Date: 16 December 2025
Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

Obgemsa

International non-proprietary name: vibegron
Pharmaceutical form: film-coated tablets
Dosage strength(s): 75 mg
Route(s) of administration: oral
Marketing authorisation holder: Pierre Fabre Pharma SA
Marketing authorisation no.: 69983
Decision and decision date: approved on 20 August 2025

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

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1 Terms, definitions, abbreviations

ADA	Anti-drug antibody
ADME	Absorption, distribution, metabolism, elimination
AE	Adverse event
ALT	Alanine aminotransferase
API	Active pharmaceutical ingredient
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical Classification System
AUC	Area under the plasma concentration-time curve
$AUC_{0\text{-}24h}$	Area under the plasma concentration-time curve for the 24-hour dosing interval
CI	Confidence interval
C_{max}	Maximum observed plasma/serum concentration of drug
CYP	Cytochrome P450
DDI	Drug-drug interaction
EMA	European Medicines Agency
ERA	Environmental risk assessment
FDA	Food and Drug Administration (USA)
GFR	Glomerular filtration rate
GI	Gastrointestinal
GLP	Good Laboratory Practice
HPLC	High-performance liquid chromatography
IC/EC_{50}	Half-maximal inhibitory/effective concentration
ICH	International Council for Harmonisation
Ig	Immunoglobulin
INN	International non-proprietary name
ITT	Intention-to-treat
LoQ	List of Questions
MA	Marketing authorisation
MAH	Marketing authorisation holder
Max	Maximum
Min	Minimum
MRHD	Maximum recommended human dose
N/A	Not applicable
NO(A)EL	No observed (adverse) effect level
OAB	Overactive bladder
PBPK	Physiology-based pharmacokinetics
PD	Pharmacodynamics
PIP	Paediatric investigation plan (EMA)
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
PSP	Pediatric study plan (US FDA)
RMP	Risk management plan
SAE	Serious adverse event
SwissPAR	Swiss Public Assessment Report
TEAE	Treatment-emergent adverse event
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)
UUI	Urge urinary incontinence

2 Background information on the procedure

2.1 Applicant's request(s) and information regarding procedure

New active substance status
The applicant requested new active substance status for vibegron in the above-mentioned medicinal product.

2.2 Indication and dosage

2.2.1 Requested indication

Obgemsa is used in adults for symptomatic therapy of overactive bladder (OAB) syndrome.

2.2.2 Approved indication

Obgemsa is used in adults for symptomatic therapy of overactive bladder (OAB) syndrome.

2.2.3 Requested dosage

Summary of the requested standard dosage:
The recommended dose is one 75 mg tablet once daily, with or without food.

Renal impairment
Mild, moderate, or severe renal impairment (15 mL/min < GFR < 90 mL/min and not requiring dialysis): No dose adjustment.
End-stage renal disease (GFR < 15 mL/min with or without haemodialysis): Vibegron has not been studied and is therefore not recommended in these patients.

Hepatic impairment
Mild to moderate hepatic impairment (Child-Pugh A and B): No dose adjustment.
Severe hepatic impairment (Child-Pugh C): no data available and therefore not recommended in this patient population.

Paediatric population
No data are available in children under 18 years of age.

2.2.4 Approved dosage

(See appendix)

2.3 Regulatory history (milestones)

Application	15 July 2024
Formal objection	6 August 2024
Response to formal objection	28 August 2024
Formal control completed	12 September 2024

Preliminary decision	13 January 2025
Response to preliminary decision	11 March 2025
Labelling corrections and/or other aspects	28 May 2025
Response to labelling corrections and/or other aspects	26 June 2025
Final decision	20 August 2025
Decision	approval

3 Medical context

Medicinal product proposed for MA. Vibegron is a ß3 adrenergic receptor agonist. Activation of the beta-3 adrenergic receptor located in the bladder detrusor muscle increases bladder capacity by relaxing the detrusor smooth muscle during bladder filling.

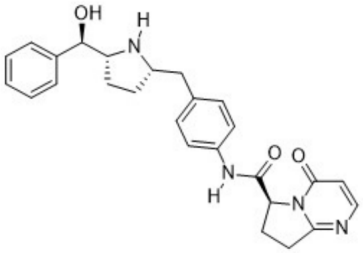
Condition addressed in the indication. Overactive bladder is a clinical syndrome characterised by urinary urgency (i.e., a sudden compelling desire to void that is difficult to defer) with or without urge urinary incontinence (UUI). The aim of therapy is to increase bladder control and thereby decrease the daily number of urinary urgency and/or incontinence episodes.

Available therapies and unmet medical need
There is a disease burden in OAB, and although a wide range of therapies is available, there is an unmet need for more effective therapy in this common medical condition. The active substance in the present application, vibegron, has a mechanism of action similar to mirabegron. Obgemsa may be crushed, e.g. for use in patients with dysphagia or administration via feeding tubes.

4 Quality aspects

4.1 Drug substance

INN: Vibegron
Chemical name: (6S)-N-[4-[[(2S,5R)-5-[(R)-hydroxy(phenyl)methyl]pyrrolidin-2- yl]methyl]phenyl]-4-oxo-7,8-dihydro-6H-pyrrolo[1,2-a]pyrimidine-6-carboxamide
Molecular formula: $C_{26}H_{28}N_4O_3$
Molecular mass: 444.538 g/mol
Molecular structure:



Physicochemical properties: Vibegron is a white to off-white to tan powder. It has four stereochemical centres.

Synthesis: The drug substance is manufactured by multiple-step chemical synthesis. The synthesis of the drug substance and the necessary in-process controls are described in detail.

Specification: To ensure consistent drug substance quality, the specifications include all relevant test parameters as recommended by the relevant ICH guidelines.

Stability: Appropriate stability data have been generated, resulting in a suitable retest period.

4.2 Drug product

Description and composition: Vibegron 75mg tablets are supplied as light green, oval, film-coated immediate release tablets debossed with V75 on one side and plain on the other.

Pharmaceutical development: Suitable pharmaceutical development data have been provided for the finished product composition and manufacturing process.

Manufacture: Vibegron film-coated tablets are manufactured by a standard process consisting of component blending, granulation, compression into tablets and film-coating. Adequate process parameters and in-process controls are defined to ensure consistent tablet quality.

Specification: Adequate tests and criteria at release and during shelf-life have been established for finished product control. The test methods applied are adequately validated according to the recommendations of the current scientific guidelines.

Container closure system: The primary container closure system used for commercial distribution of vibegron tablets is a high-density polyethylene (HDPE) bottle packaging with a child-resistant polypropylene (PP) cap, and an induction seal type liner (inner seal).

Stability: Appropriate stability data have been generated in the packaging material intended for commercial use and according to the relevant international guidelines.

4.3 Quality conclusions

Satisfactory and consistent quality of the drug substance and drug product has been demonstrated.

5 Nonclinical aspects

The Nonclinical Assessment Division conducted an abridged evaluation, which was based on the EMA assessment report EMA/CHMP/133512/2024 (approval 25 April 2024) provided by the applicant, for the marketing authorisation application for Obgemsa.

Overall, the submitted nonclinical documentation is considered appropriate to support the approval of Obgemsa in the proposed indication. The pharmaco-toxicological profile has been sufficiently characterised. All nonclinical data that are relevant for safety are adequately mentioned in the Information for healthcare professionals.
There are no safety concerns arising from impurities and excipients.
A phase II ERA assessment to determine the risk of Obgemsa to the environment is being conducted and will be provided by the end of 2025.

From the nonclinical standpoint, there is no objection to the approval of Obgemsa in the requested indication.

6 Clinical aspects

6.1 Clinical and clinical pharmacology assessment

The evaluation of the clinical and clinical pharmacological data of this application has been carried out in reliance on previous regulatory decisions by EMA. The available assessment report and respective product information from EMA were used as a basis for clinical and clinical pharmacology evaluation. For further details concerning clinical pharmacology, dosing recommendations, efficacy, and safety, see the appendix of this report.

7 Risk management plan summary

The RMP summaries contain information on the medicinal products′ safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

8 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for Obgemsa was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo.ch).

Note:
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

▼ This medicine is subject to additional monitoring. This allows for the rapid identification of new safety insights. Healthcare professionals are encouraged to report suspicion of a new or serious adverse reaction. For information on reporting side effects, see the "Undesirable effects" section.

Obgemsa

Composition

Active substances

Vibegron

Excipients

Tablet core: mannitol (E421), microcrystalline cellulose (E460), croscarmellose sodium (equivalent to 0.405 mg sodium) (E468), hydroxypropyl cellulose (E463), magnesium stearate
Film coating: indigotine (E132), hypromellose (E464), yellow iron oxide (E172), lactose monohydrate (1.575 mg), titanium dioxide (E171), triacetin

Formulation and amount of active ingredient per unit

film-coated tablet.
Each film-coated tablet contains 75 mg of Vibegron
Light green oval film-coated tablet with the embossing V75 on one side and smooth on the other side. The dimensions of the tablet are approximately 9 mm (length) x 4 mm (width) x 3 mm (height).

Indications/Uses

Obgemsa is used in adults for symptomatic therapy of overactive bladder (OAB) syndrome.

Dosage/Administration

Usual dosage

The recommended dose is 75 mg once a day.

Special dosing instructions

Patients with hepatic impairment

In patients with mild to moderate hepatic impairment (Child Pugh A and B), dose adjustment of Vibegron is not recommended. Vibegron has not been studied in patients with severely impaired hepatic function (Child Pugh C) and is therefore not recommended in this patient population (see Pharmacokinetics *section*).

Patients with renal impairment

No dose adjustment of Vibegron is recommended in patients with mild, moderate or severe renal impairment (15 mL/min < GFR < 90 mL/min and not requiring dialysis). In patients with end-stage renal disease (GFR < 15 ml/min with or without haemodialysis), Vibegron has not been studied and is therefore not recommended in these patients (see Pharmacokinetics *section*).

Children and adolescents

The safety and efficacy of Obgemsa in children and adolescents under 18 years of age have not been established. No data available.

Method of administration

To be taken with or without food. Swallow with 200-300ml of water (equivalent to one glass). Obgemsa 75 mg film-coated tablets can also be crushed and taken mixed with a tablespoon (approximately 15 ml) of soft food (e.g. applesauce) along with a glass of water.

Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in *the composition section*.

Warnings and precautions

Patients with bladder outlet obstruction and patients taking antimuscarinic drugs to treat OAB

Urinary retention has been reported in patients taking Obgemsa. The risk of urinary retention may be increased in patients with bladder outlet obstruction, with pre-existing bladder emptying disorder of other causes (such as damage to the lower bladder centerin the spinal cord), and in patients taking muscarine antagonists with Obgemsa. Signs and symptoms of urinary retention should be monitored before and during treatment with Vibegron, especially in patients with clinically significant bladder outlet obstruction, patients with predisposing conditions to bladder outlet obstruction, and in patients taking Vibegron with muscarine antagonists.
Obgemsa should be discontinued in patients who develop urinary retention.

Lactose

Patients with rare hereditary galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not use this medicine.

Sodium

This medicine contains less than 1 mmol of sodium (23 mg) per tablet, which means it is almost 'sodium-free'.

Interactions

Effect of Obgemsa on other medicinal products

In vitro data

Vibegron is not an inhibitor of CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, or CYP3A4/5 and has not caused time-dependent inhibition of these enzymes.

Vibegron is not an inducer of CYP1A2, CYP2B6, or CYP3A4.

Vibegron is an inhibitor of OCT1 *in vitro*. This interaction has not been studied *in vivo*, and the clinical relevance is currently unknown.

At clinically relevant concentrations, Vibegron did not inhibit the following transporters: P-gp, BCRP, OATP1B1, OATP1B3, OAT1, OAT3, OCT2, MATE1, or MATE2K.

Vibegron ist kein Inhibitor von UGT1A1, UGT1A3, UGT1A4, UGT1A6, UGT1A9, UGT2B7, UGT2B15 und UGT2B17.

Clinical data

A single dose of 100 mg of Vibegron increased the C_{max} and AUC of the P-gp substrate digoxin by 21% and 11%, respectively, in healthy volunteers. Serum digoxin concentrations should be monitored and used to adjust the dose of digoxin until the desired clinical effect.
When combined with sensitive P gp substrates with narrow therapeutic width, such as dabigatran texilate, apixaban or rivaroxaban, possible interactions with P gp by Vibegron should be considered.

Vibegron had no clinically relevant effect on the pharmacokinetics of tolterodine (CYP2D6 substrate), or its metabolite 5-hydroxy-tolterodine, metoprolol (CYP2D6 substrate), R- or S-warfarin (CYP2C9/CYP2C19 substrate), or an oral contraceptive (Ethinyl estradiol and levonorgestrel, CYP3A4/5 substrate).

Effect of other medicines on Obgemsa

In vitro / preclinical data

Vibegron is a substrate for cytochrome P450 (CYP) 3A4/5, several UGT enzymes and the efflux transporter P glycoprotein (P-gp).

Vibegron is not a substrate for the following transporters: BCRP, MATE1, MATE2 K, OAT1, OAT3, OCT2, OATP1B1, OATP1B3 and OCT1.

Clinical data

CYP3A4/P-gp inhibitors

Vibegron exposure (AUC) was increased by a factor of 2.1 in healthy volunteers in the presence of the potent CYP3A/P-gp inhibitor ketoconazole and by a factor of 1.6 in the presence of the moderate CYP3A/P gp inhibitor diltiazem. No dose adjustment is required when Vibegron is combined with strong and moderate CYP3A and/or P gp inhibitors.

CYP3A4/P-gp Inductors

Vibegron's AUC was not altered with repeated administration of rifampicin, a potent inducer of CYP3A/P gp, to healthy volunteers, while Vibegron's Cmax was increased by 86%. No dose adjustment is required when using Vibegron with CYP3A or P gp inducers.

Tolterodine and diltiazem also had no clinically relevant influence on the pharmacokinetics of Vibegron.

Pharmacodynamic Interactions

Concomitant use of Vibegron and metoprolol, a representative beta-blocker, or amlodipine, a representative vasodilator, did not result in clinically meaningful decreases or increases in systolic blood pressure compared to metoprolol alone or amlodipine alone.

Children and adolescents

Studies to capture interactions have only been conducted in adults.

Pregnancy, breastfeeding

Women of childbearing age

The use of Vibegron in women of childbearing potential who do not use contraception is not recommended.

Pregnancy

So far, there are no or very limited data from the use of Obgemsa in pregnant women. Animal studies have shown reproductive toxicity (see preclinical *data*).
The use of Obgemsa during pregnancy is not recommended. If a planned or diagnosed pregnancy, treatment with Obgemsa should be discontinued and, if necessary, alternative therapy should be initiated

Nursing period

It is not known whether Obgemsa/metabolites are excreted in human milk.
Animal studies have shown that Obgemsa/metabolites are excreted in milk (see preclinical *data*).
A risk to the newborn/infant cannot be ruled out.
Obgemsa should not be used during breastfeeding

Fertility

The effects of Obgemsa on fertility in humans have not been studied. Animal studies have shown no effect on the fertility of female or male rats (see preclinical data *section*).

Effect on driving ability and on the operation of machines

Obgemsa has no or negligible influence on driving ability or the ability to operate machines.

Undesirable effects

Summary of the security profile

The most commonly reported adverse reactions are UTI (6.6%), headache (5.0%), diarrhea (3.1%) and nausea (3.0%).
The frequency of adverse reactions that led to discontinuation of treatment is 0.9%. The most common adverse reactions that led to discontinuation of treatment are: headache (0.5%), constipation, diarrhea, nausea and rash (0.2% each).

List of adverse effects

The following table shows the adverse reactions observed with Vibegron from the 12-week Phase III study, the Phase III long-term extension study, (637 subjects were included in the safety population) and post-marketing data. The adverse reactions are ordered by MedDRA system organ classes and frequency according to the following convention: "very common" (≥1/10), "common" (≥1/100, <1/10), "uncommon" (≥1/1,000, <1/100), "rare" (≥1/10,000, <1/1,000), "very rare" (<1/10,000), "not known" (cannot be estimated from the available data).

Table 1: Side effects reported for Vibegron 75 mg

System organ class	Side effect	Frequency
Infections and parasitic diseases	Urinary tract infection	Frequently
Diseases of the nervous system	Headache	Frequently
Vascular diseases	Hot flush	Occasionally
Diseases of the gastrointestinal tract	Constipation, diarrhea, nausea	Frequently
Diseases of the skin and subcutaneous tissue	Rash Angioedema[b] Hypersensitivity reactions, including urticaria[b]	Occasionally Not known Not known

Diseases of the kidneys and urinary tract	Residual urine increased Urinary retention[c]	Frequently Occasionally

[a] including rash with pruritus and erythematous rash
[b] Adverse reactions identified from post-marketing surveillance
[c] including straining during urination.

Reporting suspected side effects after approval is of great importance. It enables continuous monitoring of the benefit-risk ratio of the drug. Healthcare professionals are encouraged to report any suspicion of a new or serious adverse reaction via the ElViS (Electronic Vigilance System) online portal. You can find information about this under www.swissmedic.ch.

Overdosing

The cases of overdose have been reported in a dose range between 100 mg and 375 mg per day. All adverse events observed following the reported overdose were not serious. The adverse events reported were gastrointestinal disorders, headache, and dyspnea.
If overdose is suspected, symptomatic and supportive treatment is given.

Properties/ Effects

ATC code

G04BD15
Pharmacotherapeutic group: Urologists, remedies for frequent bladder emptying and urinary incontinence.

Action

Vibegron is a selective and potent human beta 3 adrenoceptor agonist, with very low affinity for beta 1 and beta 2 adrenoreceptors. Activation of the beta 3 adrenoceptor in the detrusor muscle of the bladder increases bladder capacity by relaxing the smooth detrusor muscles during bladder filling.

Pharmacodynamics

Electrophysiology of the heart
Viberron did not show a clinically relevant prolongation of the QT interval after administration of a single dose at 5.3 times (9 times higherC_{max}) of the recommended therapeutic dose of 75 mg.

RubricClinical efficacy

The efficacy of Vibegron 75 mg was evaluated in a 12-week, double-blind, randomized, placebo, and active-controlled Phase III study (EMPOWUR) in patients with overactive bladder (OAB) and symptoms of imperative urination and high micturition frequency with or without urge incontinence. Patients were randomized to receive Vibegron 75 mg, placebo, or tolterodine Retard 4 mg orally once daily for 12 weeks. To participate in the study, patients had to meet the following criteria: symptoms of OAB for at least 3 months with an average of 8 or more micturitions per day and at least 1 urge incontinence per day or an average of 8 or more micturitions per day and an average of at least 3 episodes of imperative

urination per day. Urge incontinence was defined as any loss of urine, regardless of the amount, because the patient felt the urge or need to urinate immediately. The study population included patients who had not previously received drugs for OAB as well as patients who had been previously treated with drugs for OAB. A total of 1518 patients were randomized: 547 people in the Vibegron group, 540 in the placebo group and 431 in the tolterodine group. Up to 15% of the patients were allowed to be male. Of these 1,518 patients, 54 of the placebo-treated patients (10.0%) and 45 of the patients treated with Vibegron 75 mg (8.2%) discontinued the study. The main reason for the termination of the study was the withdrawal of consent (3.9% in the placebo group and 2.6% in the Vibegron group).

Co-primary endpoints were the changes in mean daily micturition and urge incontinence episodes at week 12 from baseline.

A total of 1515 patients received at least one daily dose of placebo (n = 540), Vibegron 75 mg (n = 545) or active control (n = 430). The majority of patients were of Caucasian descent (78%) and female (85%), with a median age of 60 (range: 18 to 93) years. 77% of the patients had urge incontinence (wet OAB) at the time of presentation. The percentage of patients who were over 65 years of age at baseline was 42.6% and 12.1% were older than 75 years.

Vibegron 75mg was effective in treating the symptoms of OAB within 2 weeks. Efficacy was maintained over the 12-week treatment period (results are shown in Table 2 below).

Table 2: Mean baseline and changes from baseline at week 12 for micturition frequency, urge incontinence episodes, imperative urinary episodes, total incontinence episodes, and micturition volume

Parameter	Placebo	Obgemsa 75 mg	Tolterodin Retard 4 mg
Average daily number of micturitions[a]			
Mean Baseline (n)	11,8 (520)	11,3 (526)	11,5 (417)
Change from baseline[b] (n)	-1,3 (475)	-1,8 (492)	-1,6 (378)
Difference to placebo	-0,5		-0,3
95% confidence interval	-0,8; -0,2		-0,6; 0,1
pValue (versus placebo)	< 0.001[d,e]		0,0988
Average daily number of urge incontinence episodes[c]			
Mean Baseline (n)	3,5 (405)	3,4 (403)	3,4 (319)
Change from baseline[b] (n)	-1,4 (372)	-2,0 (383)	-1,8 (286)
Difference to placebo	-0,6		-0,4
95% confidence interval	-0,9; -0,3		-0,7; -0,1
pValue (versus placebo)	<0.0001[d,e]		0.0123

[a] FAS-Population: Full Analysis Set. All randomized patients with OAB who received at least 1 dose of the investigational double-blind drug and for whom there was at least one evaluable change from micturition measurement at baseline.
[b] Least squares mean, adjusted for treatment, baseline, type of OAB (FAS analyses only), gender, geographic region, study date, and interaction between study date and treatment.
[c] FAS-I-Population: applied to the incontinence endpoints; Patients in the FAS population with OAB wet at baseline and at least 1 evaluable change from the urge incontinence measurement at baseline.
[d] Statistically significant.
[e] Parameters included in the multiple test procedure. The hypothesis was tested only for Vibegron placebo.

The long-term safety and efficacy of Vibegron 75 mg was evaluated for up to 52 weeks in a Phase III extension study in 505 patients who had completed the 12-week Phase III study (EMPOWUR). The clinical efficacy of Vibegron lasted for a period of 52 weeks

Pediatrics

The European Medicines Agency has granted Obgemsa a deferral of the obligation to submit results on studies in one or more paediatric age groups in the treatment of neurogenic detrusor overactivity (see section *Dosage/Use* for information on use in children and adolescents).

Pharmacokinetics

Absorption

The mean C_{max} and AUC of Vibegron increased more than dose-proportionally up to 600 mg after a single dose and 400 mg after repeated administration. The mean accumulation ratio (Rac) was 1.7 for C_{max} and 2.4 for AUC0-24h. The median T_{max} of Vibegron is approximately 1 to 3 hours.
Oral administration of Vibegron 75 mg as a crushed film-coated tablet mixed with 15 ml of applesauce did not result in clinically meaningful changes in the pharmacokinetics of Vibegron compared to administration as an intact Vibegron 75 mg film-coated tablet. Therefore, Vibegron can be crushed for administration with soft food.
Influence of food:
Taking a 75 mg tablet with a high-fat meal resulted in a 63% and 37% reduction in Vibegron's C max and AUC, respectively. The influence of food appeared to be lower at steady state (unchanged AUC and 30% lower C_{max}). In the Phase III studies to demonstrate efficacy and safety, Vibegron was administered with or without food. Accordingly, Vibegron can be taken with or without food.

Distribution

The mean apparent volume of distribution after oral administration is 9120 liters. The plasma protein binding of Vibegron in humans is approximately 50%. The average blood-plasma concentration ratio is 0.9.

Metabolism

Vibegron is metabolized via oxidation and direct glucuronidation, however, metabolization is not a major excretion pathway. Vibegron is the main circulating compound after a single application of 14C-Vibegron. An important metabolite has been detected in human plasma, a phase II glucuronide, which

accounts for 12% to 14% of total exposure. All recombinant UGT enzymes studied *in vitro* showed some metabolism of Vibegron (mainly UGT1A3, UGT1A4, UGT1A6, UGT2B10, UGT2B15). Although *in vitro* studies indicate an involvement of CYP3A4 in the oxidative metabolism of Vibegron, *in vivo* results show that these isoenzymes play a limited role in overall elimination.

Elimination

The mean terminal half-life (t1/2) after repeated administration is between 59 and 94 hours in younger and elderly subjects, and the effective half-life across all populations is 31 hours.
After oral administration of 100 mg ^{14}C Vibegron to healthy volunteers, about 59% of the radiolabeled substance was detected in the stool and 20% in the urine. Unchanged vibegron accounted for most of the radioactivity excreted (54% of the radiolabeled substance in the stool and 19% in the urine). Most of the dose found in the faeces is probably unabsorbed substance. The excretion of the unchanged substance in the urine is an important route of excretion (about 50% of the absorbed vibegron). Biliary excretion of the unchanged substance may also contribute to excretion, while hepatic metabolism appears to play a minor role.

Kinetics of special patient groups

The pharmacokinetics of Vibegron showed no clinically meaningful differences based on age (range studied: 18 to 93 years), weight, sex or ethnic origin.
Weight (studied range: 39 to 161 kg) had a moderate influence on clearance and central distribution volume in the population pharmacokinetic analysis. The increase in Vibegron exposures due to weight differences is therefore not considered clinically significant.

Liver dysfunction

Compared to subjects with normal liver function, a single dose of 100 mg of Vibegron increased mean C_{max} and AUC by 1.3 and 1.3 times, respectively, in subjects with moderately impaired hepatic function (ChildPugh B).
No dose adjustment of Vibegron is recommended in patients with mild to moderate hepatic impairment (ChildPugh A and B). Vibegron has not been studied in patients with severely impaired hepatic function (ChildPugh C) and is therefore not recommended in this patient population.

Renal dysfunction

Compared to subjects with normal renal function (GFR ≥ 90 ml/min), a single dose of 100 mg of Vibegron increased mean C_{max} and AUC by:

- 1.6 and 2.1 times in subjects with slightly impaired renal function (60 ≤ GFR < 90 ml/min),
- 2.0 and 1.6 times in subjects with moderately impaired renal function (30 ≤ GFR < 60 ml/min),
- 1.8 and 1.2 times in subjects with severely impaired renal function (GFR < 30 ml/min).

No dose adjustment of Vibegron is recommended in patients with mild, moderate, or severely impaired renal function (15 ml/min < GFR < 90 ml/min and not requiring dialysis). Vibegron has not been studied

in patients with end-stage renal disease (GFR < 15 ml/min with or without haemodialysis) and is therefore not recommended in these patients.

Children and adolescents

There are no pharmacokinetic data in children and adolescents under 18 years of age.

Preclinical data

Vibegron showed 9 and 78 times lower β3AR presence in vitro for rabbits and rats compared to humans. Therefore, the safety margins for potential β3AR-mediated effects on development or reproduction are correspondingly smaller than for nonβ3AR-related effects.
In animal studies, no effects on embryofetal development were observed following oral administration of Vibegron during the period of organogenesis at an exposure (AUC) approximately 275 times (in rats) and 285 times (in rabbits) the clinical exposure at the recommended human dose (= RHD) of 75 mg Vibegron /day. In rabbits, delayed fetal skeletal ossification and decreased fetal body weights were observed in the presence of maternal toxicity at an exposure equivalent to approximately 898 times the clinical exposure (AUC) in RHD. In rats receiving Vibegron during pregnancy and lactation, no effects on the offspring were observed at 89 times the clinical exposure to RHD. In offspring, developmental toxicity was observed in the presence of maternal toxicity at an exposure equivalent to approximately 458 times the clinical exposure (AUC) in RHD.
Radioactivity was detected in milk following administration of a single oral dose of radiolabelled Vibegron to postnatally lactating rats.
At doses up to 300 mg/kg/day associated with a systemic exposure (AUC) of at least 275 times that of humans at an RHD of 75 mg/day, no effects on fertility were observed in female or male rats. When 1 000 mg/kg/day was administered to female rats, which was associated with an estimated systemic exposure (AUC) of 1 867 times the human exposure to RHD of 75 mg/day, general toxicity, reduced fertility and decreased fertility were observed.

Other notes

Incompatibilities

Not applicable.

Durability

The medicine must only be used up to the date marked "EXP" on the package.

Special storage instructions

Do not store above 30°C.
Keep out of reach of children.

Licence number

69983 (Swissmedic).

Packs

1 bottle of 30 film-coated tablets
1 bottle of 90 film-coated tablets

Marketing authorisation holder

Pierre Fabre AG, Basel

State of information

January 2025