REPLAGAL DOSING CALCULATION

Replagal is administered at a recommended dose of 0.2 mg/kg body weight every other week by intravenous infusion over 40 minutes[1]

Determine the total volume of Replagal to be administered and the number of vials needed based on the patient's weight and the recommended dose of 0.2 mg per kg.[1]

Example:

Required information for the calculation:

- Weight of patient = 70 kg
- Each 1 ml of solution contains 1 mg of algasidase alfa
- Each vial contains 3.5 ml of Replagal concentrate

The calculation:

- 0.2 x 70 = 14 mg
- 14 mg of Replagal required = 14 ml of Replagal concentrate
- 14 ÷ 3.5 (the volume of a vial of Replagal) = 4
- 4 vials will be required for infusion

Each 1 ml of concentrate for solution contains 1 mg Replagal

Each vial of Repalagal concentrate contains 3.5 ml solution

kg	x 0.2 =	mg	=	ml	/ 3.5 =	vials
patient's weight		dose of Replagal		volume of Replagal concentrate		number of vials of Replagal concentrate

Dilute the total volume of Replagal concentrate required in 100 ml of 9 mg/ml (0.9%) sodium chloride solution for infusion

You need ____ ml Replagal concentrate from ____ vials.

1. Replagal®. Shire EU Summary of Product Characteristics 2016.

WEIGHT-BASED DOSING EXAMPLES

Replagal is administered at a recommended dose of 0.2 mg/kg body weight every other week by intravenous infusion over 40 minutes[1]

These calculations are based on the SmPC recommended doses of 0.2 mg/kg body weight every other week by intravenous infusion over 40 minutes. Example patient weights are given, this is purely illustrative in how to calculate the desired dose and number of vials required.

Body weight	Replagal dose	Calculation step (number of vials)	Actual number of vials required
60.0 kg	12 mg	3.4	4
70.0 kg	14 mg	4.0	4
72.5 kg	15.5 mg	4.1	5
77.4 kg	15.48 mg	4.4	5
84.6 kg	16.92 mg	4.8	5

1. Replagal®. Shire EU Summary of Product Characteristics 2016.

PRESCRIBING INFORMATION

Replagal™ (agalsidase alfa)

(Before prescribing please consult the Summary of Product Characteristics (SmPC))

Product Name: Replagal 1 mg/ml concentrate for solution for infusion.

Indication: Replagal is indicated for long-term enzyme replacement therapy in patients with a confirmed diagnosis of Fabry Disease (α-galactosidase A deficiency).

Dose and Administration: Replagal treatment should be supervised by a physician experienced in the management of patients with Fabry Disease or other inherited metabolic diseases. Replagal is administered at a dose of 0.2 mg/kg body weight every other week by intravenous infusion over 40 minutes. No studies in elderly patients (over 65 years of age) have been performed and no dosage regimen can presently be recommended in these patients. The safety and efficacy of Replagal in children aged 0-6 years has not yet been established. No recommendation on posology can be made. In clinical studies of children (7-18 years) who received Replagal 0.2 mg/kg every other week, no unexpected safety issues were encountered.

Contraindications: Hypersensitivity to the active

Warnings and precautions: *Idiosyncratic infusion*
with Replagal in clinical trials have experienced
17 (23.5%) paediatric patients ≥7 years of age er
infusion reaction over a period of 4.5 years of
Three of 8 (37.5%) paediatric patients <7 years c
reaction over a mean observation time of 4.2 year
uncommonly. The onset of infusion related reactions has generally occurred within the first 2-4 months after initiation of treatment with Replagal 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, medical attention must be sought immediately and appropriate actions instituted. The infusion can be temporarily interrupted (5 to 10 minutes) until symptoms subside and the infusion may then be restarted. Mild and transient effects may not require medical treatment or discontinuation of the infusion. *Hypersensitivity reactions:* If severe allergic or anaphylactic-type reactions occur, the administration of Replagal should be discontinued immediately and appropriate treatment initiated. The current medical standards for emergency treatment are to be observed. *Antibodies to the protein:* Patients may develop antibodies to the protein. A low titre IgG antibody response has been observed in approximately 24% of the male patients treated with Replagal. Based on limited data this percentage has been found to be lower (7%) in the male paediatric population. These IgG antibodies appeared to develop following approximately 3-12 months of treatment. After 12 to 54 months of therapy, 17% of Replagal treated patients were still antibody positive whereas 7% showed evidence for the development of immunologic tolerance, based on the disappearance of IgG antibodies over time. The remaining 76% were antibody negative throughout. In paediatric patients >7 yrs of age, 1/16 male patients tested positive for IgG anti-agalsidase alfa antibodies during the study. 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. Borderline IgE antibody positivity not associated with anaphylaxis has been reported in clinical trials in a very limited number of patients. *Patients with renal impairment:* The presence of extensive renal damage may limit the renal response to enzyme replacement therapy, possibly due to underlying irreversible pathological changes. In such cases, the loss of renal function remains within the expected range of the natural progression of disease.

Fertility, Pregnancy and Lactation: *Pregnancy:* There is very limited data on pregnancies exposed to Replagal. Caution should be exercised when prescribing to pregnant women. *Breast-feeding:* It is unknown whether Replagal is excreted in human milk. Caution should be exercised when prescribing to breast-feeding women. *Fertility:* No effects on male fertility were seen in reproductive studies in male rats.

Driving: Replagal has no or negligible influence on the ability to drive and use machines.

Undesirable Effects: Most commonly reported adverse reactions were infusion associated reactions, which occurred in 13.7% of adult patients treated with Replagal in clinical trials. Most undesirable effects were mild to moderate in severity. Adverse reactions reported for the 177
including 21 patients with history of end stage
rs of age) and 17 female patients. *Very common*
ng, nausea, rigors, pyrexia, pain and discomfort,
oedema, dizziness, dysgeusia, neuropathic pain,
, decreased corneal reflex, increased lacrimation,
ations, hypertension, cough, hoarseness, throat
itis, 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.

Overdosage: In clinical trials doses up to 0.4 mg/kg weekly were used, and their safety profile was not different from the recommended dose of 0.2 mg/kg biweekly.

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

Date of Revision: August 2016.

Number, Name and Address of MA Holder: EU/1/01/189/001-003. Shire Human Genetic Therapies AB, Vasagatan 7, 11120 Stockholm, Sweden.

Further information is available on request.

Replagal is a registered trade name.

Suspected adverse reactions should be reported to Shire at: globalpharmacovigilance@shire.com

Placeholder text should be replaced with the local API where required

Shire

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For HCP use only

Please refer to the full prescribing information for more details

REPLAGAL®
agalsidase alfa
CHANGING THE FACE OF FABRY DISEASE