Gemeinsamer Bundesausschuss

Justification

to 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
Vibegron (overactive bladder)

of 21 August 2025

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assess the benefit of all 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 studies the pharmaceutical company have 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 the 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 is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The relevant date for the start of the benefit assessment procedure was the first placing on the (German) market of the active ingredient vibegron on 1 October 2024 in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure (VerfO) of the G-BA.

At G-BA's request, the pharmaceutical company submitted a fixed reimbursement rate dossier in accordance with Annex VI of Chapter 5 of the VerfO at the time Obgemsa was first placed on the market in Germany. However, after reviewing the legal situation, the G-BA came to the conclusion that the requirements for implementing the simplified procedure in accordance with Section 35a, paragraph 1, sentence 4 in conjunction with paragraph 4 SGB V for the medicinal product Obgemsa are not met in the present case. By resolution of 22 November 2024, it was decided to suspend the proceedings until 1 May 2025 at the latest[1].

[1] Pharmaceuticals Directive/Annex XII: Vibegron (overactive bladder) – suspension of the benefit assessment procedure. https://www.g-ba.de/beschluesse/6910/

The pharmaceutical company submitted the final dossier to the G-BA in due time on 28 February 2025.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 2 June 2025 on the G-BA website (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 vibegron 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. In order to determine the extent of the additional benefit, the G-BA have 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 [2] was not used in the benefit assessment of vibegron.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA have 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 Vibegron (Obgemsa) in accordance with the product information

Obgemsa is indicated in symptomatic treatment of adult patients with overactive bladder (OAB) syndrome.

Therapeutic indication of the resolution (resolution of 21.08.2025):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with an overactive bladder

Appropriate comparator therapy for vibegron:

- Darifenacin or desfesoterodine or fesoterodine or mirabegron or propiverine or solifenacin or tolterodine or trospium chloride

Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA and Section 6 paragraph 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV):

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.

[2] General Methods, version 7.0 from 19.09.2023. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

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.
3. As comparator therapy, medicinal products or non-medicinal treatments for which the patient-relevant benefit has already been determined by the G-BA 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.

According to Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the determination of the appropriate comparator therapy must be based on the actual medical treatment situation as it would be without the medicinal product to be assessed. According to Section 6, paragraph 2, sentence 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the G-BA may exceptionally determine the off-label use of medicinal products as an appropriate comparator therapy or as part of the appropriate comparator therapy if it determines by resolution on the benefit assessment according to Section 7, paragraph 4 that, according to the generally recognised state of medical knowledge, this is considered a therapy standard in the therapeutic indication to be assessed or as part of the therapy standard in the medical treatment situation to be taken into account according to sentence 2, and

1. for the first time, a medicinal product approved in the therapeutic indication is available with the medicinal product to be assessed,
2. according to the generally recognised state of medical knowledge, the off-label use is generally preferable to the medicinal products previously approved in the therapeutic indication, or
3. according to the generally recognised state of medical knowledge, the off-label use for relevant patient groups or indication areas is generally preferable to the medicinal products previously approved in the therapeutic indication.

An appropriate comparator therapy may also be non-medicinal therapy, the best possible add-on therapy including symptomatic or palliative treatment, or monitoring wait-and-see approach.

<u>Justification based on the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO and Section 6, paragraph 2 AM-NutzenV:</u>

On 1. In addition to vibegron, the active ingredients darifenacin, desfesoterodine, fesoterodine, flavoxate, mirabegron, oxybutynin, propiverine, solifenacin, tolterodine and trospium chloride are approved for the present therapeutic indication.

On 2. In the present therapeutic indication, non-medicinal measures within the meaning of the Remedies Directive or the catalogue of remedies (e.g. physiotherapy) are considered as comparator therapy.

On 3. There is a resolution of the G-BA for the active ingredient mirabegron dated 20 November 2014 on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V in the present therapeutic indication.

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as reviews of clinical studies in the present indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to Section 35a SGB V".

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 therapeutic indication according to Section 35a, paragraph 7 SGB V. A joint statement by the German Society of General Practice/Family Medicine (DEGAM), the German Society of Geriatrics (DGG), the German Society of Gynaecology and Obstetrics (DGGG), the German Society of Neurology (DGN), the German Society of Urology (DGU) and the German Continence Society (DKG) is available.

The guidelines and the statements of the scientific-medical societies recommend the administration of β3-adrenoceptor agonists or anticholinergics for the symptomatic treatment of OAB syndrome. In addition, reference is made to physiotherapeutic measures (pelvic floor training).

From the group of antimuscarinics, the active ingredient oxybutynin cannot be considered as an appropriate comparator therapy due to the consistently more frequent occurrence of the adverse event of dry mouth in the direct comparator studies and the more frequent therapy discontinuation due to adverse events. The available evidence does not contain any explicit recommendations on flavoxate for adults with overactive bladder, so that the active ingredient flavoxate cannot be considered as an appropriate comparator therapy either.

Against this background, the G-BA determined the active ingredients darifenacin or desfesoterodine or fesoterodine or mirabegron or propiverine or solifenacin or tolterodine or trospium chloride as the appropriate comparator therapy for vibegron for adults with overactive bladder. The appropriate comparator therapy determined here includes several therapy options. These therapeutic alternatives are equally appropriate for the comparator therapy. The additional benefit can be demonstrated compared to one of the therapeutic alternatives mentioned.

Non-medicinal measures within the meaning of the Remedies Directive or the catalogue of remedies (e.g. physiotherapy) can contribute to alleviation of symptoms and should be offered in both study arms if indicated.

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

A change in the appropriate comparator therapy requires a resolution by the G-BA linked to the prior review of the criteria according to Chapter 5 Section 6, paragraph 3 Rules of Procedure.

2.1.3 Extent and probability of the additional benefit

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

<u>Adults with an overactive bladder</u>

An additional benefit is not proven.

Justification:

The pharmaceutical company used the randomised, controlled, double-blind RVT-901-3003 and RVT-901-3004 studies (extension study of the RVT-901-3003 study) for the assessment of the additional benefit of vibegron for the treatment of adults with overactive bladder.

RVT-901-3003 study (3003)

The randomised, controlled, double-blind, multicentre 3003 study investigated the administration of vibegron versus tolterodine or placebo in adults diagnosed with overactive bladder. The treatment phase lasted 12 weeks overall. Adults who had an existing medical diagnosis of overactive bladder (OAB; defined as "OAB dry" or "OAB wet") for at least 3 months prior to enrolment in the study were enrolled in the study. The "OAB dry" was defined as an average of ≥ 8 micturitions, an average of ≥ 3 episodes with imperative urge to urinate and an average of < 1 urge incontinence episodes (each per day). The "OAB wet" was defined as an average of ≥ 8 micturitions and an average of ≥ 1 urge incontinence episodes (each per day). If stress incontinence was present, the total number of urge incontinence episodes had to be greater than the total number of stress incontinence episodes in the diary entries from the last visit. In addition, only subjects who showed ≥ 80% compliance with self-administration of the study medication during the 2-week placebo run-in phase were enrolled. Reasons for exclusion were as follows: previous surgical intervention to correct stress incontinence, pelvic organ prolapse, treatment of benign prostatic hyperplasia in the 6 months prior to screening, injection of botulinum toxin into the urinary bladder muscles in the 9 months prior to screening, urinary bladder training or electrical stimulation in the 28 days prior to screening or plans to start such treatment during the study.

The 1,518 patients were randomised in a 5:5:4 ratio to the study arms (vibegron 75 mg, placebo or tolterodine 4 mg) at the start of the study. A 5-week screening phase, which included a 28-day washout phase, was followed by a 2-week placebo run-in phase and a 12-week treatment phase. Subsequently, the subjects either entered a 4-week follow-up phase or the 3004 extension study.

The 3003 study was conducted in the period from March 2018 to February 2019.

RVT-901-3004 extension study (3004)

The randomised, controlled, double-blind, multicentre 3004 study investigated the administration of vibegron versus tolterodine over 40 weeks. Subjects were enrolled if they had completed the 3003 study and showed at least 80% compliance with the study medication and at least 4 complete diary days in the micturition diary at week 12. In the 3004 study, the study participants remained with the respective assignment of the study medication from the 3003 study (vibegron or tolterodine). Patients who had been randomised to the placebo arm in the 3003 study were randomised in a 1:1 ratio to the vibegron or tolterodine treatment arm. The number of subjects who received vibegron and tolterodine continuously for 52 weeks was 182 and 141 patients respectively.

The 3004 study was conducted between June 2018 and July 2019 and took place exclusively in study sites in the USA.

Uncertainties of the 3003 and 3004 studies

Patient population enrolled in the 3003 study

The 3003 study enrolled patients with OAB who had to fulfil certain criteria regarding the frequency of episodes of imperative urge to urinate, urge incontinence and micturition

frequency (see study description). However, in the current guidelines[3,4,5], the diagnosis of OAB is not linked to specific requirements regarding the number of micturitions or episodes with imperative urge to urinate or urge incontinence. According to the guidelines, the focus is rather on the degree of burden caused to patients by micturition frequency.

Irrespective of this, the inclusion criteria of the 3003 study with regard to micturition frequency are considered sufficient for the presence of OAB, as they sufficiently reflect the definition of OAB according to the guidelines.

In addition, patients who had undergone urinary bladder training or electrical stimulation in the 28 days prior to screening or were planning to start such treatment during the study were excluded from participation in the 3003 study. However, this restriction does not correspond to everyday care and the S2k guidelines[3,4] also recommend these non-medical measures for this patient population.

From the information available, it remains unclear overall to what extent these non-medical measures were indicated for the study population. In addition, no specific information on the use of these measures before or during the 3003 and 3004 studies can be obtained from the study documents.

Implementation of the appropriate comparator therapy

The studies investigated the administration of vibegron versus tolterodine in adults diagnosed with OAB. According to the product information, the daily dose of tolterodine can be reduced from 4 mg to 2 mg in case of intolerance. However, no dose adjustments were permitted in the two studies. Overall, it is unclear to what extent adverse events could have been avoided in the comparator arm if dose reduction was possible.

Transition from the 3003 study to the 3004 extension study

The transition of patients from the 3003 study to the 3004 extension study is subject to the following uncertainties:

Around 10% of the 1,518 study participants enrolled in the 3003 study discontinued the study prematurely and did not have the option to switch to the extension study. The study documents show that the study discontinuations in the 3003 study occurred with comparable frequency between the study arms (vibegron, tolterodine and placebo) and for similar reasons (e.g. due to withdrawal of consent to study participation, due to lost to follow-up and due to AEs). On the basis of the available documents, it is not possible to assess whether the reasons that led the study participants to withdraw their consent differed between the study arms. Even if the percentage of subjects with such a withdrawal was rather low (2.6% in the vibegron arm, 3.0% in the tolterodine arm, 3.9% in the placebo arm), there is still uncertainty as to

[3] German Society of Gynaecology and Obstetrics, Austrian Society of Gynaecology and Obstetrics, Swiss Society of Gynaecology and Obstetrics (2022): Urinary incontinence in women, AWMF registry number 015-091, guideline class S2k, last revised December 2021, version 1.0 [online]. https://register.awmf.org/assets/guidelines/015-091l_S2k_Harninkontinenz-der-Frau_2022-03.pdf

[4] German Society of Geriatrics, German Society of Urology, German Society of Gynaecology and Obstetrics et al. (2024): Urinary incontinence in geriatric patients – diagnosis and therapy, version 7.1 (update 2024), S2k guideline [online]. https://register.awmf.org/assets/guidelines/084-001l_S2e_Harninkontinenz-bei-geriatrischen-Patienten-Diagnostik-Therapie_2024-01_1.pdf

[5] International Continence Society (2025), Factsheet: Overactive Bladder [online]. https://www.ics.org/public/factsheets/overactivebladder

whether there is an unequal distribution of reasons for discontinuation between the study arms.

In addition, it was planned that around 500 subjects of the study participants who had completed the 3003 study would be transferred to the 3004 extension study. In the publication Staskin et al., 2021[6] it was reported that 506 of 587 study participants (approx. 86%) who were the first to complete the 3003 study decided to participate in the 3004 study and also met the inclusion and exclusion criteria. Among other things, patients were not allowed to take part in the extension study if new health problems, which, in the opinion of the principal investigator, could falsify the results of the study, had arisen in the course of the previous study. The requirement that continued study participation depended on the patients' decision and the absence of an exclusion criterion can potentially lead to an impairment of structural equality, as these points may differ between the two treatment groups.

For the remaining 14% of the 587 participants in the 3003 study, no information is available on the reasons why they were excluded from participation in the extension study (e.g. whether these subjects had new health problems) or the reasons why they decided not to participate in the extension study. Since these missing reasons may be potentially informative, it therefore remains unclear whether the structural equality of the study arms is ultimately impaired.

Overall, the risk of bias across endpoints is assessed as high on the basis of these uncertainties although it is assumed that the structural equality of the study arms in the transition from the 3003 study to the 3004 extension study is not impaired to such an extent that the results could not be used for the benefit assessment.

Sub-population relevant for the benefit assessment

Only the presented sub-population that was treated with vibegron or tolterodine during the two 3003 and 3004 studies, thus continuously over a period of 52 weeks, is relevant for the present benefit assessment. This sub-population includes 182 patients in the vibegron arm and 141 patients in the tolterodine arm.

Extent and probability of the additional benefit

Mortality

There was no death in the 3003 and 3004 studies.

[6] Staskin et al. (2021), Once-Daily Vibegron 75 mg for Overactive Bladder: Long-Term Safety and Efficacy from a Double-Blind Extension Study of the International Phase 3 Trial (EMPOWUR). J Urol 2021; 205(5): 1421-1429. https://doi.org/10.1097/JU.0000000000001574

Morbidity

Health status (EQ-5D VAS)

For the endpoint of health status, collected using visual analogue scale (VAS) of the EQ-5D, there was no statistically significant difference between the treatment groups.

Symptomatology (symptom bother score, PGI-Change, PGI -Severity and PGI-Control)

Symptomatology was assessed in the studies using the symptom bother score symptom scale of the overactive bladder symptom and health-related quality of life questionnaire long form (OAB-q LF), the Patient Global Impression (PGI) - Change, the PGI-Severity and the PGI-Control. The responder analyses, which depict an improvement, were used for the benefit assessment. No results were available for the PGI-Control in Module 4. Although the pharmaceutical company submitted additional analyses on PGI-Control in the written statement procedure, these could have already been submitted in the dossier, so that the continuous data from the study report are used for the benefit assessment.

Overall, for each of the endpoints, there was no statistically significant difference between treatment groups.

Incontinence, urge incontinence, micturition frequency, imperative urge to urinate and nycturia

In the two 3003 and 3004 studies, the number of micturitions, episodes of imperative urge to urinate, incontinence and urge incontinence as well as nocturia were documented by the patients in micturition diaries 7 days before each visit. The average value per 24 hours was then calculated on the basis of the records.

In Module 4, in addition to the predefined evaluations of the change at week 52 compared to baseline, the pharmaceutical company also submitted various responder analyses, some of which were predefined and some of which were conducted post hoc. In view of the fact that the presented response thresholds sometimes differ between the endpoints and the rationale for the choice of the respective response thresholds is absent, only the continuous analyses are used for the endpoints of incontinence, urge incontinence, micturition frequency, imperative urge to urinate and nycturia.

For the endpoints of incontinence and urge incontinence respectively, there was a statistically significant difference to the advantage of vibegron compared to tolterodine based on the mean differences. However, it cannot be concluded from the associated effect estimators and 95% confidence intervals that there are clinically relevant effects with the mean difference of half an incontinence episode between the two treatment arms. This assessment is also made against the background that the advantages are not reflected in other patient-relevant endpoints such as micturition frequency, imperative urge to urinate or nycturia.

For the endpoints of micturition frequency, imperative urge to urinate and nycturia, there was no statistically significant difference between the treatment groups in each case.

Quality of life

Health-related quality of life was assessed using the OAB-q LF. The responder analyses which depict a clinically relevant improvement are used for the benefit assessment. There were no signs of statistically significant differences between the treatment groups. There was an effect modification here due to the "Age" characteristic: For subjects ≥ 65 years, there was a statistically significant improvement in quality of life in the vibegron arm compared to the tolterodine arm. For subjects < 65 years, there was still no statistically significant difference.

However, this effect modification is reflected in none of the other patient-relevant endpoints. Moreover, the medical rationale for this age limit is unclear. Overall, the results of the observed effect modification due to the "Age" characteristic are considered inadequate to derive separate statements on the additional benefit for subjects < 65 years and ≥ 65 years in the overall assessment.

Side effects

SAEs, severe AEs and discontinuation due to AEs

For the overall rates of serious adverse events (SAEs), severe AEs and discontinuation due to AEs, there was no statistically significant difference between the treatment groups in each case.

Specific AEs

Urinary tract infection and dry mouth

In detail, for the AE of urinary tract infection, there was no statistically significant difference between treatment groups. For the AE of dry mouth, there was a statistically significant difference to the advantage of vibegron compared to tolterodine.

Overall assessment

The results of the 3003 and 3004 studies are available. Only the sub-population that was treated with vibegron or tolterodine during the two studies, thus continuously over a period of 52 weeks, is considered for the assessment of the additional benefit.

There were no deaths in the studies.

For the endpoint category of morbidity, there was no statistically significant difference between the treatment groups for each of the endpoints of health status (EQ-5D VAS), symptomatology (measured using the symptom bother score, PGI-Change, PGI-Severity and PGI-Control), micturition frequency, imperative urge to urinate and nycturia. For the endpoints of incontinence and urge incontinence respectively, there was a statistically significant difference to the advantage of vibegron compared to tolterodine based on the mean differences. However, the reduction by half an incontinence episode per day is not considered to be a clinically relevant benefit. This assessment is also made against the background that the advantages are not reflected in other patient-relevant endpoints such as micturition frequency, imperative urge to urinate or nycturia.

For the endpoint category of health-related quality of life assessed using the OAB-q LF, there was no statistically significant difference between the treatment groups. There was an effect modification here due to the "Age" characteristic. For subjects ≥ 65 years, there was a statistically significant improvement in quality of life in favour of vibegron compared to tolterodine. However, the results of the observed effect modification due to the "Age" characteristic are considered inadequate to derive separate statements on the additional benefit for subjects < 65 years and ≥ 65 years in the overall assessment.

For the endpoint category of side effects, the overall rates of serious adverse events (SAEs), severe AEs and discontinuation due to AEs showed no statistically significant difference between the treatment groups in each case. In detail, for the AE of dry mouth, there was a statistically significant advantage of vibegron compared to tolterodine. In the overall assessment of the results in the side effects category, no additional benefit of vibegron compared to tolterodine was derived.

In summary, it was concluded that an additional benefit of vibegron over the appropriate comparator therapy of tolterodine was not proven for adults with overactive bladder.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product "Obgemsa" with the active ingredient "vibegron". The active ingredient vibegron is approved for the symptomatic treatment of overactive bladder in adults. The active ingredients darifenacin or desfesoterodine or fesoterodine or mirabegron or propiverine or solifenacin or tolterodine or trospium chloride were determined as the appropriate comparator therapy.

The pharmaceutical company submitted the randomised, controlled, double-blind RVT-901-3003 study and the associated RVT-901-3004 extension study. Only the sub-population that was treated with vibegron or tolterodine continuously over a period of 52 weeks during the two studies is relevant for the benefit assessment.

There were no deaths in the studies.

For the endpoint category of morbidity, there was no statistically significant difference between the treatment groups for each of the endpoints of health status, symptomatology, micturition frequency, imperative urge to urinate and nycturia. For the endpoints of incontinence and urge incontinence respectively, there was a statistically significant difference to the advantage of vibegron compared to tolterodine. However, the reduction by half an incontinence episode per day is not considered to be a clinically relevant benefit. This assessment is also made against the background that the advantages are not reflected in other patient-relevant endpoints such as micturition frequency, imperative urge to urinate or nycturia.

For health-related quality of life, there was no statistically significant difference between the treatment groups. There was an effect modification here due to the age characteristic. For subjects ≥ 65 years, there was a statistically significant improvement in quality of life in favour of vibegron compared to tolterodine. However, the results of the observed effect modification are considered inadequate to derive separate statements on the additional benefit for subjects < 65 years and ≥ 65 years in the overall assessment.

For the endpoint category of side effects, the overall rates of serious adverse events (SAEs), severe AEs and discontinuation due to AEs did not result in any statistically significant difference between the treatment groups in each case. In detail, for the AE of dry mouth, there was a statistically significant advantage of vibegron compared to tolterodine. In the overall assessment of the results in the side effects category, no additional benefit of vibegron compared to tolterodine was derived.

In summary, it was concluded that an additional benefit of vibegron over the appropriate comparator therapy of tolterodine was not proven for adults with overactive bladder.

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

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

The number of patients stated by the pharmaceutical company refers exclusively to patients who are already undergoing medicinal treatment. This assumption leads to an underestimation of the patient number, as patients who are not currently being treated but are in need of treatment are also eligible for the medicinal product to be assessed. In addition,

the prevalences stated by the pharmaceutical company for the upper and lower limits of patients with OAB syndrome treated with medication are subject to uncertainties.

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 Obgemsa (active ingredient: vibegron) at the following publicly accessible link (last access: 5 August 2025):

https://www.ema.europa.eu/en/documents/product-information/obgemsa-epar-product-information_en.pdf

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 August 2025).

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 varies from patient to patient and/or is shorter on average. The time unit "days" is used to calculate the "number of treatments/ patient/ year", time intervals between individual treatments and for the maximum treatment duration, if specified in the product information.

For the cost representation, only the dosages of the general case are considered. Patient-individual dose adjustments (e.g. because of side effects or comorbidities) are not taken into account when calculating the annual treatment costs.

Adults with an overactive bladder

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Vibegron	Continuously, 1 x daily	365.0	1	365.0
Appropriate comparator therapy				
Darifenacin	Continuously, 1 x daily	365.0	1	365.0
Desfesoterodine	Continuously, 1 x daily	365.0	1	365.0
Fesoterodine	Continuously, 1 x daily	365.0	1	365.0
Mirabegron	Continuously, 1 x daily	365.0	1	365.0
Propiverine	Continuously, 1 x daily	365.0	1	365.0
Solifenacin	Continuously, 1 x daily	365.0	1	365.0
Tolterodine	Continuously, 1 x daily	365.0	1	365.0
Trospium chloride	Continuously, 2-3 x daily	365.0	1	365.0

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					
Vibegron	75 mg	75 mg	1 x 75 mg	365.0	365 x 75 mg
Appropriate comparator therapy					
Darifenacin	7.5 mg – 15 mg	7.5 mg – 15 mg	1 x 7.5 mg – 1 x 15 mg	365.0	365 x 7.5 mg – 365 x 15 mg
Desfesoterodine	3.5 mg – 7 mg	3.5 mg – 7 mg	1 x 3.5 mg – 1 x 7 mg	365.0	365 x 3.5 mg – 365 x 7 mg
Fesoterodine	4 mg – 8 mg	4 mg – 8 mg	1 x 4 mg – 1 x 8 mg	365.0	365 x 4 mg – 365 x 8 mg
Mirabegron	50 mg	50 mg	1 x 50 mg	365.0	365 x 50 mg
Propiverine	30 mg – 45 mg	30 mg – 45 mg	1 x 30 mg – 1 x 45 mg	365.0	365 x 30 mg – 365 x 45 mg
Solifenacin	5 mg – 10 mg	5 mg – 10 mg	1 x 5 mg – 1 x 10 mg	365.0	365 x 5 mg – 365 x 10 mg
Tolterodine	4 mg	4 mg	1 x 4 mg	365.0	365 x 4 mg
Trospium chloride	15 mg	30 mg – 45 mg	1 x 30[7] mg – 1 x 45[8] mg	365.0	365 x 30 mg – 365 x 45 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. Any reference prices shown in the cost representation may not represent the cheapest available alternative.

[7] Film-coated tablet divisible into 2 equal-dose halves
[8] Film-coated tablet divisible into 3 equal-dose thirds

Costs of the medicinal products:

Adults with an overactive bladder

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					
Vibegron 75 mg	90 FCT	€ 159.61	€ 1.77	€ 8.21	€ 149.63
Appropriate comparator therapy					
Darifenacin 7.5 mg[9]	98 SRT	€ 57.55	€ 1.77	€ 3.66	€ 52.12
Darifenacin 15 mg[9]	98 SRT	€ 69.10	€ 1.77	€ 4.57	€ 62.76
Desfesoterodine 3.5 mg[9]	98 SRT	€ 56.08	€ 1.77	€ 0.00	€ 54.31
Desfesoterodine 7 mg[9]	98 SRT	€ 67.13	€ 1.77	€ 0.00	€ 65.36
Fesoterodine 4 mg[9]	100 SRT	€ 57.45	€ 1.77	€ 3.65	€ 52.03
Fesoterodine 8 mg[9]	100 SRT	€ 68.85	€ 1.77	€ 4.55	€ 62.53
Mirabegron 50 mg[9]	100 SRT	€ 63.75	€ 1.77	€ 0.00	€ 61.98
Propiverine 30 mg[9]	98 MHC	€ 60.42	€ 1.77	€ 0.00	€ 58.65
Propiverine 45 mg[9]	98 MHC	€ 67.26	€ 1.77	€ 0.00	€ 65.49
Solifenacin 5 mg[9]	90 FCT	€ 53.85	€ 1.77	€ 3.36	€ 48.72
Solifenacin 10 mg[9]	90 FCT	€ 64.36	€ 1.77	€ 4.20	€ 58.39
Tolterodine 4 mg[9]	98 MHC	€ 60.77	€ 1.77	€ 3.91	€ 55.09
Trospium chloride 30 mg[9]	100 FCT	€ 54.39	€ 1.77	€ 3.41	€ 49.21
Trospium chloride 45 mg[9]	100 FCT	€ 60.33	€ 1.77	€ 3.88	€ 54.68
Abbreviations: FCT = film-coated tablets; MHC = modified-release hard capsules; SRT = sustained release tablet; SUS = suspension					

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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.

[9] Fixed reimbursement rate

2.5 Designation of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

According to Section 35a, paragraph 3, sentence 4, the G-BA designate all medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

Basic principles of the assessed medicinal product

A designation in accordance with Section 35a, paragraph 3, sentence 4 SGB V requires that it is examined based on the product information for the assessed medicinal product whether it can be used in a combination therapy with other medicinal products in the assessed therapeutic indication. In the first step, the examination is carried out on the basis of all sections of the currently valid product information for the assessed medicinal product.

If the assessed medicinal product contains an active ingredient or a fixed combination of active ingredients in the therapeutic indication of the resolution (assessed therapeutic indication) and is approved exclusively for use in monotherapy, a combination therapy is not considered due to the marketing authorisation under Medicinal Products Act, which is why no designation is made.

A designation is also not considered if the G-BA have decided on an exemption as a reserve antibiotic for the assessed medicinal product in accordance with Section 35a, paragraph 1c, sentence 1 SGB V. The additional benefit is deemed to be proven if the G-BA have decided on an exemption for a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V; the extent of the additional benefit and its therapeutic significance are not to be assessed by the G-BA. Due to the lack of an assessment mandate by the G-BA following the resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with regard to the extent of the additional benefit and the therapeutic significance of the reserve antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

With regard to the further examination steps, a differentiation is made between a "determined" or "undetermined" combination, which may also be the basis for a designation.

A "determined combination" exists if one or more individual active ingredients which can be used in combination with the assessed medicinal product in the assessed therapeutic indication are specifically named.

An "undetermined combination" exists if there is information on a combination therapy, but no specific active ingredients are named. An undetermined combination may be present if the information on a combination therapy:

- names a product class or group from which some active ingredients not specified in detail can be used in combination therapy with the assessed medicinal product, or

- does not name any active ingredients, product classes or groups, but the assessed medicinal product is used in addition to a therapeutic indication described in more detail in the relevant product information, which, however, does not include information on active ingredients within the scope of this therapeutic indication.

Concomitant active ingredient

The concomitant active ingredient is a medicinal product with new active ingredients that can be used in combination therapy with the assessed medicinal product for the therapeutic indication to be assessed.

For a medicinal product to be considered as a concomitant active ingredient, it must be classified as a medicinal product with new active ingredients according to Section 2 paragraph 1 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with the corresponding regulations in Chapter 5 of the Rules of Procedure of the G-BA as of the date of the present resolution. In addition, the medicinal product must be approved in the assessed therapeutic indication, whereby a marketing authorisation is sufficient only for a sub-area of the assessed therapeutic indication.

Based on an "undetermined combination", the concomitant active ingredient must be attributable to the information on the product class or group or the therapeutic indication according to the product information of the assessed medicinal product in the assessed therapeutic indication, whereby the definition of a product class or group is based on the corresponding requirements in the product information of the assessed medicinal product.

In addition, there must be no reasons for exclusion of the concomitant active ingredient from a combination therapy with the assessed medicinal product, in particular no exclusive marketing authorisation as monotherapy.

In addition, all sections of the currently valid product information of the eligible concomitant active ingredient are checked to see whether there is any information that excludes its use in combination therapy with the assessed medicinal product in the assessed therapeutic indication under marketing authorisation regulations. Corresponding information can be, for example, dosage information or warnings. In the event that the medicinal product is used as part of a determined or undetermined combination which does not include the assessed medicinal product, a combination with the assessed medicinal product shall be excluded.

Furthermore, the product information of the assessed medicinal product must not contain any specific information that excludes its use in combination therapy with the eligible concomitant active ingredient in the assessed therapeutic indication under marketing authorisation regulations.

Medicinal products with new active ingredients for which the G-BA have decided on an exemption as a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V are ineligible as concomitant active ingredients. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V also applies accordingly to the medicinal product eligible as a concomitant active ingredient.

Designation

The medicinal products which have been determined as concomitant active ingredients in accordance with the above points of examination are named by indicating the relevant active ingredient and the invented name. The designation may include several active ingredients, provided that several medicinal products with new active ingredients may be used in the same combination therapy with the assessed medicinal product or different combinations with different medicinal products with new active ingredients form the basis of the designation.

If the present resolution on the assessed medicinal product in the assessed therapeutic indication contains several patient groups, the designation of concomitant active ingredients shall be made separately for each of the patient groups.

Exception to the designation

The designation excludes combination therapies for which - patient group-related - a considerable or major additional benefit has been determined by resolution according to Section 35a, paragraph 3, sentence 1 SGB V or it has been determined according to Section 35a, paragraph 1d, sentence 1 SGB V that at least considerable additional benefit of the combination can be expected. In this context, the combination therapy that is excluded from the designation must, as a rule, be identical to the combination therapy on which the preceding findings were based.

In the case of designations based on undetermined combinations, only those concomitant active ingredients - based on a resolution according to Section 35a, paragraph 3, sentence 1 SGB V on the assessed medicinal product in which a considerable or major additional benefit had been determined - which were approved at the time of this resolution are excluded from the designation.

Legal effects of the designation

The designation of combinations is carried out in accordance with the legal requirements according to Section 35a, paragraph 3, sentence 4 and is used exclusively to implement the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The designation is not associated with a statement as to the extent to which a therapy with the assessed medicinal products in combination with the designated medicinal products corresponds to the generally recognised state of medical knowledge. The examination was carried out exclusively on the basis of the possibility under Medicinal Products Act to use the medicinal products in combination therapy in the assessed therapeutic indication based on the product information; the generally recognised state of medical knowledge or the use of the medicinal products in the reality of care were not the subject of the examination due to the lack of an assessment mandate of the G-BA within the framework of Section 35a, paragraph 3, sentence 4 SGB V.

The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

Justification for the findings on designation in the present resolution:

Adults with an overactive bladder

No medicinal product with new active ingredients that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

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

At their session on 7 January 2025, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 28 February 2025, the pharmaceutical company submitted a dossier for the benefit assessment of vibegron to the G-BA in due time.

By letter dated 3 March 2025 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit 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 vibegron.

The dossier assessment by the IQWiG was submitted to the G-BA on 28 May 2025, and the written statement procedure was initiated with publication on the G-BA website on 2 June 2025. The deadline for submitting statements was 23 June 2025.

The oral hearing was held on 7 July 2025.

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 session of the Subcommittee on 12 August 2025, and the proposed draft resolution was approved.

At their session on 21 August 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	7 January 2025	Determination of the appropriate comparator therapy
Working group Section 35a	1 July 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	7 July 2025	Conduct of the oral hearing
Working group Section 35a	15 July 2025 5 August 2025	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	12 August 2025	Concluding discussion of the draft resolution
Plenum	21 August 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 21 August 2025

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

Prof. Hecken