

## **APPROVED PATIENT INFORMATION LEAFLET**

**Read all of this leaflet carefully before you start using Beriglobin P.**

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **Beriglobin P** has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

### **SCHEDULING STATUS:**

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### **PROPRIETARY NAME AND DOSAGE FORM:**

**BERIGLOBIN® P 2 ml** Solution for Injection for subcutaneous or intramuscular administration.

**BERIGLOBIN® P 5 ml** Solution for Injection for subcutaneous or intramuscular administration.

### **WHAT BERIGLOBIN® P CONTAINS:**

1 ml contains:

160 mg human normal immunoglobulin.

The other ingredients are:

Aminoacetic acid (glycine), sodium chloride, HCl or NaOH (in small amounts for pH adjustment), water for injections.

### **WHAT BERIGLOBIN® P IS USED FOR:**

Beriglobin P is used for

- Replacement therapy in adults and children in congenital (primary) immunodeficiency syndromes such as:
  - Congenital absence of antibodies (agammaglobulinaemia)
  - or antibody deficiency (hypogammaglobulinaemia).
  - Common variable immunodeficiency
  - Severe combined immunodeficiency
  - IgG subclass deficiencies with recurrent infections
- Replacement of antibodies in
  - cancer of bone marrow (myeloma) or
  - malignant illness of white blood cells (chronic lymphatic leukaemia). This disease leads to severe antibody deficiency (secondary hypogammaglobulinaemia) and recurrent infections.
- Hepatitis A prophylaxis
  - in travellers who present less than 2 weeks before possible exposure, preferably in combination with vaccination.

For long-term hepatitis A prophylaxis, active immunisation is recommended.

- in persons exposed less than 2 weeks previously.
  
- Therapy of inflammation of mucous membranes caused by radiotherapy (radiogenic mucositis).

### **BEFORE YOU USE BERIGLOBIN® P:**

The following information should be considered by you and your doctor before you use Beriglobin P.

**Do not use BERIGLOBIN® P:**

- if you are allergic (hypersensitive) to any of the components of the product.
- Please inform your doctor if you are allergic to any medicine or food.
- into a blood vessel
- into a muscle if you suffer from a disorder of blood clotting.

**Take special care with BERIGLOBIN® P:**

- if Beriglobin P is accidentally administered into a blood vessel. You could develop a severe allergic reaction (anaphylactic shock). This reaction is seen as a fall in blood pressure and shortness of breath. You could also develop blood clots (thromboembolic events);
- if you receive human normal immunoglobulin for the first time;
- if you have received another product for treatment of the same symptoms in the past;
- when treatment has been interrupted for more than eight weeks.

True hypersensitivity reactions are rare. They can occur in the very rare cases of IgA deficiency with anti-IgA antibodies. In this case you should be treated with caution.

Rarely, Beriglobin P can induce a fall in blood pressure with anaphylactic reaction. This reaction may also occur if you had tolerated previous treatment with normal human immunoglobulin.

***Thromboembolic events associated with subcutaneous substitution therapy:***

With the subcutaneous use of high doses of immunoglobulins for substitution therapy (e.g. primary immunodeficiency syndrome) there have been reports of blood clots (thromboembolic events). They may lead to heart attack (myocardial infarction), stroke, blood clots in the leg (deep venous thrombosis) and blood clots in the arteries of the lungs (pulmonary embolism).

If you have any known risk factors for developing blood clots, such as if

- you are overweight,
- you are elderly,
- you have diabetes,
- you have been bedridden for a longer time,
- you have or have already had problems with your blood vessels (vascular diseases or blockage of a vessel),
- you have or have already had kidney problems,
- you have a high blood pressure,
- you suffer from a disease which causes your blood to thicken,
- you suffer from an increased tendency for blood clotting (thrombophilia).

Please tell your doctor or health care professional prior to high-dose subcutaneous treatment with Beriglobin if at least one of these circumstances applies to you.

First symptoms of thromboembolic events can be shortness of breath, pain and swelling of a limb, numbness or weakness of an arm or leg or one side of your face, sudden confusion, or trouble speaking or understanding and chest pain. Please contact your physician immediately, if you have any of those symptoms. Please make sure that you are sufficiently hydrated before high-dose subcutaneous treatment with Beriglobin.

**Potential complications can often be avoided by ensuring that:**

- you are not sensitive to human normal immunoglobulin. The product should initially be injected slowly. The recommended infusion rate should be adhered to (see “How to use Beriglobin P”);

- you are carefully monitored for any symptoms throughout the infusion period especially if
  - you receive human normal immunoglobulin for the first time,
  - you switched from an alternative product, or
  - there has been a long interval since the previous infusion.

In these cases you should be monitored during the first infusion and for the first hour thereafter.

All other patients should be observed for at least 20 minutes after administration.

On suspicion of an allergic or anaphylactic reaction the administration has to be discontinued immediately. In case of shock the current medical standards for shock treatment have to be applied.

***Information on safety with respect to infections***

When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to patients. These include:

- careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded, and
- the testing of each donation and pools of plasma for signs of viruses/infections.

Manufacturers of these products also include steps in the processing of the blood or plasma that can inactivate or remove viruses. Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infections cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.

The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV, the AIDS virus), hepatitis B virus and hepatitis C virus (liver inflammation), and for the non-enveloped hepatitis A virus and parvovirus B19 (Sticker's disease).

Immunoglobulins have not been associated with hepatitis A or parvovirus B19 infections possibly because the antibodies against these infections, which are contained in the product, are protective.

Every time you take Beriglobin P you should record the following data in your treatment diary

- the date of administration

- the batch number of the product
- the injected volume

**Using BERIGLOBIN® P with food and drink:**

Beriglobin P can be used without regard to food and drink.

**Pregnancy and Breast-feeding:**

- Ask your doctor or pharmacist for advice before taking any medicine if you are pregnant or breast-feeding your baby.
- The safety of **BERIGLOBIN® P** for use in human pregnancy has not been established.
- Clinical experience with immunoglobulins suggests that no harmful effects on the course of pregnancy, or on the foetus and the neonate are to be expected.
- Your doctor will decide if it is suitable for you to receive Beriglobin P if you are pregnant or breast-feeding your baby.

If you are pregnant or breast feeding your baby while using **BERIGLOBIN® P**, please consult your doctor, pharmacist or other health care professional for advice.

**Driving and using machinery:**

Beriglobin P should not affect your ability to drive and use machines.

**Important information about some of the ingredients of BERIGLOBIN® P:**

Beriglobin P contains up to 110 mg sodium per dose (75 kg body weight) if the maximum daily dose is given (11,25 g = 70,3 ml). This should be taken into consideration if you are on a controlled sodium diet.

**Using other medicines with BERIGLOBIN® P:**

- Please ask your doctor or pharmacist for advice if you are taking or have recently taken any other medicines including vaccines or medicines obtained without a prescription.
- You must not mix this medicinal product with other medicinal products, solvents or diluents.
- Results of some blood tests may be affected by Beriglobin P. If you are due to receive blood tests of any sort, make sure the doctor treating you knows you are receiving Beriglobin P.

If you are taking other medicines on a regular basis, including complementary or traditional medicines, the use of **BERIGLOBIN® P** with these medicines may cause undesirable interactions. Please consult your doctor, pharmacist or other healthcare professional, for advice.

**HOW TO USE BERIGLOBIN® P:**

Always use **BERIGLOBIN® P** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

**Dosage:**

The dosage and intervals of infusion are dependent on the indication.

### **Replacement therapy:**

The product should be administered via the subcutaneous route.

Always use Beriglobin P exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Your doctor will calculate the correct dose for you taking into account your weight and response to treatment.

A loading dose of at least 1,3 to 3,1 ml/kg body weight – divided over several days – may be required. Following this, maintenance doses may be given (usually weekly) to reach a cumulative monthly dose of about 2,5 to 5 ml per kg of body weight.

### **Hepatitis A prophylaxis:**

The product is to be administered via the intramuscular route.

– Short-term prophylaxis in travellers who present less than 2 weeks before possible exposure:

For stays in endemic areas of less than 3 months a dose of 0,003 to 0,004 g/kg (0,02 ml/kg) bodyweight is recommended to be administered intramuscularly.

Beriglobin P can be given in combination with Hepatitis A vaccine, but at different sites of the body.

- Hepatitis A prophylaxis in persons exposed less than 2 weeks previously: 0,003 to 0,004 g/kg (0,02 ml/kg) bodyweight administered intramuscularly.

### **Therapy of radiogenic mucositis**

The product is to be administered via the intramuscular route.

Initially 10 ml (1600 mg), after 2 days 5 ml (800 mg) and after a further 2 days again 5 ml (800 mg). The treatment can be repeated as often as necessary.

**Administration:**

Beriglobin P is a ready-for use solution and should be administered at body temperature.

Beriglobin P is a clear solution. The colour can vary from colourless to pale-yellow up to light brown. Do not use solutions, which are cloudy or contain residues (deposits/particles).

The solution should be administered at body temperature.

Depending on the indication, human normal immunoglobulin should be administered via the subcutaneous or intramuscular route.

Subcutaneous infusion for home treatment should be initiated by a doctor experienced in the guidance of patients for home treatment.

You will be instructed in the use of a syringe driver, infusion techniques, the keeping of a treatment diary and measures to be taken in case of severe adverse events. Intramuscular injection must be given by a doctor or nurse.

Do not inject intravascularly! Note that there is an increased risk of inadvertent intravascular injection in patients who have repeatedly received intramuscular injections.

**Subcutaneous administration:**

Subcutaneous infusion for home treatment should be initiated and monitored by a physician experienced in the treatment of immunodeficiencies and in the guidance of patients for home treatment. You will be instructed

- in the use of a syringe driver,
- infusion techniques,
- the keeping of a treatment diary and
- measures to be taken in case of severe adverse events.

The recommended infusion rate is 22 ml/hour. In a clinical study with 53 patients evaluated, during the training phase under supervision of a physician, the infusion rate was increased from initially 10 ml to 22 ml/hour.

Beriglobin P should preferably be administered in the abdominal wall, thigh and/or buttocks.

No more than 15 ml should be injected into a single site. Doses over 15 ml should be divided and injected into 2 or more sites.

Your doctor will instruct you how to dispose of unused product or waste material.

**Intramuscular administration:**

Intramuscular injection must be given by a physician or nurse.

Beriglobin P should preferably be administered ventrogluteally with the patient lying down. If larger doses are required, it is advisable to administer them in divided fractions. This applies in the case of doses above 2 ml for persons up to 20 kg bodyweight and doses above 5 ml for persons above 20 kg bodyweight.

Any unused product or waste material should be disposed of in accordance with local requirements.

If you have the impression that the effect of **BERIGLOBIN® P** is too strong or too weak, talk to your doctor or pharmacist.

**If you use more BERIGLOBIN® P than you should:**

There are no known symptoms of overdose.

In the event of overdose, consult your doctor or pharmacist. If neither is available, seek help at the nearest hospital or poison control centre.

**If you forget to use BERIGLOBIN® P:**

The consequences of a skipped dose are not known.

**Effects when treatment with BERIGLOBIN® P is stopped:**

You should not experience any effects when treatment with BERIGLOBIN® P is stopped.

Please consult your doctor or pharmacist before treatment is stopped.

**POSSIBLE SIDE EFFECTS:**

Like all medicines, **Beriglobin P** can have side effects, although not everybody gets them.

Please contact your doctor immediately or go to the Emergency Department at your nearest hospital immediately if any of the listed side effects occur, or if you notice any side effects not listed in this leaflet.

The following undesirable effects have been reported in a clinical study with subcutaneous administration:

**Local reactions at the injection site:**

Very common, i.e. more than 1 out of 10 treated persons: swelling, soreness, redness, induration, local heat, itching, bruising or rash. The frequency of these local reactions declined very rapidly within the first ten infusions, when patients became used to this form of treatment.

**Immune system disorders:**

In single cases, i.e. less than 1 out of 10,000 treated persons: allergic reactions including fall in blood pressure

**Generalised reactions:**

In single cases, i.e. less than 1 out of 10,000 treated persons: e.g. chills, fever, headache, generally feeling unwell moderate back pain. unconsciousness, dizziness, rash, wheezing.

In addition to the reactions which have been observed during clinical trials, the following adverse reactions have been reported after introduction to the market:

**Immune system disorders:**

Allergic/anaphylactic reactions including difficulty breathing and skin reactions. In isolated cases these reactions can lead to a severe allergic reaction (anaphylactic shock). This may happen even if you have well tolerated previous administration with Beriglobin P or a similar product.

**Generalised reactions:**

Generalised reactions concerning the whole body e.g. nausea, vomiting, joint pain.

**Heart and vascular disorders:**

Circulatory disorders particularly if the product has been inadvertently injected into a blood vessel.

With the subcutaneous use of high doses of immunoglobulins for substitution therapy (e.g. primary immunodeficiency syndrome), vascular disorders: Formation of unwanted blood clots (arterial and venous thromboembolic events) have been reported. Symptoms of these may include:

- severe chest pain or chest pressure (heart attack)
- weakness, paralysis or numbness on one side of the body, loss of vision in one or both eyes, speech difficulties (stroke)
- cough, chest pain, rapid breathing, rapid heart rate (pulmonary embolism)
- swelling, pain, redness of the leg (deep vein thrombosis)

Not all side effects reported for this medicine are included in this leaflet. Should your general health worsen while taking this medicine, please consult your doctor, pharmacist or other health care professional for advice.

**STORAGE INSTRUCTIONS:**

Do not use Beriglobin P after the expiry date which is stated on the label and carton.

- Store in a refrigerator (+2 °C to +8 °C) and keep the container in the outer carton in order to protect from light. Do not freeze!
- The product must be inspected visually prior to administration and should not be used if there is any variation of physical appearance (see also section 3. subheading “Method of administration” and section 6. subheading “What Beriglobin P looks like and contents of the pack”).
- Once a container has been opened, its contents are to be used immediately.

Keep all medicines out of the reach and sight of children.

Return all unused medicine to your pharmacist.

**PRESENTATION OF BERIGLOBIN® P:**

**BERIGLOBIN® P 2 ml:** A single dose 2 ml clear glass ampoule packed into a carton.

**BERIGLOBIN® P 2 ml:** A single dose 2 ml pre-filled syringe packed into a carton.

**BERIGLOBIN® P 5 ml:** A single dose 5 ml clear glass ampoule packed into a carton.

**BERIGLOBIN® P 5 ml:** A single dose 5 ml pre-filled syringe packed into a carton.

**IDENTIFICATION OF BERIGLOBIN® P:**

**BERIGLOBIN® P** is a clear colourless to pale-yellow up to light brown solution.

**REGISTRATION NUMBER/REFERENCE NUMBER:**

**BERIGLOBIN® P 2 ml:**

T/30.2/608

11/30.2/0037 (Namibia)

**BERIGLOBIN® P 5 ml:**

T/30.2/609

11/30.2/0038 (Namibia)

**NAME AND ADDRESS OF REGISTRATION HOLDER OF CERTIFICATE OF**

**REGISTRATION:**

Actor Pharma (Pty) Ltd <sup>1</sup>

Unit 7, Royal Palm Business Estate

646 Washington Street, Halfway House, Midrand, 1685,

Gauteng, South Africa

On behalf of: CSL Behring GmbH, Germany

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<sup>1</sup> Company Registration number: 2008/008787/07