

Important information regarding the shortage of enzyme replacement therapy (ERT) for patients with Fabry disease

Dear Doctor,

You may be aware that Genzyme are currently facing supply issues with enzyme replacement therapy (ERT), which they reported in their press release issued on 23rd September 2009.¹ Shire HGT believes it important for physicians and patients to be fully aware that Replagal[®] 0.2 mg/kg (agalsidase alfa) is a licensed alternative to Fabrazyme[®] 1.0mg/kg (agalsidase beta) for patients with Fabry disease.

Replagal 0.2mg/kg (agalsidase alfa) is a human form of the enzyme, alpha-galactosidase A (α -Gal A), and is manufactured in a human cell line by gene activation. Clinical studies have proven Replagal 0.2mg/kg to be effective in treating many of the signs and symptoms of Fabry disease,² in stabilizing renal and cardiac function and in slowing progression of organ damage.^{2,3,4,5} Replagal 0.2mg/kg is effective for both short- and long-term treatment in men,^{2,6} women,⁵ and children (aged 7-16 years*)⁷ with Fabry disease.

We are pleased to confirm that Shire HGT currently has an adequate supply of Replagal 0.2mg/kg for both existing and anticipated future patients to receive ERT to control their Fabry disease.

Shire HGT is committed to partnering with you and the Fabry community, particularly during this critical period. Please do not hesitate to contact me, or any of my colleagues, if we can help you to ensure that your Fabry patients' treatment needs are fulfilled.

Yours sincerely,

*Studies in children between 0 and 6 years of age have not been performed, and no dosage regimen can presently be recommended in such patients.⁸

References

1. <http://www.genzyme.com/corp/media/GENZ%20PR-092309.asp>.
2. Schiffmann R, *et al.* *JAMA* 2001; **285**: 2743-9.
3. Feriozzi S, *et al.* *Am J Nephrol* 2009; **29**: 353-61.
4. Hughes DA, *et al.* *Heart* 2008; **94**: 153-8.
5. Whybra C, *et al.* *Genet Med* 2009; **11**: 441-9.
6. Beck M, *et al.* *Eur J Clin Invest* 2004; **34**: 838-44.
7. Schiffmann R, *et al.* Presented at ACMG, 25-29 March, 2009; Tampa, Florida.
8. Replagal Summary of Product Characteristics.

Abbreviated prescribing information

Please consult the Summary of Product Characteristics (SmPC) before prescribing.

Presentation: Concentrate solution for IV infusion. 1ml of concentrate for solution for infusion contains 1mg agalsidase alfa.

Indication: Long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry disease (α -galactosidase A deficiency).

Dosage and administration: Replagal 0.2mg/kg body weight by IV infusion over 40 min every other week.

Contraindications: Hypersensitivity to the active substance or any of the excipients.

Warnings and precautions: 13.7% of patients receiving 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). 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 allergic or anaphylactic-type reactions occur, discontinue Replagal immediately and initiate appropriate treatment. Patients may develop IgG antibodies to the protein. Extensive renal damage may limit the renal response to enzyme replacement therapy. Do not give Replagal together with chloroquine, amiodarone, benoquin or gentamicin because these substances can inhibit intracellular α -galactosidase activity. Studies in children aged 0–6 years have not been performed. A dose of 0.2mg/kg is suggested for older children and adolescents (7–18 years). Caution should be exercised in pregnant or breast-feeding women. **Side effects:** Most reported adverse effects have been mild to moderate. *Very common (>1/10 patients):* headache, flushes, nausea, rigors, pyrexia, pain/discomfort, fatigue; *common (>1/100, <1/10 patients):* peripheral oedema, dizziness, dysgeusia, neuropathic pain, tremor, hypersomnia, hypoesthesia, paraesthesia, increased lacrimation, tinnitus, tinnitus aggravated, tachycardia, palpitations, hypertension, cough, hoarseness, throat tightness, dyspnoea, nasopharyngitis, pharyngitis, increased throat secretion, rhinorrhoea, diarrhoea, vomiting, abdominal pain/discomfort, acne, erythema, pruritus, rash, livedo reticularis, musculoskeletal discomfort, myalgia, back pain, limb pain, peripheral swelling, arthralgia, joint swelling, aggravated fatigue, feeling hot, feeling cold, asthenia, chest pain, chest tightness, influenza-like illness, injection-site rash, malaise, decreased corneal reflex; *uncommon (>1/1000, <1/100 patients):* parosmia, angioneurotic oedema, urticaria, sensation of heaviness, decreased oxygen saturation.

Package quantity and price: Vials of 5ml (containing 3.5ml concentrate) in pack sizes of 1, 4 or 10 vials. Price: £1068.64 for 5ml vials.

Pharmaceutical precautions: Store in a refrigerator (2°C–8°C).

Marketing authorisation number and holder: EU/1/01/189/001-006. Shire Human Genetic Therapies AB, Svärdvägen 11D, SE 182 33 Danderyd, Sweden.

Legal category: POM. Further information is available in the Summary of Product Characteristics (SmPC), or on request from the marketing authorisation holder.

Date of preparation: 27th January 2009 **Item code:** INT/REP/09/0004

Adverse events should be reported. Reporting forms and information can be found at www.yellowcard.gov.uk. Adverse events should also be reported to Shire Human Genetic Therapies on +44 (0)1256 894000 or faxed on +44 (0)1256 894715 or emailed to GlobalPharmacovigilance@shire.com