Justification

Gemeinsamer Bundesausschuss

of the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive (AM-RL): Annex XII - Benefit assessment of medicinal products with new active ingredient according to Section 35a SGB V Levofloxacin/Dexamethasone (Infections and inflammations in connection with cataract surgery)

of 15 July 2021

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. This includes, in particular, the assessment of the additional benefit and its therapeutic significance. The benefit assessment is carried out on the basis of evidence provided by the pharmaceutical company, which must be submitted to the G-BA electronically, including all clinical trials the pharmaceutical company has conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

1. Approved therapeutic indications,
2. Medical benefit,
3. Additional medical benefit in relation to the appropriate comparator therapy,
4. Number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. Treatment costs for statutory health insurance funds,
6. Requirements for a quality-assured application.

The G-BA may commission the Institute for Quality and Efficiency in Health Care (IQWiG) to carry out the benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment 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 combination of active ingredient levofloxacin/dexamethasone in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure of the G-BA (VerfO) is 1 February 2021. The pharmaceutical company has 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 27 January 2021.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 3 May 2021 on the G-BA website at (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of levofloxacin/dexamethasone compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure and the addenda to the benefit assessment prepared by IQWiG. In order to determine the extent of the additional benefit, the G-BA has evaluated the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5, Section 5, paragraph 7

VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of levofloxacin/dexamethasone.

In the light of the above and taking into account the statements received and the oral hearing, the G-BA has come to the following assessment:

2.1 Additional benefit of the medicinal product in relation to the appropriate comparator therapy

2.1.1 Approved therapeutic indication of levofloxacin/dexamethasone (Ducressa) according to the product information

Ducressa eye drops solution is indicated for prevention and treatment of inflammation, and prevention of infection associated with cataract surgery in adults.

Therapeutic indication of the resolution (resolution of 15.07.2021):

see approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Patient population: Prevention and treatment of inflammation, and prevention of infection associated with cataract surgery in adults

Appropriate comparator therapy:

A combination of local antibiotic therapy (cefuroxime, polymyxin B/neomycin/gramicidin, tobramycin[2], gentamicin, neomycin[2]) in conjunction with mono- or combination anti-inflammatory therapy: Corticosteroid, e.g. rimexolone, dexamethasone, fluorometholone, prednisolone, loteprednol etabonate and/or NSAIDs, e.g. diclofenac, nepafenac, indomethacin, ketorolac

Criteria according to Chapter 5, Section 6 of the Rules of Procedure of the G-BA:

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication in accordance with the generally recognised state of medical knowledge (Section 12 SGB V), preferably a therapy for which endpoint studies are available and which has proven its worth in practical application unless contradicted by the guidelines under Section 92, paragraph 1 SGB V or the principle of economic efficiency.

In determining the appropriate comparator therapy, the following criteria, in particular, must be taken into account as specified in Chapter 5, Section 6, paragraph 3 VerfO:

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.

[1] General Methods, version 6.0 from 5.11.2020. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

[2] Only in fixed combination with dexamethasone

3. As comparator therapy, medicinal products or non-medicinal treatments for which the G-BA has already determined the patient-relevant benefit shall be preferred.
4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

Justification based on the criteria set out in Chapter 5, Section 6, paragraph 3 VerfO:

on 1. The following active ingredients are approved in the therapeutic indication: For infection prophylaxis**:** Cefuroxime, polymyxin B/neomycin/gramicidin, povidone-iodine.
For the prevention and/or treatment of inflammation:

- NSAID: Diclofenac, nepafenac, indomethacin, ketorolac, flurbiprofen
- Corticosteroids: Rimexolone, dexamethasone, fluorometholone, prednisolone, loteprednol etabonate

Combination preparations of anti-infectives and corticosteroids: Dexamethasone/neomycin, dexamethasone/gentamycin, tobramycin/dexamethasone, dexamethasone/neomycin/polymyxin B. Bromfenac is no longer available in Germany since May 2014.

on 2. A non-medicinal treatment paid by the SHI is not considered as an appropriate comparator therapy in the therapeutic indication.

on 3. There is a resolution regarding Bromfenac for the treatment of postoperative ocular inflammation following cataract extraction in adults dated 19/01/2012.

on 4. The generally accepted state of medical knowledge for the indication was established by means of a search for guidelines and systematic reviews of clinical studies. Overall, the evidence base for this indication is considered low. The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the comparator therapy in the present indication according to Section 35a paragraph 7 SGB V. Overall, the aggregated evidence suggests that the standard of care for the prevention and treatment of inflammation and infection associated with cataract surgery is a combination of local antibiotic therapy and anti-inflammatory therapy. *Anti-inflammatory* drugs can be NSAIDs*(non-steroidal anti-inflammatory* drugs) or corticosteroids. If necessary, two anti-inflammatory substances of different product classes can be combined. Since no superiority of individual agents can be derived from the available evidence, all approved agents are considered equally appropriate options for the appropriate comparator therapy. Thus, the following agents are available as antibiotic therapy: cefuroxime, polymyxin B/neomycin/gramicidin, tobramycin[3], gentamicin[3] neomycin/polymyxin B[3] or neomycin[3], as non-steroidal anti-inflammatory therapy: Diclofenac, nepafenac, indomethacin, ketorolac, flurbiprofen and as steroidal anti-inflammatory therapy: Rimexolone, dexamethasone, fluorometholone, prednisolone, loteprednol etabonate. It is assumed that considering general surgical standards, preoperative antiseptic treatment with povidone-iodine will be administered in the course of cataract surgery in both study arms. Since postoperative antibiotic therapy is not generally indicated to prevent infection in the course of cataract surgery, it is assumed that antibiotic therapy is indicated in the present therapeutic indication.

[3] Only in fixed combination with dexamethasone

In summary, the G-BA concludes that for adult patients, a combination of local antibiotic therapy (cefuroxime, polymyxin-B/neomycin/gramicidin, tobramycin[4], gentamicin[4], neomycin[4]) in conjunction with mono- or combination anti-inflammatory therapy is appropriate for the prevention and treatment of inflammation and the prevention of infections associated with cataract surgery: Corticosteroid, e.g. rimexolone, dexamethasone, fluorometholone, prednisolone, loteprednol etabonate and/or NSAID, e.g. diclofenac, nepafenac, indomethacin, ketorolac is appropriate.

The findings in Annex XII do not restrict the scope of treatment required to fulfil the medical treatment mandate.

2.1.3 Extent and probability of the additional benefit

In summary, the additional benefit of levofloxacin/dexamethasone assessed as follows:

Prevention and treatment of inflammation, and prevention of infection associated with cataract surgery in adults

An additional benefit is not proven

Justification:

For the evaluation of the additional benefit of levofloxacin/dexamethasone compared to the fixed combination tobramycin/dexamethasone in adults for the prevention and treatment of inflammation and for the prevention of infections associated with cataract surgery, the pharmaceutical company presents the randomised, endpoint-blinded study LEADER-7.

The study included subjects aged 40 years and older who had undergone surgery for senile or presenile cataract without complications. Phacoemulsification was the surgical method performed in all subjects. Subjects with eye disorders (e.g., blepharitis, conjunctivitis, or diabetic retinopathy) and systemic diseases (e.g., rheumatoid arthritis, systemic lupus erythematosus, or scleroderma with severe ocular involvement) were excluded.

Subjects received either treatment with levofloxacin/dexamethasone for 7 days followed by dexamethasone as monotherapy for another 7 days or treatment with tobramycin/dexamethasone for 14 days after cataract surgery.

Standard preoperative antiseptic treatment with povidone-iodine was documented in only about 68% of subjects, and another approximately 5% received preoperative antiseptic treatment with picloxydin. After 7 days of treatment, an ophthalmologic examination was performed. In the majority of the subjects, the postoperative healing process was already largely completed. It remains questionable whether postoperative antibiotic prophylactic therapy was indicated for all subjects in the study.

[4] Only in fixed combination with dexamethasone

Extent and probability of the additional benefit

Mortality

For the endpoint overall mortality no statistically significant difference was detected between the treatment arms.

Morbidity

Endophthalmitis

The endpoint Endophthalmitis was recorded on days 4, 8, and 15 of the study. Endophthalmitis diagnosis was based on clinical assessment of symptoms such as swollen eyelids, eye pain, conjunctival hyperaemia, decreased visual acuity, and vitreous opacities by slit-lamp examination microbiological testing of conjunctival or corneal swabs. No endophthalmitis occurred during the study.

Itching/burning, redness of the conjunctiva, tearing, and ocular pain/discomfort (each considered symptom-free)

In the LEADER-7 study, patient-reported ocular symptomatology was assessed using the TOSS instrument. The TOSS includes patient-reported assessment of 3 ocular symptoms: Itching/burning, redness of the conjunctiva and tearing. The occurrence and severity of each symptom were assessed on days 4, 8, and 15 of the study with a score ranging from 0 to 3 points. The ocular pain/discomfort score is a patient-reported assessment of ocular pain and discomfort. Again, symptom severity was assessed on days 4, 8, and 15 of the study with a score ranging from 0 to 3 points. For the endpoints, itching/burning, redness of the conjunctiva, tearing and ocular pain/discomfort (each considered as symptom-free) there were no statistically significant differences between the treatment arms at any time point. Since the subgroup of persons with diabetes was not prespecified, no separate data analysis was performed.

Decrease of visual acuity

According to local clinical practice, there is no statistically significant difference between the treatment arms for the endpoint Decrease in visual acuity, assessed with the Snellen or Early Treatment of Diabetic Retinopathy Study (ETDRS) chart.

Quality of life

No health-related quality of life endpoints were collected in the LEADER 7 study.

Side effects

SAEs and discontinuation due to AEs

There was no statistically significant difference between the treatment arms for the endpoint SAE and discontinuation due to AEs.

Overall assessment/conclusion

For adults for the prevention and treatment of inflammation as well as for the prevention of infections in connection with cataract surgery, evaluations of the direct comparator study LEADER-7 are available for the comparison of levofloxacin/dexamethasone with tobramycin/dexamethasone.

In summary, the results on mortality and morbidity results do not show statistically significant differences between the treatment arms. No endpoints were collected in the category health-related

quality of life. In the category side effects, no advantages or disadvantages can be derived for levofloxacin/dexamethasone versus tobramycin/dexamethasone overall.

An additional benefit for the combination of active ingredients levofloxacin/dexamethasone for adults for the prevention and treatment of inflammations as well as for the prevention of infections in connection with cataract surgeries, compared to the appropriate comparator therapy tobramycin/dexamethasone was consequently not proven.

2.1.4 Summary of the assessment

The present evaluation is the benefit assessment of the combination of active ingredients levofloxacin/dexamethasone versus the fixed combination tobramycin/dexamethasone in adults for the prevention and treatment of inflammation and for the prevention of infections associated with cataract surgery.

For this purpose, the pharmaceutical company presents the direct comparative study LEADER-7.

In summary, the results on mortality and morbidity results do not show statistically significant differences between the treatment arms. No endpoints were collected in the category health-related quality of life. In the category side effects, no advantages or disadvantages can be derived for levofloxacin/dexamethasone versus tobramycin/dexamethasone overall.

Overall, the results do not show statistically significant differences between the treatment groups in any endpoint category.

An additional benefit for the combination of active ingredients levofloxacin/dexamethasone for adults for the prevention and treatment of inflammations as well as for the prevention of infections in connection with cataract surgeries is therefore not proven compared to tobramycin/dexamethasone.

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

The number of patients is the target population in statutory health insurance (SHI).

The data are based on the patient numbers submitted by the pharmaceutical company in the written statement procedure. The data in the written statement in comparison with the data of the pharmaceutical company in the dossier represent, despite existing uncertainties, a more suitable approximation of the number of subjects in the SHI target population.

However, the calculated 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.

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: 15 June 2021).

The treatment of infections and inflammations associated with cataract surgery is an acute therapy that should generally last only a few days and weeks. More detailed information on the treatment duration can be found in the product information. The therapy for one eye is shown. The duration of

treatment is patient-individual. The maximum treatment costs are calculated based on the recommended maximum treatment duration.

Treatment duration:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ operated eye	Treatment duration/ treatment (days)	Days of treatment/ patient/ operated eye
Medicinal product to be assessed				
Levofloxacin/ dexamethasone	1 every 6 hours for 7 days	1	7	7
Appropriate comparator therapy				
a local antibiotic therapy				
Cefuroxime	1 at the end of the cataract surgery	1	1	1
Polymyxin B/ neomycin/ gramicidin	3 to 5 times a day 1 drop	1	5 - 7	5 - 7
Tobramycin/ dexamethasone	during the waking phases every 4 to 6 hours	1	14 - 24	14 - 24
Gentamicin/ dexamethasone (ointment)	2-3 times a day	1	Up to 14.	Up to 14.
Gentamicin/ dexamethasone (drops)	4-6 times a day	1	Up to 14.	Up to 14.
Neomycin / dexamethasone	4-6 times a day	1	Up to 21.	Up to 21.
Neomycin/ polymyxin B/ dexamethasone (drops)	Up to 6 times a day	1	Up to 21.	Up to 21.
Neomycin/ polymyxin B/ dexamethasone (ointment)	3-2 times a day	1	Up to 21.	Up to 21.
in conjunction with anti-inflammatory monotherapy or combination therapy:				

Designation of the therapy	Treatment mode	Number of treatments/ patient/ operated eye	Treatment duration/ treatment (days)	Days of treatment/ patient/ operated eye
Corticosteroid				
dexamethasone (drops)	first 2 days: 2 - 5 times a day, then 3 times a day	1	up to 14 days	up to 14 days
dexamethasone (ointment)	3 times a day	1	up to 14 days	up to 14 days
Fluorometholone	2-4 times a day, during the first 1 - two days also hourly possible	1	Up to 21.	Up to 21.
Prednisolone (drops and gel)	1 - 4 times a day, during the first 1 - two days also hourly possible.	1	Up to 14.	Up to 14.
Prednisolone (cream)	3-2 times a day	1	Patient-individual	
Prednisolone (ointment)	3-2 times a day	1	Up to 14.	Up to 14.
Loteprednol	4 times a day	1	Up to 14.	Up to 14.
and/or NSAID				
Diclofenac	3-2 times a day	1	Up to 28.	Up to 28.
Nepafenac	Once daily	1	Up to 21.	Up to 21.
Ketorolac	3 times a day	1	21 - 28	21 - 28
Flurbiprofen	4 times every 30 minutes in the 2 hours before surgery, afterwards: 4 times a day	1	7 - 14	7 - 14

Consumption:

Designation of the therapy	Dosage/ Application	Dosage/ patient/ days of treatment	Usage by potency/ day of treatment	Treatment days/ patient/ Year	Average consumption by potency/ operated eye
Medicinal product to be assessed					
Levofloxacin/dexamethasone	1 drop á 30 µl	120 µl	4 x 30 µl	7	28 x 30 µl
Appropriate comparator therapy					
a local antibiotic therapy					
Cefuroxime	1 mg	1 mg	1 x 1 mg	1	1 x 1 mg
Polymyxin B/neomycin/gramicidin	1 drop	3-5 drops	3-5 drops	5 - 7	15-35 drops
Tobramycin/dexamethasone	1 drop every 4-6 h during the day	1 drop[5]	3-5 drops	14 - 24 days	42 - 120 drops
Gentamicin/dexamethasone (ointment)	patient-individual			Up to 14.	patient-individual
Gentamicin/dexamethasone (drops)	1 drop	4– 6 drops	4– 6 drops	Up to 14.	up to 84 drops
Neomycin/dexamethasone	1 drop	4– 6 drops	4– 6 drops	Up to 21.	up to 126 drops
Neomycin/polymyxin B/dexamethasone (drops)	1 drop	up to 6 drops	up to 6 drops	Up to 21.	up to 126 drops
Neomycin/polymyxin B/dexamethasone (ointment)	patient-individual			Up to 21.	patient-individual
in conjunction with anti-inflammatory monotherapy or combination therapy:					
Corticosteroid					
dexamethasone (drops)	1 drop	3 drops[6]	3 drop	Up to 14.	up to 42 drops

[5] In the first 24 to 48 hours, the dosage can be increased to one drop every two hours during the waking phases
[6] On the first 2 days, 2 to 5 times a day 1 drop, afterwards 3 times a day 1 drop.

Designation of the therapy	Dosage/ Application	Dosage/ patient/ days of treatment	Usage by potency/ day of treatment	Treatment days/ patient/ Year	Average consumption by potency/ operated eye
dexamethasone (ointment)	patient-individual			Up to 14.	Patient-individual
Fluorometholone	1 drop	2 -4 drops [7]	2 -4 drops	Up to 21.	up to 84 drops
Prednisolone (drops and gel)	1 drop	1 -4 drops	1 -4 drops	Up to 14.	up to 56 drops
Prednisolone (cream and ointment)	patient-individual				patient-individual
Loteprednol	1-2 drops	4– 8 drops	4– 8 drops	Up to 14.	up to 112 drops
and/or NSAID					
Diclofenac	1 drop	3-5 drops	3-5 drops	Up to 28.	up to 140 drops
Nepafenac	1 drop 3 mg/ml	1 drop	1 drop 3 mg/ml	Up to 21.	up to 21 drops
Ketorolac	1 drop	3 drop	3 drop	21- 28	63– 84 drops
Flurbiprofen	1 drop	4 drops[8]	4 drop	7 - 14 days	32– 60 drops

Costs:

Costs of the medicinal product:

In order to improve comparability, the costs of the medicinal products were approximated both based on 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 based on consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated based on the costs per pack after deduction of the statutory rebates. In general, it is assumed that a pack, unless in single doses, is designed for the therapy of one operated eye. Cefuroxime is covered as a single dose in the course of the surgery by the flat rates for material costs agreed in the material cost agreements for outpatient cataract surgery of the Associations of Statutory Health Insurance Physicians, and no further costs are incurred as a result of the drug.

[7] During the first 1 - 2 days also hourly possible

[8] 1 drop should be placed in the eye about every half hour for a period of 2 hours before the surgery. After surgery: 1 drop applied 4 times a day for 2 weeks (but at least one week).

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate § 130 SGB V	Rebate § 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Levofloxacin/dexamethasone	5 ml ATR	€ 22.42	€ 1.77	€ 0.63	€ 20.02
Appropriate comparator therapy					
a local antibiotic therapy					
Cefuroxime	No additional costs, as included in the flat rate for outpatient cataract surgery				
Polymyxin B/neomycin/gramicidin	5 ml ATO	€ 17.87	€ 1.77	€ 0.53	€ 15.57
Tobramycin/dexamethasone	5 ml ATR	€ 17.86	€ 1.77	€ 0.71	€ 15.38
Gentamicin/dexamethasone (ointment)	3 ml AUS	€ 13.74	€ 1.77	€ 0.34	€ 11.63
Gentamicin/dexamethasone (drops)	5 ml ATR	€ 14.72	€ 1.77	€ 0.39	€ 12.56
Neomycin / dexamethasone	5 ml ATR	€ 15.40	€ 1.77	€ 0.24	€ 13.39
Neomycin/polymyxin B/dexamethasone (drops)	5 ml ATR	€ 19.31	€ 1.77	€ 0.87	€ 16.67
Neomycin/polymyxin B/dexamethasone (ointment)	3.5 g OFF	€ 19.31	€ 1.77	€ 0.87	€ 16.67
Corticosteroid					
Dexamethasone (drops)	5 ml ATR	€ 14.09	€ 1.77	€ 0.14	€ 12.18
Dexamethasone (ointment)	5 AUS	€ 18.04	€ 1.77	€ 0.39	€ 15.88
Fluorometholone	5 ml ATR	€ 14.97	€ 1.77	€ 0.51	€ 12.69
Prednisolone (drops 5 mg)	10 ml ATR	€ 14.83	€ 1.77	€ 0.22	€ 12.84
Prednisolone (drops 10 mg)	5 ml ATR	€ 15.71	€ 1.77	€ 0.22	€ 13.72
Prednisolone (gel)	5 g AUG	€ 15.01	€ 1.77	€ 0.23	€ 13.01
Prednisolone (cream)	5 g CRE	€ 30.01	€ 1.77	€ 8.92	€ 19.32
Prednisolone (ointment)	5 g OFF	€ 18.65	€ 1.77	€ 0.42	€ 16.46
Loteprednol	5 ml ATR	€ 19.25	€ 1.77	€ 0.47	€ 17.01
NSAID					
Diclofenac	5 ml ATR	€ 17.21	€ 1.77	€ 0.29	€ 15.15
Nepafenac 3 mg/ml	3 ml ATR	€ 29.38	€ 1.77	€ 1.02	€ 26.59
Ketorolac	5 ml ATR	€ 17.64	€ 1.77	€ 0.31	€ 15.56
Flurbiprofen	20 X0.4 ml ATR	€ 32.28	€ 1.77	€ 1.18	€ 29.33

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate § 130 SGB V	Rebate § 130a SGB V	Costs after deduction of statutory rebates
Abbreviations: ATO = eye and ear drops; ATR = eye drops; AUG = eye gel; AUS = eye ointment; CRE = cream					

Last revised LAUER-TAXE®: 15 June 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 standard expenditure in the course of the treatment are not shown.

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

3. Bureaucratic costs

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

At its session on 8 September 2020, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 27 February 2021, the pharmaceutical company submitted a dossier for the benefit assessment of levofloxacin/dexamethasone to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 28 January 2021 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefits of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient levofloxacin/dexamethasone.

The dossier assessment by the IQWiG was submitted to the G-BA on 29 April 2021, and the written statement procedure was initiated with publication on the website of the G-BA on 3 May 2021. The deadline for submitting written statements was 25 May 2021.

The oral hearing was held on 7 June 2021.

By letter dated 8 June 2021, the IQWiG was commissioned with a supplementary assessment of data submitted in the written statement procedure. The addenda prepared by IQWiG was submitted to the G-BA on 24 June 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 the 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 were discussed at the session of the subcommittee on 6 July 2021, and the proposed resolution was approved.

At its session on 15 July 2021, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal product	8 September 2020	Determination of the appropriate comparator therapy
Working group Section 35a	2 June 2021	Information on written statement procedures received; preparation of the oral hearing
Subcommittee Medicinal product	7 June 2021 8 June 2021	Conduct of the oral hearing, Commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	16 June 2021 30 June 2021	Consultation on the dossier assessment by the IQWiG, evaluation of the written statement procedure
Subcommittee Medicinal product	6 July 2021	Concluding discussion of the draft resolution
Plenum	15 July 2021	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 15 July 2021

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

Prof. Hecken