Gemeinsamer Bundesausschuss

Justification

of the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V:
Satralizumab
(neuromyelitis optica spectrum disorders, anti-aquaporin-4IgG seropositive, ≥ 12 years)

of 6 January 2022

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assesses the benefit of reimbursable medicinal products with new active ingredients.

For medicinal products for the treatment of a rare disease (orphan drugs) that are approved according to Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999, the additional medical benefit is considered to be proven through the grant of the marketing authorisation according to Section 35a paragraph 1, sentence 11, 1st half of the sentence German Social Code, Book Five (SGB V), the additional medical benefit is considered to be proven through the grant of the marketing authorisation. Evidence of the medical benefit and the additional medical benefit in relation to the appropriate comparator therapy do not have to be submitted (Section 35a, paragraph 1, sentence 11, 2nd half of the sentence SGB V). Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V thus guarantees an additional benefit for an approved orphan drug, although an assessment of the orphan drug in accordance with the principles laid down in Section 35a paragraph 1, sentence 3, No. 2 and 3 SGB V in conjunction with Chapter 5 Sections 5 et seq. of the Rules of Procedure (VerfO) of the G-BA has not been carried out. In accordance with Section 5, paragraph 8 AM-NutzenV, only the extent of the additional benefit is to be quantified indicating the significance of the evidence.

However, the restrictions on the benefit assessment of orphan drugs resulting from the statutory obligation to the marketing authorisation do not apply if the turnover of the medicinal product with the SHI at pharmacy sales prices and outside the scope of SHI-accredited medical care, including VAT exceeds € 50 million in the last 12 calendar months. According to Section 35a paragraph 1, sentence 12 SGB V, the pharmaceutical company must then, within three months of being requested to do so by the G-BA, submit evidence according to Chapter 5, Section 5, subsection 1–6 VerfO, in particular regarding the additional medical benefit in relation to the appropriate comparator therapy as defined by the G-BA according to Chapter 5 Section 6 VerfO and prove the additional benefit in comparison with the appropriate comparator therapy.

In accordance with Section 35a paragraph 2 SGB V, the G-BA decides whether to carry out the benefit assessment itself or to commission the Institute for Quality and Efficiency in Health Care (IQWiG). Based on the legal requirement in Section 35a paragraph 1 sentence 11 SGB V that the additional benefit of an orphan drug is considered to be proven through the grant of the marketing authorisation the G-BA modified the procedure for the benefit assessment of orphan drugs at its session on 15 March 2012 to the effect that, for orphan drugs, the G-BA initially no longer independently determines an appropriate comparator therapy as the basis for the solely legally permissible assessment of the extent of an additional benefit to be assumed by law. Rather, the extent of the additional benefit is assessed exclusively on the basis of the approval studies by the G-BA indicating the significance of the evidence. Rather, the extent of the additional benefit is assessed exclusively on the basis of the marketing authorisation studies by the G-BA, indicating the significance of the evidence.

Accordingly, at its session on 15 March 2012, the G-BA amended the mandate issued to the IQWiG by the resolution of 1 August 2011 for the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a paragraph 2 SGB V to that effect that, in the case of orphan drugs, the IQWiG is only commissioned to carry out a benefit assessment in the case of a previously defined comparator therapy when the sales volume of the medicinal product concerned has exceeded the legal limit of € 50 million and is therefore subject to an unrestricted benefit assessment (cf. Section 35a paragraph 1, sentence 12 SGB

V). According to Section 35a paragraph 2 SGB V, the assessment by the G-BA must be completed within three months of the relevant date for submission of the evidence and published on the internet.

According to Section 35a paragraph 3 SGB V, the G-BA decides on the benefit assessment within three months of its publication. The resolution is to be published on the internet and forms part of the Pharmaceuticals Directive.

2. Key points of the resolution

The relevant date for the first placing on the (German) market of the active ingredient satralizumab in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure of the G-BA (VerfO) is 15 July 2021. The pharmaceutical company submitted the final dossier to the G-BA in accordance with Section 4, paragraph 3, number 1 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM- NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 1 VerfO on 5 July 2021.

Satralizumab as monotherapy or in combination with immunosuppressive therapy for the treatment of neuromyelitis optica spectrum disorders in adults and adolescents aged 12 years and above who are anti-aquaporin-4IgG seropositive is approved as a medicinal product for the treatment of rare diseases under Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999.

In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional benefit is considered to be proven through the grant of the marketing authorisation. The extent of the additional benefit and the significance of the evidence are assessed on the basis of the marketing authorisation studies by the G-BA.

The G-BA carried out the benefit assessment and commissioned the IQWiG to evaluate the information provided by the pharmaceutical company in Module 3 of the dossier on treatment costs and patient numbers. The benefit assessment was published on 15 October 2021 together with the IQWiG assessment on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA has adopted its resolution on the basis of the pharmaceutical company's dossier, the dossier assessment carried out by the G-BA, the IQWiG assessment of treatment costs and patient numbers (IQWiG G21-22) and the statements made in the written statements and oral hearing process, as well of the amendment drawn up by the G-BA on the benefit assessment.

In order to determine the extent of the additional benefit, the G-BA has assessed the studies relevant for the marketing authorisation considering their therapeutic relevance (qualitative) in accordance with the criteria laid down in Chapter 5, Section 5, paragraph 7, sentence 1, numbers 1 – 4 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of satralizumab.

[1] General Methods, version 6.0 from 05.11.2020. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

2.1 Additional benefit of the medicinal product

2.1.1 Approved therapeutic indication of Satralizumab (Enspryng) in accordance with the product information

Enspryng is indicated as a monotherapy or in combination with immunosuppressive therapy (IST) for the treatment of neuromyelitis optica spectrum disorders (NMOSD) in adult and adolescent patients from 12 years of age who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive.

Therapeutic indication of the resolution (resolution of 6 January 2022):

see the approved therapeutic indication

2.1.2 Extent of the additional benefit and significance of the evidence

In summary, the additional benefit of satralizumab is assessed as follows:

Adult and adolescent patients from 12 years of age with neuromyelitis optica spectrum disorders (NMOSD) who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive

Hint for a minor additional benefit

Justification:

The pharmaceutical company presents the SAkuraStar and SAkuraSky studies for the assessment of the additional benefit of satralizumab.

SAkuraStar

SAkuraStar is a randomised, double-blind, phase III study followed by an open-label extension period to investigate the efficacy and safety of satralizumab as monotherapy compared to placebo in the treatment of adults with NMOSD. 95 subjects were randomised in a 2:1 ratio to the treatment groups, of whom 64 had an AQP4-Ab positive status. Randomisation was stratified by previous therapy for prevention of a relapse (B-cell depletion; immunosuppressants/other) and last relapse in the year before baseline (first relapse; recurrent relapse). The AQP4-Ab status was not a stratification characteristic during randomisation.

The study treatment comprised 120 mg satralizumab as monotherapy or placebo in the form of a subcutaneous injection in the 0th, 2nd and 4th week and every 4 weeks thereafter and was given until the occurrence of a protocol-defined relapse or the end of the double-blind study period. Subsequently, there was the possibility of being treated with satralizumab within the framework of an OLE (open-label extension) study.

The primary endpoint of the SAkuraStar study was defined as "time to occurrence of a protocol-defined relapse" during the double-blind study phase. Other endpoints included disability progression, visual acuity, fatigue, pain, suicidality and the occurrence of adverse events.

Relevant patient population (AQP4-Ab-positive) of the SAkuraStar study

The evaluation-relevant study population of the SAkuraStar study consisted of 64 adult, AQP4-Ab-positive NMOSD patients, of whom 41 were randomised to satralizumab and 23 to placebo (ITT population). Study participants were from the USA (satralizumab 68% and placebo 52%), Asia (12% and 22%) and Europe/other (20% and 26%). The median age was 47 years in the satralizumab arm and 43 years in the placebo arm. In the age group ≥ 65 years, only one subject was examined in the satralizumab arm. In accordance with the distribution in the population, according to which significantly more women than men are affected by NMOSD (approx. 9:1), more women (76 and 96%) than men (24 and 4%) were enrolled in the study. The observed differences in patient characteristics between treatment arms may result from the small sample size and consideration of the sub-population relevant to the assessment.

According to the inclusion criteria, the study participants had to have had at least one documented relapse in the last 12 months before screening, with the onset of the last relapse > 30 days ago. In the majority of those examined (88% and 83% respectively), the last disease relapse before baseline was a recurrent relapse. The median EDSS score was 4 in the satralizumab arm and 3.5 in the placebo arm. Information on the annual relapse rate or duration of disease is not available.

SAkuraSky

SAkuraSky is a randomised, double-blind, phase III study followed by an open-label extension period to investigate the efficacy and safety of satralizumab in combination with basic immunosuppressive therapy compared to placebo plus basic immunosuppressive therapy in the treatment of adults and adolescents aged 12 years and above with NMOSD. 83 patients were randomised in a 1:1 ratio to satralizumab or placebo, of which 55 had an AQP4-Ab positive status. Randomisation was stratified by region (Asia; Europe/other) and annual relapse rate at baseline (1; > 1). The AQP4-Ab status was not a stratification characteristic during randomisation.

The study treatment comprised 120 mg satralizumab or placebo as a subcutaneous injection in combination with basic immunosuppressive therapy in the 0th, 2nd and 4th week and every 4 weeks thereafter until the occurrence of a relapse treated with emergency therapy and/or a protocol-defined relapse or until the end of the double-blind study period. Basic immunosuppressive therapy consisted of monotherapy with azathioprine, mycophenolate mofetil (MMF) or oral corticosteroids stable for at least 8 weeks at the time of enrolment in the study. For subjects < 18 years of age, the combinations azathioprine plus oral corticosteroids or MMF plus oral corticosteroids were also allowed.

After the occurrence of a protocol-defined relapse or a relapse treated with emergency therapy, the double-blind study period ended for the study participants. All patients had the option of being treated with satralizumab during the open-label extension period.

The primary endpoint of the SAkuraSky study was defined as "time to occurrence of a protocol-defined relapse" during the double-blind study period. Other endpoints included disability progression, visual acuity, fatigue, pain and the occurrence of adverse events.

Relevant patient population (AQP4-Ab-positive) of the SAkuraSky study

The assessment-relevant study population of the SAkuraSky study consisted of 52 adults and 3 adolescents with AQP4-Ab-positive NMOSD, of whom 27 subjects were randomised to

satralizumab and 28 to placebo (in adolescents 1 verum, 2 placebo) (ITT population). Those studied were from Asia (satralizumab 48% and placebo 46%) and Europe/other (52% and 54%). The median age was 44 years in the satralizumab arm and 45 years in the placebo arm. Only women were enrolled in the study.

According to the inclusion criteria, the study participants had to have had at least 2 documented relapses in the last 2 years before screening, of which at least one relapse had to have occurred in the last 12 months. About half of the patients enrolled in the study had an annual relapse rate of 1 or a relapse rate of > 1. The median EDSS score was 4 in the satralizumab arm and 3.5 in the placebo arm. Information on the duration of disease is not available.

Mortality

There were no deaths in the studies.

Morbidity

Disease relapses
NMOSD is a relapsing disease. The patients suffer from persistent neurological deficits which are a consequence of incompletely remitted relapses. Accordingly, the avoidance or reduction of disease relapses is patient-relevant.

The primary endpoint of both studies was "time to occurrence of a protocol-defined relapse" during the double-blind study period. In addition, the disease relapses were presented using two further operationalisations: Percentage of subjects without protocol-defined relapse and annual relapse rate (protocol-defined relapses). Patients who experienced a disease relapse had to leave the double-blind, controlled study phase, so that only the first disease relapse was recorded in each case. Therefore, the operationalisations "percentage of subjects without protocol-defined relapse" and "annual relapse rate" do not provide any additional information. Consequently, only the operationalisation "time to occurrence of a protocol-defined relapse" is presented for the assessment.

Disease relapse was defined as the new onset or deterioration of neurological symptoms related to NMOSD. A protocol-defined disease relapse was identified in a multi-step process: 1. report of suspicion of a potential relapse by the treating study staff, 2. EDSS relapse assessment by the investigating study staff, 3. review by a blinded endpoint committee.

In both studies, there was a statistically significant and clinically relevant advantage of satralizumab compared to placebo for the assessment-relevant sub-population in terms of time to occurrence of a protocol-defined relapse. In the marketing authorisation procedure, the EMA used various sensitivity analyses for this endpoint (including "clinical relapses", "treated clinical relapses" and "protocol-defined disease relapses with evaluation of emergency-treated relapses and intensification of basic therapy as events"). Although the stability of the effect observed in the primary analyses could not be comprehensively supported by the sensitivity analyses, the pre-specified, primary analysis with strictly defined criteria for a standardised and mostly objective assessment of a relapse represents the methodologically more valid evaluation.

Disability progression (EDSS-based)
Progression of disability is a patient-relevant endpoint. The EDSS is a tool to describe the severity of disability in neurodegenerative diseases. The determination of the EDSS score is based on the neurological examination of 7 functional systems or the identification of limitations in these functions as well as the assessment of walking ability.

For time to EDSS progression, the SAkuraStar study showed a statistically significant advantage of satralizumab as monotherapy compared to placebo. Treatment with satralizumab in combination with basic immunosuppressive therapy did not result in a statistically significant difference compared to placebo plus basic immunosuppressive therapy in the SAkuraSky study.

Visual acuity (Snellen test)
The loss of visual acuity associated with optic neuritis is a relevant symptom in NMOSD. Accordingly, visual acuity or the preservation thereof is assessed as patient-relevant. The Snellen eye test is a tool for determining visual acuity.

For both studies, due to the high proportion of missing values from study week 48, only descriptive data at baseline and week 24 could be considered, from which no conclusions on the effects of satralizumab on visual acuity can be derived.

Quality of life

SF-36
Quality of life was not recorded in the present evaluations after the occurrence of a relapse. Accordingly, in both studies, the percentage of subjects in the evaluation, related to the ITT population, in at least one of the two study arms was already < 70% at the first survey time point after baseline (week 24). The results of the SF-36 are therefore assessed as not valid for the ITT population. The effect of satralizumab on quality of life can therefore not be assessed.

Side effects

The assessment of AE was continuous throughout the study. The evaluations presented refer to the observation period from the day of the first dose to the day of the data cut-off, the day prior to the start of treatment in the open-label extension period, the end of the study or, for subjects with no follow-up, the day of the last contact (whichever came first). Due to the strongly differing duration of observation between the treatment groups, a comparison of the event rates would lead to biased results. The pharmaceutical company therefore submitted time-to-event analysis (from an occurrence of 10 events per comparison) using an unstratified Cox regression model.

For the relevant sub-population, there were no statistically significant differences in the evaluation of serious adverse events (SAE) between the treatment arms in either study. For

severe AEs, there was no statistically significant difference between the study arms in the SAkuraStar study, and no effect estimator could be calculated in the SAkuraSky study due to the low number of events. No effect estimator could be calculated for AEs that led to discontinuation of the study medication due to too low event numbers.

Overall assessment

For the benefit assessment of satralizumab for the treatment of adults and adolescents aged 12 years and above with NMOSD who are AQP4 IgG-seropositive, results of the two randomised, double-blind and placebo-controlled phase III SAkuraStar and SAkuraSky studies are available. In the SAkuraStar study, adults were studied as part of monotherapy, and in the SAkuraSky study, adults and adolescents aged 12 years and above were studied in combination with basic immunosuppressive therapy. The relevant sub-population comprises AQP4 IgG-seropositive patients and thus, approx. 67% of the total population in both studies.

There were no deaths in both studies.

In the morbidity category, both studies showed a statistically significant advantage in favour of satralizumab over placebo in the endpoint disease relapses in time to occurrence of a protocol-defined relapse. Due to the methodologically more valid significance of the protocol-defined relapses, the additionally performed sensitivity analyses do not question the positive effect of satralizumab on the reduction of disease relapses.

For the endpoint of (EDSS-based) disability progression, there was also a statistically significant advantage with respect to time to EDSS progression in the SAkuraStar study in favour of satralizumab as monotherapy over placebo, whereas there was no statistically significant difference between treatment arms in the SAkuraSky study. For the endpoint of visual acuity, only descriptive data are available. No assessable data are available for other patient-relevant endpoints in the indication, such as fatigue and pain. Overall, the advantages in the endpoints of disease relapses and disability progression are assessed to be low in magnitude.

No assessable data are available in the quality of life category.

In the side effects category, there were no statistically significant differences for serious AEs in both studies and for severe AEs in the SAkuraStar study.

In the overall assessment of the available results on the patient-relevant endpoints, the G-BA classifies the extent of the additional benefit of satralizumab for the treatment of adults and adolescents aged 12 years and older with NMOSD, who are AQP4-IgG seropositive, as being low, based on the criteria in Section 5, paragraph 8, sentences 1, number 2 in conjunction with Section 5, paragraph 7, sentence 1, number 4 AM-NutzenV.

Significance of the evidence

This assessment is based on the results of the randomised, double-blind and placebo-controlled SAkuraStar and SAkuraSky studies.

The risk of bias at the study level is rated as unclear for each of the two studies. Limitations include observed GCP violations in the conduct of both studies, which were critically discussed by the EMA in the EPAR.

Since NMOSD is usually associated with repeated and often severe disease relapses, patients in the German health care context are usually given immunotherapy from the first relapse onwards to prevent further relapses. However, in the SAkuraStar study, the patients in the control arm were treated only with placebo, with the exception of pain therapy. In the SAkuraSky study, the patients mostly received monotherapy with oral corticosteroids or monotherapy with azathioprine as part of the basic immunosuppressive therapy. It can therefore be assumed that the patients in both studies did not receive a therapy for their NMOSD disease that corresponds to the currently regarded standard of care.

In the overall assessment, the uncertainties mentioned with regard to the significance of the evidence result in a hint of an additional benefit.

2.1.3 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product "Enspryng" with the active ingredient satralizumab.

Enspryng has been approved as an orphan drug for the treatment of adults and adolescents aged 12 years and above with neuromyelitis optica spectrum disorders (NMOSD) who are anti-aquaporin-4 IgG (AQP4 IgG) seropositive, as monotherapy or in combination with immunosuppressive therapy.

For this patient group, the pharmaceutical company presents results of the RCTs SAkuraStar and SAkuraSky. In the SAkuraStar study, adults were studied as part of monotherapy, and in the SAkuraSky study, adults and adolescents aged 12 years and above were studied in combination with basic immunosuppressive therapy. The relevant sub-population in each case comprises AQP4 IgG-seropositive patients.

There were no deaths in both studies

In the morbidity category, the endpoint "time to occurrence of a protocol-defined relapse" showed a statistically significant advantage in favour of satralizumab in both studies. For the endpoint "time to EDSS progression", one study showed a statistically significant advantage in favour of satralizumab. Overall, the advantages in the endpoints of disease relapses and disability progression are assessed to be low in magnitude.

No assessable data are available for the quality of life category.

For the results of the endpoint category of side effects, no statistically significant differences were observed for serious AEs and severe AEs.

The significance of the data presented is fraught with uncertainty since the patients in the comparator arm of both studies did not receive a therapy for NMOSD that corresponds to the current standard of care and the risk of bias at study level is also unclear.

In the overall assessment, a hint of minor additional benefit is identified.

2.2 Number of patients or demarcation of patient groups eligible for treatment

The information on the number of patients (approx. 460 – 5050) is based on the target population in statutory health insurance (SHI). The data follow the representations of the pharmaceutical company and the assessment of IQWiG.

Uncertainties exist, in particular, with regard to deviating prevalence data from the literature, the estimate based on cases treated exclusively as full inpatients and outdated diagnostic criteria with regard to the evaluation of the NEMOS register.

Overall, the upper limit tends to be overestimated.

2.3 Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Enspryng (active ingredient: satralizumab) at the following publicly accessible link (last access: 18 November 2021):
https://www.ema.europa.eu/en/documents/product-information/enspryng-epar-product-information_en.pdf

Treatment with satralizumab should be initiated and monitored by a specialist in neurology or by a specialist in neurology and psychiatry or by a specialist in paediatrics and adolescent medicine with specialisation in neuropaediatrics and experience in the treatment of neuromyelitis optica spectrum disorders.

In accordance with the European Medicines Agency (EMA) requirements regarding additional risk minimisation measures, the pharmaceutical company must provide a patient identification card. This contains, in particular, information and warnings about the risk of infections.

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 1 December 2021).

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration is patient-individual and/or is shorter on average. The time unit "days" is used to calculate the "number of treatments/ patient/ years", time intervals between individual treatments and for the maximum treatment duration, if specified in the product information.

In general, initial induction regimens are not taken into account for the cost representation, since the present indication is a chronic disease with a continuous need for therapy and, as a rule, no new titration or dose adjustment is required after initial titration.

For dosages depending on body weight, the average body measurements from the official representative statistics "Microcensus 2017 – body measurements of the population" were

applied (average body weight of adults: 77.0 kg; average body weight of 12-year-olds: 47.1 kg).[2]

The maximum daily doses specified in the SAkuraSky marketing authorisation study were used for the dosage of the concomitant active ingredients. This is an upper limit, patient-individual dosages may be lower. For the oral corticosteroids, prednisolone was also presented as an example based on the dosage data.

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ years	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Satralizumab	1 x every 28 days	13	1	13
Possibly in combination with:				
Prednisolone	1 x daily	365	1	365
Azathioprine	1 x daily	365	1	365
Mycophenolate mofetil	2 x daily	365	1	365

Consumption:

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Satralizumab	120 mg	120 mg	1 x 120 mg	13	13 x 120 mg
Possibly in combination with:					
Prednisolone	15 mg	15 mg	1 x 10 mg+	365	365 x 10 mg+

[2] Federal Statistical Office, Wiesbaden 2018: http://www.gbe-bund.de/

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
			1 x 5 mg		365 x 5 mg
Azathioprine	3 mg/kg = 141.3 mg	150 mg	1 x 100 mg + 1 x 50 mg	365	365 x 100 mg + 365 x 50 mg
	231 mg	225 mg	2 x 100 mg + 1 x 25 mg		730 x 100 mg + 365 x 25 mg
Mycophenolate mofetil	1.5 g	3 g	6 x 500 mg	365	2190 x 500 mg

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates.

Costs of the medicinal products:

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Satralizumab 120 mg	3 SFI	€ 29,841.89	€ 1.77	€ 1,701.00	€ 28,139.12
Prednisolone 10 mg[3]	100 TAB	€ 17.54	€ 1.77	€ 0.51	€ 15.26
Prednisolone 5 mg[3]	100 TAB	€ 15.16	€ 1.77	€ 0.33	€ 13.06
Azathioprine 100 mg[3]	100 FCT	€ 57.74	€ 1.77	€ 3.69	€ 52.28

[3] Fixed reimbursement rate

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Azathioprine 50 mg[3]	100 FCT	€ 40.40	€ 1.77	€ 2.32	€ 36.31
Azathioprine 25 mg[3]	100 FCT	€ 29.50	€ 1.77	€ 1.46	€ 26.27
Mycophenolate mofetil 500 mg[3]	250 FCT	€ 465.58	€ 1.77	€ 35.95	€ 427.86
Abbreviations: FCT = film-coated tablets; SFI = solution for injection; TAB = tablets					

LAUER-TAXE® last revised: 1 December 2021

Costs for additionally required SHI services:

Only costs directly related to the use of the medicinal product are taken into account. If there are regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be taken into account as costs for additionally required SHI services.

Medical treatment costs, medical fee services, and costs incurred for routine examinations (e.g. regular laboratory services such as blood count tests) that do not exceed the standard expenditure in the course of the treatment are not shown.

Because there are no regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, no costs for additionally required SHI services had to be taken into account.

3. Bureaucratic costs calculation

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

4. Process sequence

On 5 July 2021, the pharmaceutical company submitted a dossier for the benefit assessment of satralizumab to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 VerfO.

The benefit assessment of the G-BA was published on 15 October 2021 together with the IQWiG assessment of treatment costs and patient numbers on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. The deadline for submitting written statements was 5 November 2021.

The oral hearing was held on 22 November 2021.

An amendment to the benefit assessment with a supplementary assessment was submitted on 6 December 2021.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the SHI umbrella organisation, and representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The evaluation of the written statements received and the oral hearing was discussed at the subcommittee session on 21 December 2021, and the draft resolution was approved.

At its session on 6 January 2022, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal product	12 October 2021	Information of the benefit assessment of the G-BA
Working group Section 35a	16 November 2021	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal product	22 November 2021	Conduct of the oral hearing
Working group Section 35a	30 November 2021 14 December 2021	Consultation on the dossier assessment by the G-BA, the assessment of treatment costs and patient numbers by the IQWiG, and the evaluation of the written statement procedure
Subcommittee Medicinal product	21 December 2021	Concluding discussion of the draft resolution
Plenum	6 January 2022	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 6 January 2022

Federal Joint Committee (G-BA)
in accordance with Section 91 SGB V
The Chair

Prof. Hecken