

## Journal of Dermatological Treatment



ISSN: (Print) (Online) Journal homepage: <a href="https://www.tandfonline.com/loi/ijdt20">https://www.tandfonline.com/loi/ijdt20</a>

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**To cite this article:** Matthias Augustin , Daniel Wirth , Jörg Mahlich , Alicia N. Pepper & Cheryl Druchok (2020): Cost per responder analysis of guselkumab versus targeted therapies in the treatment of moderate to severe plaque psoriasis in Germany, Journal of Dermatological Treatment, DOI: 10.1080/09546634.2020.1793891

To link to this article: <a href="https://doi.org/10.1080/09546634.2020.1793891">https://doi.org/10.1080/09546634.2020.1793891</a>

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### ARTICLE 3 OPEN AG



# Cost per responder analysis of guselkumab versus targeted therapies in the treatment of moderate to severe plaque psoriasis in Germany

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#### **ABSTRACT**

**Background:** The fully human monoclonal antibody guselkumab is an effective treatment option for patients with moderate to severe psoriasis.

**Objective:** The objective of this study was to examine the cost per responder of guselkumab compared with other targeted therapies for the treatment of moderate to severe plaque psoriasis in Germany.

**Methods:** A one-year cost per responder model was developed based on efficacy and safety data from a published network meta-analysis. Drug, treatment administration, resource use, and adverse event costs were included in the analysis. The primary analysis assessed the cost per Psoriasis Area and Severity Index (PASI) 90 responder at week 16. Additional analyses were conducted at year 1. In the year 1 analyses, treatment response was assessed at the end of the induction period (week 16) to determine which patients continued onto maintenance therapy (responders) and which patients moved onto a subsequent adalimumab or secukinumab therapy (non-responders).

**Results:** At week 16, the cost per PASI 90 responder was lower for guselkumab than all comparators except adalimumab and brodalumab. Similarly, in the year 1 analyses, guselkumab had a lower cost per PASI 90 responder than all comparators except brodalumab.

**Conclusions:** Guselkumab is a cost-effective therapy option in Germany.

#### **ARTICLE HISTORY**

Received 1 July 2020 Accepted 4 July 2020

#### **KEYWORDS**

Guselkumab; psoriasis; biologic; cost per responder

#### Introduction

Psoriasis is a painful chronic dermatologic condition characterized primarily by autoimmune-mediated inflammation of the skin (1). The most common form of the condition is plaque-type psoriasis, which affects  $\sim\!80$  to 90% of patients (2). The prevalence of psoriasis in Germany is around 2.5% (3–5). Approximately 25% of the patients have moderate to severe psoriasis (3,4), typically defined as a body surface area (BSA)  $>\!10\%$  and a Psoriasis Area and Severity Index (PASI) score  $>\!10$  (6).

Psoriasis is associated with substantial clinical and economic burden. It has a negative impact on health-related quality of life (7–9) and is associated with several comorbidities (10). Psoriasis is associated with substantial costs related to therapy, resource use, and lost productivity (11). Cost-of-illness studies conducted in Germany have shown that mean total annual costs of psoriasis management were approximately  $7000 \in$ , a considerable economic burden on society, public payers, and individuals (12,13). A more recent study conducted in Germany reported a similar mean total annual costs, with a greater proportion of the costs attributed to systemic drug costs, including targeted therapies, than in previous studies (14).

Targeted therapies are typically recommended for patients with moderate to severe psoriasis when other therapeutic options, including conventional systemic therapies, have not demonstrated satisfactory therapeutic success, are not tolerated, or are contraindicated (6). The most recent recommendations suggest that newer therapies can also be used as first-line treatments. In Germany, several targeted therapies are available for the treatment of moderate to severe plaque psoriasis and have been shown to be highly efficacious (15). These include: tumor necrosis factor alpha inhibitors (TNF- $\alpha$ ) (e.g. adalimumab, etanercept, and infliximab), interleukin 17 (IL-17) inhibitors (e.g. brodalumab, ixekizumab, and secukinumab), an IL-12/23 inhibitor (i.e. ustekinumab), IL-23 inhibitors (e.g. guselkumab and tildrakizumab), and a targeted small molecule (i.e. apremilast).

Guselkumab is a targeted therapy indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy (16). It is a fully human monoclonal antibody that binds selectively to the p19 subunit of the extracellular IL-23 protein with high specificity and affinity. Compared with the mechanisms of action for other targeted therapies, inhibition of IL-23 may provide a more targeted and upstream blockade of the inflammatory pathway involved in psoriasis. Clinical trials have demonstrated superior short-term

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efficacy versus placebo and adalimumab, and superior longterm efficacy versus adalimumab and secukinumab (17–19). Compared with other targeted therapies, network meta-analyses (NMAs) suggest guselkumab is one of the most effective thera-

Targeted therapies, while efficacious are costly, and as psoriasis is a chronic disease it is important to consider their economic value. The objective of this study was to examine the cost effectiveness of guselkumab compared with other targeted therapies for the treatment of moderate to severe plaque psoriasis in Germany using a cost per responder model.

#### Materials and methods

#### Population and response definition

The population of interest for the model were adults with moderate to severe psoriasis who are candidates for systemic therapy. The mean body weight (21) and the percentage of patients in Germany weighing more than 100 kg (21), were used to accurately cost infliximab and ustekinumab. The response definition used in the model was the Psoriasis Area and Severity Index (PASI) 90 response. The index scores psoriasis based on lesion severity (redness, thickness, and scaling) and affected skin surface area (22). A PASI 90 response is defined as a greater than or equal to 90% improvement in PASI score from baseline. While a PASI 75 response (i.e. 75% improvement in PASI score from baseline) was previously considered the treatment target, PASI 90 is becoming the new standard for treatment efficacy as more efficacious targeted therapies become available (23-26). Greater PASI responses are associated with improved healthrelated quality of life and are a common treatment goal for patients (24,25).

#### **Comparators**

Targeted therapies currently reimbursed in Germany were included as comparators in the model: adalimumab 40 mg every two weeks (Q2W), apremilast 30 mg twice daily (BID), brodalumab 210 mg Q2W, etanercept 50 mg once weekly (QW) (twice weekly for the first 12 weeks), infliximab 5 mg/kg every eight weeks (Q8W), ixekizumab 80 mg Q2W, secukinumab 300 mg monthly, tildrakizumab 100 mg every 12 weeks (Q12W), and ustekinumab Q12W (45 mg for <100 kg and 90 mg for >100 kg). Dosing regimens for each therapy were based on European Medicines Agency (EMA) Summary of Product Characteristics (SmPCs) (16,27-36).

#### Model structure and analyses

A one-year cost per responder model was developed in Microsoft Excel® 2016 (Microsoft®, Redmond, WA, USA) to compare guselkumab with other reimbursed targeted therapies in the first-line treatment of moderate to severe psoriasis. In the primary analysis, costs and treatment response (PASI 90) were assessed at the end of the induction period (week 16). Secondary analyses were also conducted at year 1. The treatment response at week 16 was used to determine which patients continued onto maintenance therapy (responders) and which patients moved onto a subsequent therapy (non-responders). PASI 90 responders continued the current treatment until the end of one year. Patients who did not achieve a PASI 90 response moved to a subsequent therapy and remained on that therapy for the duration of the time horizon. Adalimumab and secukinumab were selected as the subsequent therapies in the year 1 analyses because they are the therapies most commonly switched to after first-line treatment in Germany (37). Discontinuation from second-line treatment was not considered in the model; patients remained on treatment until the end of the one-year time horizon.

Scenario analyses were also conducted using an alternative responder definition, PASI 75, and using different subsequent therapies in the year 1 analyses.

#### Model inputs

Treatment efficacy was based on a published NMA of biologics for the treatment of moderate to severe psoriasis during induction (20). The NMA was informed by a systematic literature review that identified published phase 3 randomized controlled trials (RCTs) of infliximab, adalimumab, etanercept, ustekinumab, guselkumab, tildrakizumab, brodalumab, ixekizumab, secukinumab, apremilast, and biosimilar treatments. At the time of the systematic literature review (SLR), phase 3 RCT data were not published for risankizumab or certolizumab, therefore they were not included in the NMA. The absolute probability of a PASI 90 response from the NMA was used to define the number of treatment responders. The results of the NMA suggested that guselkumab had the second highest probability of a PASI 90 response (Table 1) compared to other treatments.

Several costs were considered in the model: drug costs, treatment administration costs, resource use costs, adverse event costs, and non-responders costs (year 1 analyses only). All costs are reported in 2020 Euros.

Drug costs were calculated based on the Lauer-Taxe March 2020 (38). Costs for etanercept, adalimumab, and infliximab were assumed to be the cost of their respective biosimilars.

Table 1. Costs, efficacy, and safety inputs per drug.

Treatment	Formulation (mg)	Formulation costs (€) <sup>a</sup>	PASI 90 response (%) <sup>b</sup>	Probability of SAEs (during induction) (%) <sup>b</sup>
Guselkumab	100	3044.92	73.01	2.35
Adalimumab	40	441.01	51.73	2.34
Apremilast	30	19.49	11.11	2.70
Brodalumab	210	691.98	71.20	1.60
Etanercept	50	279.39	24.89	1.97
Infliximab	100	560.64	56.57	4.59
Ixekizumab	80	1391.32	74.02	1.99
Secukinumab	300	1723.91	61.80	2.34
Tildrakizumab	100	3477.77	39.91	1.71
Ustekinumab	45 or 90	4891.92	46.44	1.66

<sup>&</sup>lt;sup>a</sup>Formulation costs obtained from the Lauer-Taxe (38).

<sup>&</sup>lt;sup>b</sup>Absolute probabilities from Cameron et al. (20).

Table 2. Resource use costs and frequency of use during the induction period.

Resource	Costs per resource (€) <sup>a</sup>	GUS, BRO, IXE, TIL	ADA, ETA	APR	IFX	SEC	UST
Dermatologist visit	15.71	2	2	2	3	2	2
Tuberculosis QuantiFERON/Interferon-gamma assay	58.00	1	1	0	1	1	1
Chest x-ray	10.00	1	1	1	1	1	1
Hepatitis B/C serology	5.50	0	1	0	1	0	1
Full blood count	1.10	2	3	2	4	3	2
Liver function test	2.70	2	3	2	4	3	2
Test for urea and electrolytes	1.50	2	2	2	3	2	2

<sup>a</sup>Unit costs were obtained from the uniform value scale (39).

ADA: adalimumab; APR: apremilast; BRO: brodalumab; ETA: etanercept; GUS: quselkumab; IFX: infliximab; IXE: ixekizumab; SEC: secukinumab; TIL: tildrakizumab; UST: ustekinumab.

Table 3. Summary of week 16 costs (€).

	Drug costs	Treatment administration costs	Resource use costs	AE costs	Total costs
Guselkumab	9135	0	110	88	9333
Adalimumab	4410	0	119	88	4617
Apremilast	4247	0	52	102	4400
Brodalumab	6228	0	110	60	6398
Etanercept	7823	0	119	74	8016
Infliximab .	11,213	383	140	173	11,909
lxekizumab	11,131	0	110	75	11,315
Secukinumab	12,067	0	114	88	12,269
Tildrakizumab	6956	0	110	64	7130
Ustekinumab	9784	0	116	62	9962

Drug costs for infliximab included drug wastage (i.e. the cost of full vials was used). A treatment administration costs was also applied to patients who received infliximab (95.81 € per intravenous administration) (39).

Resource use costs were also considered in the model. Resources included: dermatologist visits, tuberculosis QuantiFERON/Interferon-gamma assay, chest x-ray, hepatitis B/C serology, full blood count, liver function test, and test for urea and electrolytes (39). The frequency of use during the induction period varied and was based on respective SmPCs (16,27-36), German S3-guidelines (15), and expert clinical opinion (Table 2). For the maintenance period, the frequency of use was the same for all therapies: biannual dermatologist visits, full blood counts, liver function tests, and tests for urea and electrolytes.

The cost of adverse events was also included in the model. The absolute probability of a serious adverse event (SAE) was informed by the SAE NMA conducted by Cameron et al. (20) (Table 1). The cost of a SAE was based on a weighted average cost of all SAEs (40) that occurred in the guselkumab phase 3 clinical trials, VOYAGE 1 and VOYAGE 2 (41,42) (3182.43 €) (Table S1).

A non-responder cost for additional healthcare resource use was also considered in the model for the year 1 analyses. This cost was applied to patients who failed to respond to the firstline therapy. It was applied at the start of the subsequent therapy on a weekly basis for 16 weeks. The cost was based on the annual cost of health care (inpatient treatment, medication, and outpatient treatment) in patients with psoriasis not adequately controlled by conventional systemic therapies (12). The cost was inflated from 2004 to 2020 and converted to a weekly cost (133.82 €).

#### **Results**

#### Week 16

The primary analysis at week 16 demonstrated that total costs were lower for guselkumab compared to infliximab, ixekizumab,

secukinumab, and ustekinumab (Table 3). Drug costs contributed the most to the total costs, with treatment administration, resource use, and AE costs making up only a small proportion of the total costs (Table 3). Guselkumab had greater efficacy (i.e. higher absolute probability of PASI 90 response) than all comparators except ixekizumab (Table 1). The cost per PASI 90 responder ranged from 8926 € for adalimumab to 39,607 € for apremilast (Figure 1). The cost per PASI 90 responder was 12,783 € for guselkumab, which was lower than all comparators except adalimumab and brodalumab (Figure 1). The cost per PASI 90 responder for guselkumab was 2504 € to 26,823 € lower compared with the other targeted therapies. Scenario analyses showed that trends in results were similar when PASI 75 was used to define a responder (results not shown).

#### Year 1

In alignment with the week 16 analyses, the drug costs made up the greatest proportion of the total costs over one year (Table S2). In the year 1 analyses, the cost per PASI 90 responder ranged from 26,175 € to 140,055 € and 30,973 € to 234,955 € when adalimumab and secukinumab were selected as subsequent therapies, respectively (Figure 2). The cost per PASI 90 responder was greater when secukinumab was selected as a subsequent therapy. Scenario analyses showed that trends in results were consistent across other subsequent therapy selections (results not shown).

Like the week 16 analyses, guselkumab had a lower cost per PASI 90 responder than all comparators except brodalumab (Figure 2). In contrast to the week 16 analyses, adalimumab had a higher cost per PASI 90 responder than guselkumab when the cost of a subsequent therapy (secukinumab) for non-responders was also considered. The cost per PASI 90 responder for guselkumab was 2383 € to 201,204 € lower compared with other targeted therapies.

Trends in results for the year 1 analyses were similar for scenario analyses that used PASI 75 as a responder definition. In

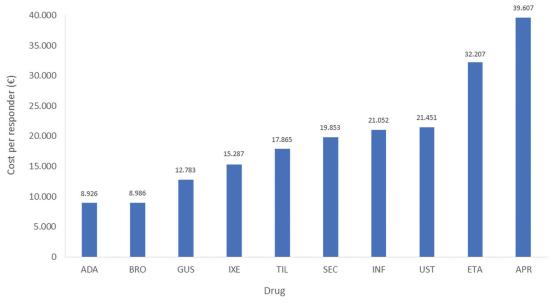


Figure 1. Cost per PASI 90 responder per drug at week 16. ADA: adalimumab; APR: apremilast; BRO: brodalumab; ETA: etanercept; GUS: guselkumab; IFX: infliximab; IXE: ixekizumab; SEC: secukinumab; TIL: tildrakizumab; UST: ustekinumab.

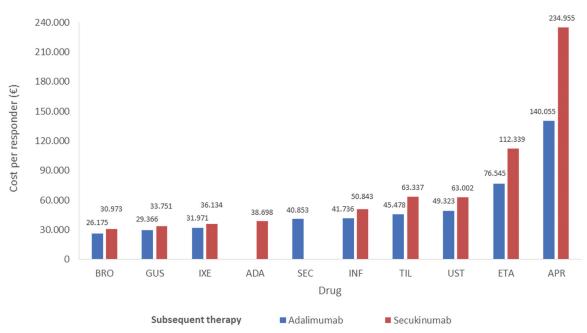


Figure 2. Cost per PASI 90 responder per drug at year 1 with adalimumab and secukinumab as subsequent therapies. ADA: adalimumab; APR: apremilast; BRO: brodalumab; ETA: etanercept; GUS: guselkumab; IFX: infliximab; IXE: ixekizumab; SEC: secukinumab; TIL: tildrakizumab; UST: ustekinumab.

the scenario using PASI 75, all comparators had a higher cost per responder than guselkumab, except for adalimumab, which contrasts with the PASI 90 year 1 analyses, where only brodalumab had a lower cost per responder than guselkumab (results not shown).

#### **Discussion**

This study is the first to demonstrate the economic value of guselkumab in Germany. Guselkumab had a lower cost per PASI 90 responder than apremilast, etanercept, infliximab,

ixekizumab, secukinumab, tildrakizumab, and ustekinumab at 16 weeks and over one year of treatment. Only brodalumab and adalimumab had lower cost per PASI 90 responder at week 16 than guselkumab because they were associated with much lower drug costs. The year 1 analyses demonstrated that irrespective of the subsequent therapy, guselkumab had a lower cost per PASI 90 responder compared to all therapies, except brodalumab.

The results of these analyses generally align with the results of a similar analysis that also examined the cost per PASI 90 responder for targeted therapies in Germany (43). The cost per

PASI 90 responder for secukinumab and ustekinumab over 16 weeks and one year were similar across studies; both analyses suggested secukinumab had a lower cost per PASI 90 responder than ustekinumab. Absolute cost per responder results for adalimumab, etanercept, and infliximab were not as comparable across studies because biosimilar costs were assumed in the current analyses, whereas only a proportion of etanercept and infliximab costs were attributed to biosimilar costs in Augustin et al. (43). However, the relative order of therapies with respect to increasing cost per responder (adalimumab, infliximab, and etanercept, respectively) aligns between both the studies. The current model also included additional targeted therapies that were not included in Augustin et al. (43): guselkumab, apremilast, brodalumab, ixekizumab, tildrakizumab.

The results of the model also align with similar analyses conducted in other countries. However, like Augustin et al. (43), most previous analyses have only included adalimumab, etanercept, infliximab, secukinumab, and ustekinumab, so comparisons are limited. A Spanish study found that secukinumab and ustekinumab had a lower cost per responder than adalimumab, etanercept, and infliximab (44). In Puig et al. (44), etanercept had the highest cost per responder, which aligns with the current study if considering only those treatments that were consistent across studies. Etanercept was also shown to have the highest cost per responder in two studies from the United States (US) (45,46). Cost per responder analyses that included ixekizumab found that it had one of the lowest cost per responder, in alignment with the current model results (45,47). Guselkumab was not included in the studies discussed above. A US cost per responder study based on head-to-head clinical data, did however show that guselkumab had a lower cost per PASI 90 responder than adalimumab at one year (48). Two other US analyses, which used naïve indirect comparisons of efficacy, showed that guselkumab also had a lower cost per PASI 90 responder than ixekizumab and secukinumab over one year (49,50). A United Kingdom cost per responder study based on head-to-head clinical data showed similar results: guselkumab had a lower cost per PASI 90 responder than secukinumab at all timepoints assessed from week 12 to 48 (51).

Given the chronic nature of psoriasis, it is important to examine the economic value of targeted therapies over a longer time horizon. In addition to demonstrating the economic benefit of guselkumab over one year, the year 1 analyses were designed to explore the impact of various subsequent therapies on the cost per responder. The year 1 analyses showed that trends in results were consistent across subsequent therapy selections. As expected, the cost per PASI 90 responder was greater when a higher cost subsequent therapy, such as secukinumab, was selected compared to a less costly therapy, such as biosimilar adalimumab.

There are limitations with the current model. The model uses published list prices, therefore any confidential rebates that are provided in individual or selective contracts are not captured. Moreover, the response rates that were used in the current model are based on clinical trial data and do not necessarily reflect real world clinical practice in Germany. A recent claims data analysis found that 80% of patients who initiated treatment with ustekinumab were still on therapy after one year (52), suggesting that a higher response rate may be achieved in the real world compared to the current model (46%). Using higher response rates in the model would lower the cost per

responder, so the current results are likely a conservative estimate.

There are also limitations with the year 1 analyses. In the model, patients who were non-responders at week 16 received the same subsequent therapy for the remainder of the year. Discontinuation and efficacy of the subsequent therapy were not considered because real-world data beyond first-line treatment are limited. In clinical practice, however, patients who do not respond to treatment would likely cycle through other therapies until an effective one was found. With several targeted therapies available, treatment with multiple lines of therapy is now common clinical practice (53,54). A more complex modeling approach than a cost per responder model is needed to capture the cost effectiveness associated with a sequence of treatments and responses.

Future models may consider longer time horizons to capture the current clinical practice where multiple lines of therapy are used. Future analyses may also consider comparisons versus the newest targeted therapies indicated for moderate to severe psoriasis, certolizumab pegol and risankizumab. These comparators were not considered in the current study because they were not included in the NMA used to inform comparative efficacy, as it was conducted before their EMA approval and the availability of published phase 3 clinical trial data.

In conclusion, guselkumab had a lower cost per PASI 90 responder than almost all targeted therapies, suggesting it is a cost-effective treatment option for moderate to severe psoriasis in Germany.

#### **Disclosure statement**

EVERSANA received financial support from Janssen-Cilag, Germany for the conduct of this study. MA has served as consultant to companies that manufacture drugs for the treatment of psoriasis, including AbbVie, Almirall, Amgen, Biogen (Biogen Idec), Boehringer Ingelheim, Celgene, Centocor, Eli Lilly and Company, Janssen-Cilag, LEO Pharma, Medac, MSD (formerly Essex, Schering-Plough), Mundipharma, Novartis, Pfizer (formerly Wyeth), Pohl Boskamp, Sandoz, and XenoPort. DW and JM are employees of Janssen-Cilag. ANP and CD are employees of EVERSANA. EVERSANA consults for various pharmaceutical, medical device, and biotech companies.

#### **Funding**

This study was supported by Janssen-Cilag, Germany.

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#### Data availability statement

The data are available on reasonable request to the corresponding author.

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