

Replagal infusion 3.5 mg / 3.5 ml**Takeda (Pty) LTD**

Approved Patient Information Leaflet

Scheduling Status:**S4**

REPLAGAL 1 mg/ml concentrate for solution for infusion

agalsidase alfa

Sugar free

Read all of this leaflet before you are given REPLAGAL.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor pharmacist, nurse or other health care provider.

What is in this leaflet

1. What REPLAGAL is and what it is used for
2. What you need to know before you take REPLAGAL
3. How to take REPLAGAL
4. Possible side effects
5. How to store REPLAGAL
6. Contents of the pack and other information

1. What REPLAGAL is and what it is used for

Active ingredient: agalsidase alfa

Inactive ingredients: Sodium phosphate monobasic, monohydrate; Polysorbate 20; Sodium chloride; Sodium hydroxide and Water for injections.

The active substance in REPLAGAL is agalsidase alfa (1mg/ml). Agalsidase alfa is a form of the human enzyme α -galactosidase. It is produced by switching on the gene for α -galactosidase A in cells.

REPLAGAL is used to treat Fabry disease. It is used as enzyme replacement therapy when the level of enzyme in the body is lower than normal as in Fabry disease.

2. What you need to know before you use REPLAGAL**REPLAGAL should not be administered to you:**

If you are allergic (hypersensitive) to agalsidase alfa or any of the other ingredients of REPLAGAL.

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42 Warnings and Precautions**43 Tell your doctor or health care provider before being given the infusion:**

44 If you notice any of the effects below during or after an infusion you should tell your doctor
45 immediately:

- 46 • high fever, chills, fast heart rate;
- 47 • vomiting;
- 48 • light-headedness;
- 49 • hives
- 50 • swelling of your hands, feet, ankles, face, lips, mouth or throat which may cause difficulty in
51 swallowing or breathing;

52 Your doctor may stop the infusion temporarily (5 –10 min) until the symptoms go away and then begin
53 the infusion again.

54

55 Your doctor may also treat the symptoms with other medicines (antihistamines or corticosteroids).

56 Most of the time you can still be given REPLAGAL even if these symptoms occur.

57

58 If you experience a severe allergic (anaphylactic-type) reaction, the administration of REPLAGAL will
59 be immediately discontinued and an appropriate treatment will have to be initiated by your doctor.

60

61 If treatment with REPLAGAL makes your body produce antibodies this will not stop REPLAGAL
62 working and the antibodies may disappear with time.

63

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65 Children and Adolescents

66 REPLAGAL has not yet been studied in children less than 6 years old and there is only limited clinical
67 data in children 7-18 years old. No unexpected safety issues were encountered in the studies with
68 REPLAGAL in children 7-18 years of age.

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72 Other medicines and REPLAGAL:

73 Always tell your healthcare provider if you are taking other medicines on a regular basis, including
74 complementary or traditional medicines, the use of REPLAGAL with these medicines may cause
75 undesirable interactions. Tell your doctor or pharmacist if you are taking any other medicines,
76 including any you have bought at your pharmacy, supermarket or health food shop. Please consult
77 your doctor, pharmacist or other healthcare professional for advice.

78

79 REPLAGAL with food and drink:

80 Interactions with food or drink are unlikely.

81

82 Pregnancy and breastfeeding:

83 If you are pregnant or breast-feeding your baby while taking this medicine, please consult your doctor,
84 pharmacist or other health care professional for advice.

85

86 Very limited clinical data on pregnancies exposed to REPLAGAL have shown no adverse effects on
87 the mother and newborn child.

88

89 Driving and using machinery:

90 You may drive and operate machinery whilst on REPLAGAL.

91

92 Sodium

93 This medicine contains 14.2 mg sodium (main component of cooking/table salt) in each vial. This is
94 equivalent to 0.7 % of the recommended maximum daily dietary intake of sodium for an adult.

95

96 Keeping a record

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98 In order to improve the traceability of biological medicines, the name and batch number of the
99 administered product should be clearly recorded by your healthcare professional. Speak with your
100 healthcare professional if you are not sure.

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103 3. How to use REPLAGAL

104 Always take REPLAGAL exactly as your doctor has told you. You should check with your doctor if
105 you are unsure.

106

107 While remaining under the medical doctors supervision, Replagal can be self-administered (by you or
108 your caregiver) after appropriate training by the treating medical doctor and/or nurse.

109 Self-administration should occur in the presence of a responsible adult.

110

111 The usual dose is an infusion of 0,2 mg for every kg you weigh. This would be about 14 mg or 4 vials
112 (glass bottles) of REPLAGAL for an average size (70 kg) individual. The infusion will be given every
113 two weeks.

114

115 REPLAGAL has to be diluted in 9 mg/ml (0.9%) sodium chloride solution before use. After dilution
116 REPLAGAL is given in a vein, usually in your arm.

117

118 Each time you are treated it will take 40 minutes for REPLAGAL to be given to you in a vein. Your
119 treatment will be supervised by a doctor who specialises in the treatment of Fabry disease.

120

121 If you have the impression that the effect of REPLAGAL is too strong or too weak, talk to your doctor
122 or pharmacist.

123

124 If you take more REPLAGAL than you should:

125 Since a health care provider will administer REPLAGAL, he/she will control the dosage. However, in
126 the event of overdosage, your doctor will manage the overdosage

127

128 If you forget to have REPLAGAL:

129 Since a health care provider will administer REPLAGAL, it is unlikely that the dose will be missed. If,
130 however, you have missed a REPLAGAL infusion, please contact your doctor

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135 4. Possible side effects

136 REPLAGAL can have side effects. Not all side effects reported for REPLAGAL are included in this
137 leaflet.

138 Most side effects of REPLAGAL are mild to moderate. More than 1 in 10 people (frequency “very
139 common”) may have a reaction during or following an infusion of REPLAGAL. These effects include
140 chills, headache, nausea, fever, tiredness, unsteadiness, difficulty breathing, shaking, cough and
141 vomiting. However some effects may be serious and may need treatment. Infusion related reactions
142 involving the heart including heart muscle ischemia and heart failure, may occur in patients with Fabry
143 disease involving the heart structures (frequency “not known” (cannot be estimated from the available
144 data)). Your doctor may stop the infusion temporarily (5 - 10 min) until the symptoms go away and
145 then begin the infusion again. Your doctor may also treat the symptoms with other medicines
146 (antihistamines or corticosteroids). Most of the time you can still be given Replagal even if these
147 symptoms occur.

148

149 List of other side effects:

150 Very common: may affect more than 1 in 10 people

151 - swelling in the tissue (eg legs, arm)

152 - tingling or numbness or pain in fingers or toes

153 - ear ringing

154 - palpitations

155 - Sore throat

156 - abdominal pain, diarrhoea

157 - rash at the infusion site

158 - back or limb pain, muscle pain, joint pain

159 - chest pain, cold symptoms, fever, feeling sick

160

161 Common: may affect up to 1 in 10 people:

162 - change in the taste of food, prolonged sleep

163 - eyes tearing

164 - increased ear ringing

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- 165 - increased heart rate, heart rhythm problems
- 166 - increased blood pressure, low blood pressure, facial flushing (redness)
- 167 - hoarseness, or tight throat, runny nose
- 168 - abdominal discomfort
- 169 - acne, red or itchy or mottled skin, excessive sweating
- 170 - muscle and bone discomfort, swelling of the extremities or joints
- 171 - hypersensitivity
- 172 - chest tightness, increased feeling lack of energy, feeling cold or hot, flu-like symptoms, discomfort
- 173
- 174
- 175 Uncommon: may affect up to 1 in 100 people:
- 176 - severe allergic (anaphylactic-type) reaction
- 177 - blink reflex abnormal
- 178 - increased heart rate
- 179 - low level of oxygen in your blood and sticky throat secretions
- 180 - sense of smell is different)
- 181 - collection of fluid under the skin may lead to swelling of body parts, lace-like discoloration of the skin
- 182 eg in the leg
- 183 - sensation of heaviness
- 184 - injection site rash

185

186 Should your general health worsen while taking REPLAGAL, or if any of the side effects gets serious,

187 or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

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Children and adolescents

190 Side effects reported in children were in general similar to those reported in adults. However, infusion

191 related reactions (fever, difficulty breathing, chest pain) and pain aggravated occurred more

192 frequently.

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196 **Reporting of side effects**

197 If you get side effects, talk to your doctor. You can also report side effects to SAHPRA via the “**6.04**
198 **Adverse Drug Reaction Reporting Form**”, found online under SAHPRA’s publications:
199 <https://www.sahpra.org.za/Publications/Index/8>. By reporting side effects, you can help provide more
200 information on the safety of REPLAGAL

201

202

203 **5. How to store REPLAGAL**

204 • Store in a refrigerator (2 °C – 8 °C).

205 • Do not freeze.

206 • STORE ALL MEDICINES OUT OF REACH OF CHILDREN

207 • Do not use REPLAGAL after the expiry date which is stated on the label after the letters EXP.

208 The expiry date refers to the last day of that month.

209 • Do not use REPLAGAL if you notice that there is discolouration or other foreign particles present.

210 • Return all unused medicine to your pharmacist

211 • Do not dispose of unused medicine in drains and sewerage systems (e.g. toilets)

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217 **6 Contents of the pack and other information**218 **What REPLAGAL contains**

219

220 The active substance is agalsidase alfa.

221

222 The other ingredients are:

223 Sodium phosphate monobasic

224 Monohydrate

225 Polysorbate 20

226 Sodium chloride

227 Sodium hydroxide

228 Water for injection.

229

230 **What REPLAGAL looks like and contents of the pack**

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231 Your medicine is available in clear, transparent 5 ml glass vials containing 3,5 mg/ 3,5 ml of
232 agalsidase alfa. The vials are closed with a grey rubber stopper and sealed with a one-piece
233 aluminium seal and white flip-off cap. Pack sizes of 1, 4 or 10 vials are available.

234

235 REPLAGAL is a clear and colourless solution and essentially free of particles. Finished product may
236 develop a minute amount of fine particulate matter during storage.

237

238

239 Holder of Certificate of Registration

240 Takeda (Pty) Ltd

241 Building A, Monte Circle

242 64 Monte Casino Boulevard,

243 Fourways

244 2191

245 South Africa

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280 The following information is intended for medical or healthcare professionals only:

281 **Instructions for use, handling and disposal**

- 282 1. Calculate the dose and number of REPLAGAL vials needed.
- 283 2. Dilute the total volume of REPLAGAL concentrate required in 100 ml 9 mg/ml sodium chloride
284 solution for infusion (0,9%w/v). Care must be taken to ensure the sterility of the prepared
285 solutions since REPLAGAL does not contain any preservative or bacteriostatic agent; aseptic
286 technique must be observed. Once diluted, the solution should be mixed gently but not
287 shaken.
- 288 3. The solution should be inspected visually for particulate matter and discolouration prior to
289 administration.
- 290
- 291 4. Administer the infusion solution over a period of 40 minutes using an intravenous line with an
292 integral filter. Since no preservative is present, it is recommended that administration is
293 started as soon as possible and within 3 hours of dilution. However, the chemical and
294 physical stability of the diluted solution has been demonstrated for 24 hours at 25°C.
- 295 5. Do not infuse REPLAGAL concomitantly in the same intravenous line with other agents.
- 296 6. For single use only. Any unused product or waste material should be disposed of in accordance with
297 local requirements.
- 298