REPLAGAL® (AGALSIDASE ALFA) 1 MG/ML CONCENTRATE FOR SOLUTION FOR INFUSION. PRESCRIBING INFORMATION FOR GREAT BRITAIN (ENGLAND, SCOTLAND, WALES), NORTHERN IRELAND & REPUBLIC OF IRELAND
Refer to Summary of Product Characteristics (SmPC) before prescribing

Presentation: 1 ml contains 1 mg of agalsidase alfa. **Indication:** Long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry Disease (α-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. Method of administration: Dilute the total volume of Replagal concentrate required (see posology) in 100 ml of 9 mg/ml (0.9%) sodium chloride solution for infusion. Care must be taken to ensure the sterility of the prepared solutions since Replagal does not contain any preservative or bacteriostatic agent. Once diluted, the solution should be mixed gently but not shaken and used immediately. Visually inspect the solution for particulate matter and discolouration prior to use. Do not infuse in the same IV line with other agents. The name and batch number of the administered product should be clearly recorded. 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 0.2kg/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 ≥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 α-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 (≥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 (≥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 (MA):** GB: PLGB 30560/0003; NI & ROI: EU/1/01/189/001-003. **Name and address of MA holder:** GB: Shire Human Genetic Therapies AB, Box 30143, 104 25 Stockholm, Sweden. NI & ROI: Shire Human Genetic Therapies AB, Lindhagensgatan 120, 112 51 Stockholm, Sweden. Additional information is available on request at:

MedinfoEMEA@takeda.com. **PI approval code:**
pi-01604. **Date of preparation:** July 2021.
Replagal is a registered trade name.

GB & NI: Adverse events should be reported. Reporting forms and information can be found at: www.mhra.gov.uk/yellowcard.
ROI: Adverse events should be reported to the Pharmacovigilance Unit at the Health Products Regulatory Authority. Reporting forms and information can be found at: www.hpra.ie.
GB, NI and ROI: Adverse events should also be reported to Takeda UK Ltd at: AE.GBR-IRL@takeda.com