

Prescribing Information for Mirabegron Astellas 25 mg prolonged-release tablets & 50 mg prolonged-release tablets (mirabegron) is found below.

Prescribing information for VESICARE™ (solifenacin succinate) film-coated tablets is found on page 4.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Astellas Pharma Ltd. on 0800 783 5018.

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Prescribing Information: Mirabegron Astellas 25 mg prolonged-release tablets & 50 mg prolonged-release tablets (mirabegron)

Presentation: Prolonged-release tablets containing 25 mg or 50 mg mirabegron.

Indication: Symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with overactive bladder (OAB) syndrome. Treatment of neurogenic detrusor overactivity (NDO) in paediatric patients aged 3 to less than 18 years.

Posology and administration: The tablet should be taken with liquids, swallowed whole and is not to be chewed, divided, or crushed. **OAB:** The recommended dose is 50 mg orally once daily in adults (including elderly patients), with or without food. Mirabegron should not be used in paediatrics for OAB. **NDO:** Mirabegron Astellas prolonged-release tablets may be administered to patients weighing ≥ 35 kg. The recommended starting dose is 25 mg orally daily with food, increasing to a maximum of 50 mg once daily after 4 – 8 weeks if needed. **Missed dose:** Patients should take any missed doses, unless > 12 hours have passed since the missed dose; if > 12 hours have passed, the missed dose can be skipped, and the next dose taken at the usual time. Evaluate patients for treatment continuation / dose adjustment at least annually during long-term therapy, or more frequently if indicated.

Renal & hepatic impairment: Mirabegron Astellas is not recommended for use in patients with end stage renal disease (eGFR < 15 ml/min/1.73

m² or patients requiring haemodialysis) or severe hepatic impairment (Child-Pugh Class C). A dose of 25 mg once daily is recommended in some patients with renal / hepatic impairment (see SPC Section 4.2 for information on dosing recommendations for these patients).

Contraindications: Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1 of the SPC. Severe uncontrolled hypertension defined as systolic blood pressure ≥ 180 mm Hg and/or diastolic blood pressure ≥ 110 mm Hg.

Warnings and Precautions: Renal impairment: Mirabegron has not been studied in patients with ESRD (eGFR < 15 ml/min/1.73 m²) or patients requiring haemodialysis and, therefore, it is not recommended for use in this patient population. Data are limited in patients with severe renal impairment (eGFR 15 to 29 ml/min/1.73 m²); based on a pharmacokinetic study (see section 5.2) a dose of 25 mg once daily is recommended in this population. This medicinal product is not recommended for use in patients with severe renal impairment (eGFR 15 to 29 ml/min/1.73 m²) concomitantly receiving strong CYP3A inhibitors (see SPC section 4.5). Hepatic impairment: Mirabegron has not been studied in patients with severe hepatic impairment (Child-Pugh Class C) and, therefore, it is not recommended for use in this patient population. This medicinal product is not recommended for use in patients with moderate hepatic impairment (Child-Pugh B) concomitantly receiving strong CYP3A inhibitors (see SPC section 4.5). Hypertension: Overactive bladder in adults: Mirabegron can increase blood pressure. Blood pressure should be measured at baseline and periodically during treatment with mirabegron, especially in hypertensive patients. Data are limited in patients with stage 2 hypertension (systolic blood pressure ≥ 160 mm Hg or diastolic blood pressure ≥ 100 mm Hg). Neurogenic detrusor overactivity in the paediatric population: Mirabegron can increase blood pressure in paediatric patients. Blood pressure increases may be larger in children (3 to less than 12 years of age) than in adolescents (12 to less than 18 years of age). Blood pressure should be measured at baseline and periodically during treatment with mirabegron. Patients with congenital or acquired QT prolongation: Mirabegron, at therapeutic doses, has not demonstrated clinically relevant QT prolongation in clinical studies (see section 5.1 of the SPC). However, since patients with a known history of QT prolongation or patients who are taking medicinal products known to prolong the QT interval were not included in these studies, the effects of mirabegron in these patients is unknown. Caution should be exercised when administering mirabegron in these patients. Patients with bladder outlet obstruction and patients taking antimuscarinics medicinal products for OAB: Urinary retention in patients with bladder outlet obstruction

(BOO) and in patients taking antimuscarinic medicinal products for the treatment of OAB has been reported in postmarketing experience in patients taking mirabegron. A controlled clinical safety study in patients with BOO did not demonstrate increased urinary retention in patients treated with mirabegron; however, mirabegron should be administered with caution to patients with clinically significant BOO. Mirabegron should also be administered with caution to patients taking antimuscarinic medicinal products for the treatment of OAB.

Interactions: Interaction studies have only been performed in adults. Caution is advised if mirabegron is co-administered with medicinal products with a narrow therapeutic index and significantly metabolised by CYP2D6. Caution is also advised if mirabegron is co-administered with CYP2D6 substrates that are individually dose titrated. In patients with mild to moderate renal impairment or mild hepatic impairment, concomitantly receiving strong CYP3A inhibitors, the recommended dose is 25 mg once daily. Mirabegron is not recommended in patients with severe renal impairment (eGFR 15 to 29 ml/min/1.73 m²) or patients with moderate hepatic impairment (Child Pugh Class B) concomitantly receiving strong CYP3A inhibitors. For patients who are initiating a combination of mirabegron and digoxin (P-gp substrate), the lowest dose for digoxin should be prescribed initially (see the SPC for full prescribing information). The potential for inhibition of P-gp by mirabegron should be considered when mirabegron is combined with sensitive P-gp substrates. Increases in mirabegron exposure due to drug-drug interactions may be associated with increases in pulse rate.

Pregnancy and lactation: Mirabegron Astellas is not recommended in women of childbearing potential not using contraception and is not recommended during pregnancy. Mirabegron Astellas should not be used during breast-feeding.

Undesirable effects: Summary of the safety profile: The safety of mirabegron was evaluated in 8433 adult patients with OAB, of which 5648 received at least one dose of mirabegron in the phase 2/3 clinical program, and 622 patients received mirabegron for at least 1 year (365 days). In the three 12-week phase 3 double blind, placebo-controlled studies, 88% of the patients completed treatment with this medicinal product, and 4% of the patients discontinued due to adverse events. Most adverse reactions were mild to moderate in severity. The most common adverse reactions reported for adult patients treated with mirabegron 50 mg during the three 12-week phase 3 double blind, placebo-controlled studies are tachycardia and urinary tract infections. The frequency of tachycardia was 1.2% in patients receiving mirabegron 50 mg. Tachycardia led to discontinuation in 0.1% patients receiving mirabegron 50 mg. The frequency of urinary tract infections was 2.9% in

patients receiving mirabegron 50 mg. Urinary tract infections led to discontinuation in none of the patients receiving mirabegron 50 mg. Serious adverse reactions included atrial fibrillation (0.2%). Adverse reactions observed during the 1-year (long term) active controlled (muscarinic antagonist) study were similar in type and severity to those observed in the three 12-week phase 3 double blind, placebo-controlled studies.

Adverse reactions: The following list reflects the adverse reactions observed with mirabegron in adults with OAB in the three 12-week phase 3 double blind, placebo-controlled studies. The frequency of adverse reactions is defined as follows: very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$) and not known (cannot be established from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. The adverse events are grouped by MedDRA system organ class. *Infections and infestations:* Common: Urinary tract infection, Uncommon: Vaginal infection, Cystitis. *Psychiatric disorders:* Not known (cannot be estimated from the available data): Insomnia*, Confusional state*. *Nervous system disorders:* Common: Headache*, Dizziness*. *Eye disorders:* Rare: Eyelid oedema. *Cardiac disorders:* Common: Tachycardia, Uncommon: Palpitation, Atrial fibrillation. *Vascular disorders:* Very rare: Hypertensive crisis*. *Gastrointestinal disorders:* Common: Nausea*, Constipation*, Diarrhoea*, Uncommon: Dyspepsia, Gastritis, Rare: Lip oedema. *Hepatobiliary disorders:* Uncommon: GGT increased, AST increased, ALT increased. *Skin and subcutaneous tissue disorders:* Uncommon: Urticaria, Rash, Rash macular, Rash papular, Pruritus, Rare: Leukocytoclastic vasculitis, Purpura, Angioedema*. *Musculoskeletal and connective tissue disorders:* Uncommon: Joint swelling. *Renal and urinary disorders:* Rare: Urinary retention*. *Reproductive system and breast disorders:* Uncommon: Vulvovaginal pruritus. *Investigations:* Uncommon: Blood pressure increased.

*observed during post-marketing experience.

Paediatric population The safety of mirabegron tablets and oral suspension was evaluated in 86 paediatric patients aged 3 to less than 18 years with neurogenic detrusor overactivity in a 52-week, open-label, baseline-controlled, multicentre, dose titration study. The most commonly reported adverse reactions observed in the paediatric population were urinary tract infection, constipation, and nausea. In the paediatric patients with NDO, no severe adverse reactions were reported. The safety of mirabegron tablets and oral suspension was evaluated in 26 paediatric patients aged 5 to less than 18 years of age

with overactive bladder in a 12-week, double-blind, randomised, multicentre, parallel group, placebo-controlled sequential dose titration study. The most commonly reported adverse reactions observed in the paediatric population were nasopharyngitis, fatigue and mood swing. Overall, the safety profile in children and adolescents is similar to that observed in adults.

Prescribers should consult the full SPC in relation to other adverse reactions.

Overdose: Treatment for overdose should be symptomatic and supportive. In the event of overdose, pulse rate, blood pressure, and ECG monitoring is recommended.

Basic NHS Cost: Mirabegron 50 mg x 30 = £29; Mirabegron 25 mg x 30 tablets = £29.

Legal classification: POM.

Marketing Authorisation number(s): PLGB 00166/0415-0416.

Marketing Authorisation Holder: Astellas Pharma Ltd., 300 Dashwood Lang Road, Bourne Business Park, Addlestone, United Kingdom, KT15 2NX.

Date of Preparation of Prescribing information: January 2026.

Document number: MAT-GB-MIR-2025-00264.

Further information available from: Astellas Pharma Ltd, Medical Information: 0800 783 5018.

For full prescribing information, please see the Summary of Product Characteristics, which may be found at: www.medicines.org.uk.

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Prescribing information: VESICARE™ (solifenacin succinate) film-coated tablets

For full prescribing information, refer to the Summary of Product Characteristics (SPC)

Presentation: VESICARE film-coated tablets containing 5 mg or 10 mg solifenacin succinate. **Indication:** Symptomatic treatment of urge incontinence and/or increased urinary frequency and urgency as may occur in patients with overactive bladder syndrome.

Posology and Administration: Adults, including the elderly: The recommended dose is 5 mg solifenacin succinate once daily. If needed, the dose may be increased to 10 mg once daily. VESICARE should not be used in children. VESICARE should be taken orally and should be swallowed whole with liquids. It can be taken with or without food. Renal impairment: No dose adjustment is necessary for patients with mild to moderate renal impairment (creatinine clearance > 30 ml/min). Patients with severe renal impairment (creatinine clearance ≤ 30 ml/min) should be treated with caution and receive no more than 5 mg once daily. Hepatic impairment: No dose adjustment is necessary for patients with mild hepatic impairment. Patients with moderate hepatic impairment (Child-Pugh score of 7 to 9) should be treated with caution and receive no more than 5 mg once daily. Effect of CYP3A4 inhibitors: The maximum dose of VESICARE should be limited to 5 mg when treated simultaneously with ketoconazole or therapeutic doses of other potent CYP3A4 inhibitors e.g. ritonavir, nelfinavir, itraconazole.

Contraindications: Solifenacin is contraindicated in patients with urinary retention, severe gastro-intestinal condition (including toxic megacolon), myasthenia gravis or narrow-angle glaucoma and in patients at risk for these conditions. Patients hypersensitive to the active substance or to any of the excipients listed in 6.1 of the SPC, patients undergoing haemodialysis, patients with severe hepatic impairment, patients with severe renal impairment or moderate hepatic impairment and who are on treatment with a potent CYP3A4 inhibitor, e.g. ketoconazole.

Warnings and Precautions: Other causes of frequent urination (heart failure or renal disease) should be assessed before treatment with VESICARE. If urinary tract infection is present, an appropriate antibacterial therapy should be started. VESICARE should be used with caution in patients with: clinically significant bladder outflow obstruction at risk of urinary retention; gastrointestinal obstructive disorders; risk of decreased gastrointestinal motility; severe renal impairment (creatinine clearance ≤ 30 ml/min), and doses should not exceed 5 mg for these patients; moderate hepatic impairment (Child-Pugh score of 7 to 9), and doses should not exceed 5 mg for these patients; concomitant use of a potent CYP3A4 inhibitor, e.g. ketoconazole; hiatus hernia/gastro-oesophageal

reflux and/or who are concurrently taking medicinal products (such as bisphosphonates) that can cause or exacerbate oesophagitis; autonomic neuropathy. QT prolongation and Torsade de Pointes have been observed in patients with risk factors, such as pre-existing long QT syndrome and hypokalaemia. Safety and efficacy have not yet been established in patients with a neurogenic cause for detrusor overactivity. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product. Angioedema with airway obstruction has been reported in some patients on solifenacin succinate. If angioedema occurs, solifenacin succinate should be discontinued and appropriate therapy and/or measures should be taken. Anaphylactic reaction has been reported in some patients treated with solifenacin succinate. In patients who develop anaphylactic reactions, solifenacin succinate should be discontinued and appropriate therapy and/or measures should be taken. The maximum effect of VESICARE can be determined after 4 weeks at the earliest.

Effects on ability to drive and use machines: Since solifenacin, like other anticholinergics may cause blurred vision, and, uncommonly, somnolence and fatigue, the ability to drive and use machines may be negatively affected.

Interactions: Concomitant medication with other medicinal products with anticholinergic properties may result in more pronounced therapeutic effects and undesirable effects. An interval of approximately one week should be allowed after stopping treatment with VESICARE, before commencing other anticholinergic therapy. The therapeutic effect of solifenacin may be reduced by concomitant administration of cholinergic receptor agonists. Solifenacin can reduce the effect of medicinal products that stimulate the motility of the gastro-intestinal tract, such as metoclopramide and cisapride. Solifenacin is metabolised by CYP3A4, the maximum dose of VESICARE should be restricted to 5 mg, when used simultaneously with ketoconazole or therapeutic doses of other potent CYP3A4 inhibitors (e.g. ritonavir, nelfinavir, itraconazole). Since solifenacin is metabolised by CYP3A4, pharmacokinetic interactions are possible with other CYP3A4 substrates with higher affinity (e.g. verapamil, diltiazem) and CYP3A4 inducers (e.g. rifampicin, phenytoin, carbamazepin).

Pregnancy and lactation: No clinical data are available from women who became pregnant while taking solifenacin. Caution should be exercised when prescribing to pregnant women. The use of VESICARE should be avoided during breast-feeding.

Undesirable effects: Summary of the safety profile: Due to the pharmacological effect of solifenacin, VESICARE may cause

anticholinergic undesirable effects of (in general) mild or moderate severity. The frequency of anticholinergic undesirable effects is dose related. The most commonly reported adverse reaction with VESICARE was dry mouth. It occurred in 11% of patients treated with 5 mg once daily, in 22% of patients treated with 10 mg once daily and in 4% of placebo-treated patients. The severity of dry mouth was generally mild and did only occasionally lead to discontinuation of treatment. In general, medicinal product compliance was very high (approximately 99%) and approximately 90% of the patients treated with VESICARE completed the full study period of 12 weeks treatment. **Adverse reactions:** The frequency of adverse reactions is defined as follows: very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$) and not known (cannot be estimated from the available data). The adverse events are grouped by MedDRA system organ class. **Infections and infestation:** Uncommon: urinary tract infection, cystitis. **Immune system disorders:** Not known: anaphylactic reaction*. **Metabolism and nutrition disorders:** Not known: decreased appetite*, hyperkalaemia*. **Psychiatric disorders:** Very rare: hallucinations*, confusional state*, Not known: delirium*. **Nervous system disorders:** Uncommon: somnolence, dysgeusia, Rare: dizziness*, headache*. **Eye disorders:** Common: blurred vision, Uncommon: dry eyes, Not known: glaucoma*. **Cardiac disorders:** Not known: Torsade de Pointes*, electrocardiogram QT prolonged*, atrial fibrillation*, palpitations*, tachycardia*. **Respiratory, thoracic and mediastinal disorders:** Uncommon: nasal dryness, Not known: dysphonia*. **Gastrointestinal disorders:** Very common: dry mouth, Common: constipation, nausea, dyspepsia, abdominal pain, Uncommon: gastro-oesophageal reflux diseases, dry throat, Rare: colonic obstruction, faecal impaction, vomiting*, Not known: ileus*, abdominal discomfort*. **Hepatobiliary disorders:** Not known: liver disorder*, liver function test abnormal*. **Skin and subcutaneous tissue disorders:** Uncommon: dry skin, Rare: pruritus*, rash*, Very rare: erythema multiforme*, urticaria*, angioedema*, Not known: exfoliative dermatitis*. **Musculoskeletal and connective tissue disorders:** Not known: Muscular weakness*. **Renal and urinary disorders:** Uncommon: difficulty in micturition, Rare: urinary retention, Not known: renal impairment*. **General disorders and administration site conditions:** Uncommon: fatigue, peripheral oedema. * observed post-marketing. Prescribers should consult the SPC in relation to other adverse reactions.

Overdose: Overdosage with solifenacin succinate can potentially result in severe anticholinergic effects. The highest dose of solifenacin succinate accidentally given to a single patient was 280 mg in a 5 hour period, resulting in mental status changes not requiring hospitalization. In the

event of overdose with solifenacin succinate the patient should be treated with activated charcoal. Gastric lavage is useful if performed within 1 hour, but vomiting should not be induced. As with other antimuscarinics, in case of overdosing, specific attention should be paid to patients with known risk for QT-prolongation (i.e. hypokalaemia, bradycardia and concurrent administration of medicinal products known to prolong QT-interval) and relevant pre-existing cardiac diseases (i.e. myocardial ischaemia, arrhythmia, congestive heart failure).

Basic NHS Cost: VESICARE 5 mg x 30 = £27.62, VESICARE 10 mg x 30 tablets = £35.91

Legal classification: POM

Marketing Authorisation number(s): VESICARE 5mg: PL 00166/0197. VESICARE 10 mg: PL 00166/0198 **Marketing Authorisation Holder:** Astellas Pharma Ltd. 300 Dashwood Lang Road, Bourne Business Park, Addlestone, United Kingdom, KT15 2NX

Date of Preparation of Prescribing information: December 2022

Document number: MAT-UK-VES-2022-00002

Further information available from: Astellas Pharma Ltd. Medical Information: 0800 783 5018.

For full prescribing information, please see the Summary of Product Characteristics, which may be found at www.medicines.org.uk

United Kingdom

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