Zorginstituut Nederland

> Return address PO Box 320, 1110 AH Diemen

To the Minister of Health, Welfare and Sport
P.O. Box 20350
2500 EJ THE HAGUE

National Health Care Institute
Research, Development and Medicinal Products
Medicinal Products Team

Willem Dudokhof 1
1112 ZA Diemen
PO Box 320
1110 AH Diemen
www.zorginstituutnederland.nl
> Return address PO Box 320, 1110 AH Diemen

T +31 (0)20 797 85 55

Contact
P. Bloemen
warcg@zinl.nl

Our reference
2025019192

Date 20 August 2025
Re: Package advice lock procedure medicinal product guselkumab (Tremfya®) for Crohn's disease

Dear Ms Jansen,

The National Health Care Institute advises you on the assessment of guselkumab (Tremfya®) for the treatment of Crohn's disease. This advice was prompted by the placement of guselkumab in the lock procedure for expensive medicinal products. We advise you to include guselkumab in the health insurance package.

Condition
Crohn's disease is characterised by inflammation of the intestines, with a varying pattern of flare-ups and quiet periods. The inflammation is caused by an uninhibited immune response against bacteria in the intestines. Untreated, these inflammations can affect several layers of the intestinal wall and adjacent organs. Patients are particularly affected by abdominal pain and diarrhoea. The quality of life of patients with Crohn's disease is lower than that of the general population. Crohn's disease affects 331 per 100,000 people. Crohn's disease is treated with topical corticosteroids, systemic corticosteroids, and, in case of inadequate response, tumour necrosis factor alpha inhibitors (TNF-alpha inhibitors). If patients also fail to respond adequately to TNF-alpha inhibitors, ustekinumab, vedolizumab, upadacitinib, risankizumab, and mirikizumab are recommended. All these medical management treatments with different mechanisms of action are intended to induce and maintain disease remission.

Registered indication
Guselkumab (Tremfya®) is indicated for the treatment of adult patients with moderately to severely active Crohn's disease who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic treatment.

In addition, guselkumab (Tremfya®) is registered for plaque psoriasis, psoriatic arthritis, and ulcerative colitis. Guselkumab (Tremfya®) is already being reimbursed for plaque psoriasis and psoriatic arthritis[1]. In July 2025, the National Health Care Institute advised you to reimburse guselkumab (Tremfya®) for

[1] Government Gazette 2025, 15098 | Overheid.nl > Official Statements

certain patients with ulcerative colitis from the basic healthcare package[2].

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Claim by the marketing authorisation holder
Guselkumab (Tremfya®) has a similar value to risankizumab in the treatment of adults with moderately to severely active Crohn's disease who have not responded (adequately) to or are intolerant to a biological medicinal product.

Package advice

The National Health Care Institute recommends that guselkumab (Tremfya®) for the treatment of adult patients with moderately to severely active Crohn's disease who have had an inadequate response, lost response, or were intolerant to biological treatment, be included in the basic healthcare package. The National Health Care Institute has determined that guselkumab meets the legal criterion of established medical science and medical practice for the above indication and that it is equivalent to standard treatment with ustekinumab, vedolizumab, upadacitinib, risankizumab and mirikizumab. Given the equal value, the starting point for inclusion in the package is an equal price.

We explain the preparation of this package advice below.

General
At your request, the National Health Care Institute assesses whether care should be part of the standard health insurance package from the perspective of the basic healthcare package paid from joint premiums.

The National Health Care Institute assesses based on the four package criteria[3]: effectiveness[4], cost-effectiveness[5], necessity[6] and feasibility[7]. The marketing authorisation holder was consulted during the process.

Comprehensive weighting of package criteria
Effectiveness
Established medical science and medical practice
In patients who have had an inadequate response to, lost response, or are intolerant to a TNF-alpha inhibitor, one of the alternative biologicals may be chosen. Since the National Health Care Institute has previously assessed that ustekinumab is similar to other biologicals used after failure on a TNF-alpha inhibitor, and there are direct comparative studies of guselkumab versus ustekinumab, the National Health Care Institute compares guselkumab to ustekinumab in this assessment.

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[2] Advice - reimburse guselkumab (Tremfya®) for the treatment of ulcerative colitis | Advice | National Health Care Institute

[3] Real-world package management 4 (2023). National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl.

[4] Assessment of the established medical science and medical practice (2023). National Health Care Institute. Via www.zorginstituutnederland.nl.

[5] Healthcare cost-effectiveness report (2024) National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl.

[6] Necessity is related to both the medical need due to the severity of a disease for the patient (burden of disease) and the need to insure something. See the report on real-world package management 4 (2023).

[7] The package criterion of feasibility deals with whether it is feasible or sustainable to include a specific form of care in the basic healthcare package. It is therefore mainly a test of a number of implementation aspects such as the healthcare organisation, support, ethical and legal aspects, budget impact and so on. See the report on real-world package management 4 (2023).

In two identical randomised studies (RCTs) GALAXI-2 and GALAXI-3, guselkumab was directly compared with ustekinumab and placebo in adult patients with moderately to severely active Crohn's disease who have not responded (adequately) or were intolerant to conventional therapy or biological treatment.

In the intravenous induction phase, no clinically relevant differences were found between guselkumab and ustekinumab at week 12 in the patient group who had an endoscopic response and remained in clinical remission (Annex 1, Table 1). In the subcutaneous maintenance phase at Week 48, results on endoscopic response, endoscopic remission, and clinical remission were comparable to numerically better with guselkumab compared to ustekinumab (Annex 1, Table 2). The results in patients who previously failed biological treatment were similar to those in patients who had not previously received biological treatment (Annex 1, Table 3). The adverse effects profile of guselkumab is also similar to ustekinumab. On this basis, the National Health Care Institute concludes that guselkumab is equivalent to ustekinumab.

Given the similar value between ustekinumab and the other medicinal products used after failure on a TNF-alpha inhibitor, the National Health Care Institute concludes that guselkumab is an equivalent alternative to ustekinumab, vedolizumab, upadacitinib, risankizumab, and mirikizumab.

Cost-effectiveness
Due to its equal value, the National Health Care Institute has not assessed its cost-effectiveness.

Budget impact analysis
As 5 medicinal products are already available and being reimbursed for the above indication, the National Health Care Institute has not prepared a comprehensive budget impact analysis for guselkumab for pragmatic reasons.

Between 2020 and 2024, the number of patients with active Crohn's disease being treated increased by an average of 22% per year. The physicians' association expects this trend to stabilise in the coming years. At present, nearly 7,500 patients are treated with ustekinumab, vedolizumab, risankizumab or upadacitinib (see Annex 2 for a distribution overview). The patent for ustekinumab has already expired, and that of vedolizumab will expire soon (Q1/2 2026). With the availability and development of biosimilars for these medicinal products, the number of users for both agents could increase further. The National Health Care Institute therefore notes that the introduction of biosimilars may limit the room for newer products, such as guselkumab.

The total average cost per patient of guselkumab has been estimated at €18,203 in the starting year and €16,171 in subsequent maintenance years. For ustekinumab, these costs are estimated at €16,441 in the starting year of treatment and €14,559 in the maintenance years (for the justification of these numbers, see Annex 2). However, the National Health Care Institute assumes that the sector has established price arrangements, which means that the prices actually paid are lower than the list prices. When similar price arrangements are also made for guselkumab, the National Health Care Institute expects the budget impact to be neutral. It is important to note that initial non-responders to the standard dosage are treated with a higher dose of guselkumab. Based on the list price, this costs almost twice as much as mirikizumab.

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Other considerations
In Dutch practice, according to the physicians' association, a second biological, including guselkumab, will be a treatment option if patients have not responded (adequately) or were intolerant to a TNF-alpha inhibitor. The package advice is based on this input from the physicians' association and relates to patients who have previously used a biological, usually a TNF-alpha inhibitor. The physicians' association has a lot of experience with anti-TNF-alpha inhibitors, but the choice is (also) motivated by price. The physicians' association has indicated that the unique preference for a TNF-alpha inhibitor may change if the price goes down after the patent for ustekinumab expires. Taking this input into account, the National Health Care Institute reports that the GALAXI studies were conducted with patients who were using either conventional therapy or a biological prior to the study. Based on these studies, the National Health Care Institute can conclude that the equivalent value of guselkumab with ustekinumab applies to the entire study population and thus also to patients who previously only used conventional therapy.

Should you need any further information, please do not hesitate to contact us. The explanation of the PT assessment is given in Annexes 1 and 2.

Yours sincerely,

M.J. Janssen
Chairperson of the Executive Board

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Annex 1

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Explanation effectiveness assessment
In the two identical, randomised, double-blind, phase III studies GALAXI-2 and GALAXI-3, guselkumab was directly compared to ustekinumab and placebo in adult patients with moderately to severely active Crohn's disease who have not responded (adequately) or were intolerant to conventional therapy or biological treatment.

In the intravenous induction phase, no clinically relevant differences were found between guselkumab and ustekinumab at week 12 in the patient group who had an endoscopic response and remained in clinical remission (Table 1).

Table 1. Effectiveness of guselkumab and ustekinumab compared to placebo at **Week 12 (induction phase)** in the pooled GALAXI-2 and GALAXI-3 dataset

	Placebo (n=148)	**Guselkumab 200 mg combined[a] (n=582)**	**Ustekinumab[b] (n=291)**
Clinical remission			
n (%)	28 (19)	274 (47)	137 (47)
Adjusted treatment difference, % (95% CI)		28 (21;36)	29 (20;37)
Nominal p-value		<0.001	<0.001
Endoscopic response			
n (%)	18 (12)	215 (37)	98 (34)
Adjusted treatment difference, % (95% CI)		25 (19;31)	22 (15;30)
Nominal p-value		<0.001	0.001

[a]Patients assigned to either guselkumab group; until assessment at Week 12, guselkumab patients had received only guselkumab 200 mg intravenously.
[b]Induction dose IV 6 mg/kg at week 0, then maintenance dose SC 90 mg at week 8

Clinical remission: CDAI Score <150; endoscopic response: ≥50% improvement from baseline in SES-CD score or SES-CD score ≤2

CI, confidence interval, CDAI, Crohn's Disease Activity Index; IV, intravenous, SC, subcutaneous; SES-CD, Simple Endoscopic Score for Crohn's Disease

In the subcutaneous maintenance phase at Week 48, results on clinical remission, endoscopic response, and endoscopic remission were similar to better with guselkumab compared to ustekinumab (Table 2). The results in patients who had previously failed on biological treatment were similar to those in the overall population (Table 3).

Table 2. Effectiveness of guselkumab over ustekinumab at **Week 48 (maintenance phase)** in the pooled GALAXI-2 and GALAXI-3 dataset

	Guselkumab 100 mg[a]	**Guselkumab 200 mg[b]**	**Ustekinumab[c]**	**Difference guselkumab 100 mg and ustekinumab, % (95% CI)**	**Difference guselkumab 200 mg and ustekinumab, % (95% CI)**
n GALAXI-2	143	146	143		
n GALAXI-3	143	150	148		
Clinical remission (%)	187/286 (65)	208/296 (70)	183/291 (63)	3 (-5;10) p=0.512	7 (0;15) p=0.058
Endoscopic response (%)	137/286 (48)	156/296 (53)	108/291 (37)	11 (3;19) p=0.0085	16 (8;23) p<0.0001
Endoscopic remission (%)	95/286 (33)	110/296 (37)	72/291 (25)	9 (1;16) p=0.024	12 (5;20) p=0.0011

[a]Induction dose IV 200 mg at weeks 0, 4, 8; then maintenance dose SC 100 mg every 8 weeks of weeks 16-40
[b]Induction dose IV 200 mg at weeks 0, 4, 8; then maintenance dose SC 200 mg every 4 weeks of weeks 12-40
[c]Induction dose IV ~6 mg/kg at week 0; then maintenance dose SC 90 mg every 8 weeks of weeks 8-40

Clinical remission: CDAI Score <150; endoscopic response: ≥50% improvement from baseline in SES-CD score or SES-CD score ≤2; endoscopic remission: SES-CD score ≤4, ≥2 points reduction from baseline, and no SES-CD subscore >1 in any individual component

CI, confidence interval, CDAI, Crohn's Disease Activity Index; IV, intravenous, SC, subcutaneous; SES-CD, Simple Endoscopic Score for Crohn's Disease

Table 3. Effectiveness of guselkumab compared to ustekinumab at **Week 48 (maintenance phase)** in the pooled GALAXI-2 and GALAXI-3 dataset in patients who do not react (adequately) or who do not tolerate biological treatment.

	Guselkumab 100 mg[a]	**Guselkumab 200 mg[b]**	**Ustekinumab[c]**	**Difference guselkumab 100 mg and ustekinumab, % (95% CI)**	**Difference guselkumab 200 mg and ustekinumab, % (95% CI)**
Clinical remission (%)	93/153 (61)	94/147 (64)	82/156 (53)	8 (-3;19)	12 (0;23)
Endoscopic response (%)	66/153 (43)	69/147 (47)	49/156 (31)	11 (1;22)	15 (5;26)
Endoscopic remission (%)	43/153 (28)	42/147 (29)	32/156 (21)	8 (-2;17)	8 (-1;18)

[a]Induction dose IV 200 mg at weeks 0, 4, 8; then maintenance dose SC 100 mg every 8 weeks of weeks 16-40
[b]Induction dose IV 200 mg at weeks 0, 4, 8; then maintenance dose SC 200 mg every 4 weeks of weeks 12-40
[c]Induction dose IV ~6 mg/kg at week 0; then maintenance dose SC 90 mg every 8 weeks of weeks 8-40

Clinical remission: CDAI Score <150; endoscopic response: ≥50% improvement from baseline in SES-CD score or SES-CD score ≤2; endoscopic remission: SES-CD score ≤4, ≥2 points reduction from baseline, and no SES-CD subscore >1 in any individual component

CI, confidence interval, CDAI, Crohn's Disease Activity Index; IV, intravenous, SC, subcutaneous; SES-CD, Simple Endoscopic Score for Crohn's Disease

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Annex 2

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Distribution treatment of patients with Crohn's disease with secondary line biological
In 2024, the majority of patients on a secondary-line biological were treated with ustekinumab (~60%), followed by vedolizumab (~30%) (Vektis data). The remaining patients were treated with the newer products risankizumab (~6%) and upadacitinib (~4%). The marketing authorisation holder expects guselkumab to take 5% to 7.5% of the total market.

Rationale for the costs for guselkumab and ustekinumab per year
The estimate, described in the letter, is based on list prices, the distribution between intravenous and subcutaneous induction therapy (90% versus 10%), and the distribution between the low (100 mg every 8 weeks from week 16) and high (200 mg every 4 weeks from week 16) maintenance dose (80% versus 20%). Based on the input of the physicians' association regarding the dosage and ratio of intravenous versus subcutaneous, the cost per patient per year of ustekinumab is €16,441 in the starting year of treatment and €14,559 in the maintenance years. In the reimbursement advice of mirikizumab[8], the National Health Care Institute states that the total cost per patient of the standard treatments amounts to €16,661 to €20,808 in the starting year of treatment and €13,422 to €16,276 for the maintenance years.