 | | |

| Results of QUASAR (NCT04033445) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Estimated absolute difference in effect | | | Estimated relative difference in effect | | | Description of methods used for estimation | References |
| **Outcome** | **Study arm** | **N** | **Result (CI)** | **Difference** | **95% CI** | ***P* value** | **Difference [a]** | **95% CI** | ***P* value** | | |
| | Guselkumab 200 mg SC q4w | 88 | n = 47 (53.4%) (CI: 43.0%, 63.8%) | N/A | N/A | N/A | 35.4% | 22.7%, 48.0% | <0.001 | p-values were based on the Cochran-Mantel-Haenszel test, stratified by clinical remission status at maintenance baseline (Yes/No), and induction treatment (guselkumab 400 mg IV, guselkumab 200 mg IV, placebo IV crossover to guselkumab 200 mg IV). | |
| CFB in IBDQ total score, BMSL-naïve subgroup (week M-44) | Placebo SC | 105 | -22.14 (3.34) (-28.7,-15.6), <0.0001 | N/A | N/A | N/A | Reference | | | Least squares means are derived based on a pairwise comparison Mixed-effects Model for Repeated Measures (MMRM) with N number of subjects with IBDQ measurements at baseline and at Week 44. Analyses were performed without stratification to avoid numerical issues. | Johnson & Johnson (9) |
| | Guselkumab 100 mg SC q8w | 103 | -2.199 (3.36) (-8.82,4.421), 0.5137 | N/A | N/A | N/A | 19.944 | 10.61, 29.28 | <0.0001 | | |
| | Placebo SC | 105 | -21.58 (3.46) (-28.4,-14.8), <0.0001 | N/A | N/A | N/A | Reference | | | | |
| | Guselkumab 200 mg SC q4w | 93 | -0.863 (3.66) (-8.07, 6.342), 0.8138 | N/A | N/A | N/A | 20.714 | 10.79, 30.64 | <0.0001 | | |

| Results of QUASAR (NCT04033445) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Estimated absolute difference in effect | | | Estimated relative difference in effect | | | Description of methods used for estimation | References |
| **Outcome** | **Study arm** | **N** | **Result (CI)** | **Difference** | **95% CI** | ***P* value** | **Difference [a]** | **95% CI** | ***P* value** | | |
| CFB in IBDQ total score, BMSL-experienced subgroup (week M-44) | Placebo SC | 74 | -33.37 (3.65) (-40.6,-26.2), <0.0001 | N/A | N/A | N/A | Reference | | | Least squares means are derived based on a pairwise comparison Mixed-effects Model for Repeated Measures (MMRM) with N number of subjects with IBDQ measurements at baseline and at Week 44. Analyses were performed without stratification to avoid numerical issues. | Johnson & Johnson (9) |
| | Guselkumab 100 mg SC q8w | 73 | 0.742 (3.64) (-6.44,7.923), 0.8388 | N/A | N/A | N/A | 34.110 | 23.91, 44.31 | <0.0001 | | |
| | Placebo SC | 74 | 34.61 (3.69); (-41.9,-27.3), <0.0001 | N/A | N/A | N/A | Reference | | | | |
| | Guselkumab 200 mg SC q4w | 105 | -6.292 (3.48) (-13.2,0.572), 0.072 | N/A | N/A | N/A | 28.320 | 18.31, 38.33 | <0.0001 | | |
| Any serious adverse event, BMSL-naïve subgroup (Week M-44) | Placebo SC | 109 | n = 1 (0.9%) | N/A | N/A | N/A | N/A | N/A | N/A | N/A | Johnson & Johnson (9) |
| | Guselkumab 100 mg SC q8w | 104 | n = 3 (2.9%) | N/A | N/A | N/A | N/A | N/A | N/A | | |

| Results of QUASAR (NCT04033445) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Estimated absolute difference in effect | | | Estimated relative difference in effect | | | Description of methods used for estimation | References |
| **Outcome** | **Study arm** | **N** | **Result (CI)** | **Difference** | **95% CI** | ***P* value** | **Difference [a]** | **95% CI** | ***P* value** | | |
| | Guselkumab 200 mg SC q4w | 96 | n = 5 (5.2%) | N/A | N/A | N/A | N/A | N/A | N/A | | |
| Any serious adverse event, BMSL-experienced subgroup (Week M-44) | Placebo SC | 78 | n = 0 (0.0%) | N/A | N/A | N/A | N/A | N/A | N/A | N/A | Johnson & Johnson (9) |
| | Guselkumab 100 mg SC q8w | 75 | n = 2 (2.7%) | N/A | N/A | N/A | N/A | N/A | N/A | | |
| | Guselkumab 200 mg SC q4w | 87 | n = 6 (6.9%) | N/A | N/A | N/A | N/A | N/A | N/A | | |

Abbreviations: AE = adverse event; BMSL = biological and targeted synthetic medicine; CI = confidence interval; COVID-19 = coronavirus disease-19; ICE = intercurrent event; IBDQ = Inflammatory Bowel Disease Questionnaire; IV = intravenous; M = maintenance; N/A = not applicable; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.

Notes:

[a] Adjusted treatment difference.

[b] ICE Strategies: Subjects who had an ostomy or colectomy (ICE 1), a prohibited change in UC medications (ICE 2), or discontinued study agent due to lack of efficacy or an AE of worsening of UC (ICE 3) prior to the designated timepoint were considered not to have achieved any of the key efficacy endpoints shown at the designated timepoint. For subjects who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine (ICE 4) prior to the designated timepoint, their observed values were used, if available. Subjects who experienced ICE 5 (discontinued study agent due to reasons other than those in ICEs 3 and 4) prior to the designated timepoint were considered not to have achieved any of the key efficacy endpoints shown at the designated timepoint.

[c] Nonresponder imputation for missing data: Subjects who were missing one or more of the components pertaining to an endpoint at the designated timepoint were considered not to have achieved the endpoint. Subjects who had an unevaluable biopsy (i.e., a biopsy that was collected, but could not be assessed due to sample preparation or technical errors) were considered not to have achieved the histology endpoints.

[d] ICE Strategies: Subjects who had an ostomy or colectomy (ICE 1), a dose adjustment (including a sham dose adjustment) (ICE 2), a prohibited change in UC medications (ICE 3), or discontinued study agent due to lack of efficacy or an AE of worsening of UC (ICE 4) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44. For subjects who discontinued study agent due to COVID-19 related reasons (excluding COVID-19 infection) or regional crisis in Russia and Ukraine (ICE 5) prior to Week M-44, their observed values (if available) were used. Subjects who experienced ICE 6 (discontinued study agent due to reasons other than those in ICEs 4 and 5) prior to Week M-44 were considered not to have achieved any of the key efficacy endpoints shown at Week M-44.

Source: Janssen Research & Development, 2023 (43); Janssen Research & Development, 2024 (8); Johnson & Johnson (9).

# Appendix C. Comparative analysis of efficacy

N/A

# Appendix D. Literature searches for the clinical assessment

N/A

# Appendix E. Clinical basis for comparison

In Table 37, we present our suggestion for the placement of guselkumab in the DMC's clinical sequence of medications for adult patients with moderate to severe UC who are BMSL-naïve (corresponding to Table 1-1 in Medicinrådet, 2024 (46)).

**Table 37 Suggestion for the DMC's clinical sequence of medications for adult patients with moderate to severe UC who are BMSL-naïve**

| BMSL-naïve patients | Drug | Administration and dose |
|---|---|---|
| Use among at least 70% of the population* | Golimumab (SC) | Induction dose: 200 mg at Week 0, 100 mg at Week 2.<br><br>Maintenance dose: 50 mg (< 80 kg); 100 mg (≥ 80 kg) q4w. |
| | Guselkumab (IV + SC) | Induction dose (IV): 200 mg at Week 0, Week 4, and Week 8.<br><br>Maintenance dose (SC): 100 mg starting at Week 16 and q8w. |
| | Infliximab (IV) | Induction dose: 5 mg/kg at Week 0, 2, and 6.<br><br>Maintenance dose: 5 mg/kg q8w. |
| | Vedolizumab (IV) | Induction dose: 300 mg at Week 0, 2, and 6.<br><br>Maintenance dose: 300 mg q8w. |
| | Vedolizumab (IV + SC) | Induction dose (IV): 300 mg at Week 0 and 2.<br><br>Maintenance dose (SC): 108 mg at Week 6, hereafter 108 every 2 weeks. |
| Consider | Adalimumab (SC) | Induction dose: 160 mg at Week 0, 80 mg at Week 2.<br><br>Maintenance dose: 40 mg every 2 weeks. |
| | Mirikizumab (IV + SC) | Induction dose (IV): 300 mg at Week 0, 4, and 8.<br><br>Maintenance dose (SC): 200 mg q4w. |
| | Ustekinumab (IV + SC) | Induction dose (IV): 260 mg (≤55 kg); 390 mg (>55 kg - ≤85 kg); 520 mg (>85 kg) at Week 0. |

| | | |
|---|---|---|
| | | Maintenance dose (SC): 90 mg at Week 8, hereafter every 12 weeks. |
| Do not use routinely | Etrasimod (per os) | Induction and maintenance dose: 2 mg etrasimod once daily |
| | Filgotinib (per os) | Induction and maintenance dose: 200 mg etrasimod once daily |
| | Ozanimod (per os) | Induction and maintenance dose: Day 1-4: 0,23 mg once daily. Day 5-7: 0,46 mg once daily. Day 8 and hereafter: 0,92 mg once daily. |
| | Tofacitinib (per os) | Induction dose: 10 mg twice daily for 8 weeks.<br>Maintenance dose: 5 mg twice daily. |
| | Upadacitinib (per os) | Induction dose: 45 mg once daily for 8 weeks (and up to 16 weeks with extended induction)<br>Maintenance dose: 15 or 30 mg once daily. |

Abbreviations: BMSL = biological and targeted synthetic medicine; DMC = Danish Medicines Council; IV = intravenous; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.
Notes: * The percentage describes the proportion of the patient population that should, at a minimum, begin treatment with the medication recommended as the first choice in the treatment recommendation. ¤ No conclusion has been made regarding whether the medication can be considered equivalent. Any potential choice between them will depend on a clinical assessment.
Source: Based on Table 1-1 in Medicinrådet, 2024 (46).

In Table 38, we present our suggestion for the placement of guselkumab in the DMC's clinical sequence of medications for adult patients with moderate to severe UC who are BMSL-experienced (corresponding to Table 1-3 in Medicinrådet, 2024 (46)).

**Table 38 Suggestion for the DMC's clinical sequence of medications for adult patients with moderate to severe UC who are BMSL-experienced**

| BMSL-experienceed patients | Drug | Administration and dose |
|---|---|---|
| Use among at least 70% of the population* | Adalimumab (SC) | Induction dose: 160 mg at Week 0, 80 mg at Week 2.<br>Maintenance dose: 40 mg every 2 weeks. |
| | Golimumab (SC) | Induction dose: 200 mg at Week 0, 100 mg at Week 2.<br>Maintenance dose: 50 mg (< 80 kg); 100 mg (≥ 80 kg) q4w. |

| | | |
|---|---|---|
| | Guselkumab (IV + SC) | Induction dose (IV): 200 mg at Week 0, Week 4, and Week 8.<br><br>Maintenance dose (SC): 100 mg starting at Week 16 and q8w. |
| | Infliximab (IV) | Induction dose: 5 mg/kg at Week 0, 2, and 6.<br><br>Maintenance dose: 5 mg/kg q8w. |
| | Mirikizumab (IV + SC) | Induction dose (IV): 300 mg at Week 0, 4, and 8.<br><br>Maintenance dose (SC): 200 mg q4w. |
| | Ustekinumab (IV + SC) | Induction dose (IV): 260 mg (≤55 kg); 390 mg (>55 kg - ≤85 kg); 520 mg (>85 kg) at Week 0.<br><br>Maintenance dose (SC): 90 mg at Week 8, hereafter every 12 weeks. |
| | Vedolizumab (IV) | Induction dose: 300 mg at Week 0, 2, and 6.<br><br>Maintenance dose: 300 mg q8w. |
| | Vedolizumab (IV + SC) | Induction dose (IV): 300 mg at Week 0 and 2.<br><br>Maintenance dose (SC): 108 mg at Week 6, hereafter 108 every 2 weeks. |
| Consider ¤ | Etrasimod (per os) | Induction and maintenance dose: 2 mg etrasimod once daily |
| | Filgotinib (per os) | Induction and maintenance dose: 200 mg etrasimod once daily |
| | Ozanimod (per os) | Induction and maintenance dose: Day 1-4: 0,23 mg once daily. Day 5-7: 0,46 mg once daily. Day 8 and hereafter: 0,92 mg once daily. |
| | Tofacitinib (per os) | Induction dose: 10 mg twice daily for 8 weeks.<br><br>Maintenance dose: 5 mg twice daily. |
| | Upadacitinib (per os) | Induction dose: 45 mg once daily for 8 weeks (and up to 16 weeks with extended induction)<br><br>Maintenance dose: 15 or 30 mg once daily. |

Abbreviations: BMSL = biological and targeted synthetic medicine; DMC = Danish Medicines Council; IV = intravenous; q4w = every 4 weeks; q8w = every 8 weeks; SC = subcutaneous; UC = ulcerative colitis.
Notes: * The percentage describes the proportion of the patient population that should, at a minimum, begin treatment with the medication recommended as the first choice in the treatment recommendation. ¤ No

conclusion has been made regarding whether the medication can be considered equivalent. Any potential choice between them will depend on a clinical assessment.
Source: Based on Table 1-3 in Medicinrådet, 2024 (46).

Medicinrådet

**Danish Medicines Council**
**Secretariat**
Dampfærgevej 21-23, 3rd floor
DK-2100 Copenhagen Ø

+ 45 70 10 36 00
medicinraadet@medicinraadet.dk

www.medicinraadet.dk