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

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.

**Example:**

1. **Weight of patient = 70 kg**
2. **Each 1 ml of solution contains 1 mg of alglucosidase alfa**
3. **Each vial contains 3.5 ml of Replagal concentrate**

**The calculation:**
- \(0.2 \times 70 = 14\) mg Replagal required
- \(14\) mg of Replagal required = \(14\) ml of Replagal concentrate
- \(14 \div 3.5\) (the volume of a vial of Replagal) = 4
- 4 vials will be required for infusion

**Required information for the calculation:**
- Weight of patient = 70 kg
- Each 1 ml of solution contains 1 mg of alglucosidase alfa
- Each vial contains 3.5 ml 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.

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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

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.

<table>
<thead>
<tr>
<th>Body weight</th>
<th>Replagal dose</th>
<th>Calculation step (number of vials)</th>
<th>Actual number of vials required</th>
</tr>
</thead>
<tbody>
<tr>
<td>60.0 kg</td>
<td>12 mg</td>
<td>3.4</td>
<td>4</td>
</tr>
<tr>
<td>70.0 kg</td>
<td>14 mg</td>
<td>4.0</td>
<td>4</td>
</tr>
<tr>
<td>72.5 kg</td>
<td>15.5 mg</td>
<td>4.1</td>
<td>5</td>
</tr>
<tr>
<td>77.4 kg</td>
<td>15.48 mg</td>
<td>4.4</td>
<td>5</td>
</tr>
<tr>
<td>84.6 kg</td>
<td>16.92 mg</td>
<td>4.8</td>
<td>5</td>
</tr>
</tbody>
</table>


Please refer to the full prescribing information for more details.
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 substance, IgG antibodies or IgE antibodies to agalsidase alfa, or a previous history of severe allergic reaction to Replagal.

Warnings and precautions: Idiosyncratic infusion related reactions with Replagal in clinical trials have experienced 17 (23.5%) paediatric patients ≥7 years of age en infusion reaction over a period of 4.5 years of treatment. Three of 8 (37.5%) paediatric patients <7 years of age experienced an infusion reaction over a mean observation time of 4.2 years. 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) have 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 subsides and the infusion may then be restarted. Mild and transient effects may not require medical treatment. Rare non-allergic, non-immune mediated, infusion associated anaphylactic reactions have been reported. Anaphylactic reactions are usually preceded by urticaria, angioedema, dyspnea, laryngeal edema, bronchospasm, hypotension, and cardiovascular collapse. Immediate medical assistance is required in cases of anaphylaxis. IgG anti-agalsidase alfa antibodies have been 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 breastfeeding 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 paediatric patients (including 21 patients with history of end stage renal disease) were similar to those observed in adult patients. In adult patients, 5 patients (all treated with ≥0.4 mg/kg weekly) had a positive test 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.

Undesirable Effects:

Very common

Hypersensitivity reactions:

- Angioedema
- Anaphylaxis
- Urticaria
- Rhinitis
- Fever

Common

- Fatigue
- Asthenia
- Cough
- Headache

Occasional

- Myalgia
- Arthralgia
- Myositis

Rare

- Anemia
- Gastrointestinal symptoms
- Diarrhea
- Abdominal pain/discomfort

Infrequent

- Conjunctivitis
- Tinnitus

Further information is available on request.

Number, Name and Address of MA Holder: EU/1/01/189/001-003. Shire Human Genetic Therapies AB, Vasagatan 7, 11220 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

Shire

For HCP use only

Please refer to the full prescribing information for more details.

Job code: C-APROM//INT//0405 | Date of preparation: June 2017

CHANGING THE FACE OF FABRY DISEASE