

**REPLAGAL® (AGALSIDASE ALFA) 1 MG/ML  
CONCENTRATE FOR SOLUTION FOR  
INFUSION. PRESCRIBING INFORMATION FOR  
GREAT BRITAIN (ENGLAND, SCOTLAND,  
WALES)**

**Refer to Summary of Product Characteristics  
(SmPC) before prescribing**

**Presentation:** 1 ml contains 1 mg of agalsidase alfa. Each vial of 3.5 ml of concentrate contains 3.5mg of agalsidase alfa **Indication:** Long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry Disease ( $\alpha$ -galactosidase A deficiency). **Dosage and administration:** Treatment should be supervised by a physician experienced in the management of patients with Fabry Disease or other inherited metabolic diseases. Replagal home infusion, and administration by the patient or patient's caregiver (self-administration), may be considered for patients who are tolerating their infusions well. The decision to have a patient move to home infusion and/or self-administration should be made after evaluation and recommendation by the treating physician. Any patients experiencing adverse events during the home infusion/ self-administration need to immediately stop the infusion process and seek the attention of a healthcare professional. **Posology:** Replagal is administered at a dose of 0.2 mg/kg body weight by IV infusion over 40 min every other week. No dosage regimen in children aged 0-6 years or elderly patients over 65 years can presently be recommended as safety and efficacy have not yet been sufficiently established. In children aged 7-18 years, Replagal 0.2mg/kg every other week led to no unexpected safety issues. **Renal and hepatic impairment:** No dosage adjustment is recommended for patients with renal impairment or those on dialysis or post-kidney transplantation; however extensive renal damage (eGFR <60mL/min) may limit the renal response to enzyme replacement therapy. No data is available in hepatic impairment. **Contraindications:** Hypersensitivity to the active substance or any of the excipients. **Warnings and precautions:** 13.7% of adult patients treated with Replagal in clinical trials had idiosyncratic infusion-related reactions (generally within 2–4 months of starting treatment although later onset [after 1 year] has been reported as well). Four of 17 paediatric patients  $\geq 7$  years of age and 3 of 8 paediatric patients <7 years experienced at least one infusion reaction over a period of approximately 4 years of treatment. These effects have decreased with time. If mild or moderate acute infusion reactions occur, seek medical attention immediately. The infusion can be temporarily interrupted (for 5–10 minutes) until symptoms subside. If severe hypersensitivity or anaphylactic-type reactions occur, discontinue Replagal immediately and initiate appropriate treatment. A review of cardiac

events showed that infusion reactions may be associated with hemodynamic stress triggering cardiac events in patients with pre-existing cardiac manifestations of Fabry disease. Patients may develop IgG antibodies to the protein. A low titre antibody response was seen in approximately 24% of male patients treated with Replagal, the remaining 76% remained antibody negative throughout. In paediatric patients >7 yrs of age, 1/16 male patients tested positive for IgG anti-agalsidase alfa antibodies. No increase in the incidence of adverse events was detected for this patient. In paediatric patients <7 yrs of age, 0/7 male patients tested positive for IgG anti-agalsidase alfa antibodies. IgE antibody positivity not associated with anaphylaxis has been reported in clinical trials in a very limited number of patients. **Sodium:** This medicinal product contains 14.2 mg sodium per vial, equivalent to 0.7% of the WHO recommended maximum daily intake of 2 g sodium for an adult. **Interactions:** Replagal should not be co-administered with chloroquine, amiodarone, benoquin or gentamicin since these substances have the potential to inhibit intra-cellular  $\alpha$ -galactosidase activity. **Fertility, pregnancy and lactation:** There is very limited data on pregnancies exposed to Replagal, therefore, caution should be exercised. Use with caution during breast-feeding. **Undesirable effects: Very common ( $\geq 1/10$ ):** peripheral oedema, headache, dizziness, neuropathic pain, tremor, hypoesthesia, paraesthesia, tinnitus, palpitations, dyspnoea, cough, nasopharyngitis, pharyngitis, vomiting, nausea, abdominal pain, diarrhoea, rash, arthralgia, pain in limb, myalgia, back pain, chest pain, rigors, pyrexia, pain, asthenia, fatigue; **Common ( $\geq 1/100$ , <1/10):** dysgeusia, hypersomnia, increased lacrimation, tinnitus aggravated, tachycardia, atrial fibrillation, hypertension, hypotension, flushing, hoarseness, throat tightness, rhinorrhoea, abdominal discomfort, urticaria, erythema, pruritus, acne, hyperhidrosis, musculoskeletal discomfort, peripheral swelling, joint swelling, hypersensitivity, chest tightness, aggravated fatigue, feeling hot, feeling cold, influenza-like illness, discomfort, malaise; **Other Serious undesirable effects:** anaphylactic reaction, myocardial ischaemia, heart failure. **Refer to the SmPC for details on full side effect profile and interactions. UK Basic NHS price:** Vials of 5 ml (containing 3.5 ml concentrate) in a pack size of 1 vial. £1049.94 for one 5 ml vial. **Legal Classification:** POM. **Marketing authorisation number(s):** PLGB 30560/0003. **Business responsible for sale and supply:** Takeda UK Limited, 1 Kingdom Street, London, W2 6BD, United Kingdom. **PI approval code:** pi-02177. **Date of preparation:** December 2022. Replagal is a registered trade name

Job code: C-APROM/GB/REP/0080

Date of Preparation: December 2022

Adverse events should be reported. Reporting forms and information can be found at: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard). Adverse events should also be reported to Takeda UK Ltd at: [AE.GBR-IRL@takeda.com](mailto:AE.GBR-IRL@takeda.com)

**REPLAGAL® (AGALSIDASE ALFA) 1 MG/ML  
CONCENTRATE FOR SOLUTION FOR  
INFUSION. PRESCRIBING INFORMATION FOR  
NORTHERN IRELAND**

**Refer to Summary of Product Characteristics  
(SmPC) before prescribing**

**Presentation:** 1 ml contains 1 mg of agalsidase alfa. Each vial of 3.5 ml of concentrate contains 3.5mg of agalsidase alfa. **Indication:** Long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry Disease ( $\alpha$ -galactosidase A deficiency). **Dosage and administration:** Treatment should be supervised by a physician experienced in the management of patients with Fabry Disease or other inherited metabolic diseases. Replagal home infusion, and administration by the patient or patient's caregiver (self-administration), may be considered for patients who are tolerating their infusions well. The decision to have a patient move to home infusion and/or self-administration should be made after evaluation and recommendation by the treating physician. Any patients experiencing adverse events during the home infusion/ self-administration need to immediately stop the infusion process and seek the attention of a healthcare professional. **Posology:** Replagal is administered at a dose of 0.2 mg/kg body weight by IV infusion over 40 min every other week. No dosage regimen in children aged 0-6 years or elderly patients over 65 years can presently be recommended as safety and efficacy have not yet been sufficiently established. In children aged 7-18 years, Replagal 0.2mg/kg every other week led to no unexpected safety issues. **Renal and hepatic impairment:** No dosage adjustment is recommended for patients with renal impairment or those on dialysis or post-kidney transplantation; however extensive renal damage (eGFR <60mL/min) may limit the renal response to enzyme replacement therapy. No data is available in hepatic impairment. **Contraindications:** Hypersensitivity to the active substance or any of the excipients. **Warnings and precautions:** 13.7% of adult patients treated with Replagal in clinical trials had idiosyncratic infusion-related reactions (generally within 2–4 months of starting treatment although later onset [after 1 year] has been reported as well). Four of 17 paediatric patients  $\geq 7$  years of age and 3 of 8 paediatric patients <7 years experienced at least one infusion reaction over a period of approximately 4 years of treatment. These effects have decreased with time. If mild or moderate acute infusion reactions occur, seek medical attention immediately. The infusion can be temporarily interrupted (for 5–10 minutes) until symptoms subside. If severe hypersensitivity or anaphylactic-type reactions occur, discontinue Replagal immediately and initiate appropriate treatment. A review of cardiac

events showed that infusion reactions may be associated with hemodynamic stress triggering cardiac events in patients with pre-existing cardiac manifestations of Fabry disease. Patients may develop IgG antibodies to the protein. A low titre antibody response was seen in approximately 24% of male patients treated with Replagal, the remaining 76% remained antibody negative throughout. In paediatric patients >7 yrs of age, 1/16 male patients tested positive for IgG anti-agalsidase alfa antibodies. No increase in the incidence of adverse events was detected for this patient. In paediatric patients <7 yrs of age, 0/7 male patients tested positive for IgG anti-agalsidase alfa antibodies. IgE antibody positivity not associated with anaphylaxis has been reported in clinical trials in a very limited number of patients. **Sodium:** This medicinal product contains 14.2 mg sodium per vial, equivalent to 0.7% of the WHO recommended maximum daily intake of 2 g sodium for an adult. **Interactions:** Replagal should not be co-administered with chloroquine, amiodarone, benoquin or gentamicin since these substances have the potential to inhibit intra-cellular  $\alpha$ -galactosidase activity. **Fertility, pregnancy and lactation:** There is very limited data on pregnancies exposed to Replagal, therefore, caution should be exercised. Use with caution during breast-feeding. **Undesirable effects: Very common ( $\geq 1/10$ ):** peripheral oedema, headache, dizziness, neuropathic pain, tremor, hypoesthesia, paraesthesia, tinnitus, palpitations, dyspnoea, cough, nasopharyngitis, pharyngitis, vomiting, nausea, abdominal pain, diarrhoea, rash, arthralgia, pain in limb, myalgia, back pain, chest pain, rigors, pyrexia, pain, asthenia, fatigue; **Common ( $\geq 1/100$ , <1/10):** dysgeusia, hypersomnia, increased lacrimation, tinnitus aggravated, tachycardia, atrial fibrillation, hypertension, hypotension, flushing, hoarseness, throat tightness, rhinorrhoea, abdominal discomfort, urticaria, erythema, pruritus, acne, hyperhidrosis, musculoskeletal discomfort, peripheral swelling, joint swelling, hypersensitivity, chest tightness, aggravated fatigue, feeling hot, feeling cold, influenza-like illness, discomfort, malaise; **Other Serious undesirable effects:** anaphylactic reaction, myocardial ischaemia, heart failure. **Refer to the SmPC for details on full side effect profile and interactions. UK Basic NHS price:** Vials of 5 ml (containing 3.5 ml concentrate) in a pack size of 1 vial. £1049.94 for one 5 ml vial. **Legal Classification:** POM. **Marketing authorisation number(s):** EU/1/01/189/001-003. **Business responsible for sale and supply:** Takeda UK Limited, 1 Kingdom Street, London, W2 6BD, United Kingdom. **PI approval code:** pi 02117. **Date of preparation:** December 2022. Replagal is a registered trade name

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