CSL Behring

SCHEDULING STATUS S4

NS2 (Namibia)

PROPRIETARY NAMES 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.

COMPOSITION

1 ml contains:

Human protein	160,0 mg
thereof immunoglobulins G at least	95 %

Distribution of IgG subclasses:
IgG, ca. 61 %
IgG, ca. 28 %
IgG, ca. 5 %
IgG, ca. 6 %
IgA max. 1,7 mg/ml
Antibodies to hepatitis A virus at least 100 IU.

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

PHARMACOLOGICAL CLASSIFICATION

A 30.1 Biologicals – Antibodies.

PHARMACOLOGICAL ACTION

Pharmacodynamic properties:

Normal human immunoglobulin contains mainly immunoglobulin G (IgG), having a broad spectrum of antibodies against various infectious agents. BERIGLOBIN P contains the immunoglobulin G antibodies present in the healthy population. It is usually prepared from the pooled plasma of at least 1 000 donors. It has a distribution of immunoglobulin G subclasses closely proportional to that in native human plasma. Adequate doses of this medicinal product may restore abnormally low immunoglobulin G levels to the normal range.

Pharmacokinetic properties:

With subcutaneous administration of human normal immunoglobulin, peak levels are achieved in the recipient's circulation after approximately 2 days.
Data from a clinical study (n = 60) show that trough levels of approximately 8 to 9 g/l (n = 53) in the plasma can be maintained by weekly doses between 0,05 and 0,15 g (0,3 to 0,9 ml) BERIGLOBIN P per kg bodyweight. This is commensurate to a monthly cumulative dosage of 0,2 to 0,6 g per kg bodyweight.
With intramuscular administration BERIGLOBIN P is bioavailable in the recipient's circulation after a delay of approximately 2 to 3 days.
IgG and IgG-complexes are broken down in the cells of the reticuloendothelial system.

INDICATIONS

Replacement therapy in adults and children in primary immunodeficiency syndromes such as:

- Congenital agammaglobulinaemia and hypogammaglobulinaemia, including therapy-induced.
- Common variable immunodeficiency.
- Severe combined immunodeficiency.
- IgG subclass deficiencies with recurrent infections.

Replacement therapy in myeloma or chronic lymphocytic leukaemia with severe 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 radiogenic mucositis

CONTRA-INDICATIONS

Hypersensitivity to any of the components of the product.
BERIGLOBIN P must not be administered intramuscularly in cases of disorders of haemostasis.

WARNINGS

Do not inject intravascularly!
If BERIGLOBIN P is accidentally administered into a blood vessel, patients could develop shock or thromboembolic events. When administering intramuscularly it is recommended to ensure by aspiration that no vessel has been penetrated.
The recommended infusion rate stated under "DOSAGE AND DIRECTIONS FOR USE" should be adhered to.

INTERACTIONS

Live attenuated virus vaccines:

Immunoglobulin administration may impair for a period of at least 6 weeks and up to 3 months the efficacy of live attenuated virus vaccines such as measles, rubella, mumps, and varicella vaccines.
After administration of BERIGLOBIN P, an interval of at least 3 months should elapse before vaccination with live attenuated virus vaccines. In the case of measles, this impairment may persist for up to 1 year. Therefore patients receiving measles vaccines should have their antibody status checked.

Interference with serological testing:

It has to be considered that when serological test results are interpreted, the transitory rise of passively transferred antibodies after immunoglobulin injection may result in positive test results.
Passive transmission of antibodies to erythrocyte antigens, e.g., A, B and D, may interfere with some serological tests for red cell allo-antibodies (e.g. Coombs test), reticulocyte count and haptoglobin.

PREGNANCY AND LACTATION

There are no controlled clinical trials on the use in human pregnancy. Therefore, the administration of this medicinal product to pregnant women or breastfeeding mothers should be carefully considered.
Long lasting 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.

DOSAGE AND DIRECTIONS FOR USE

Dosage:

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

Replacement therapy:

The product should be administered via the subcutaneous route.
The dosage may need to be individualised for each patient dependent on the pharmacokinetic and clinical response. The following dosage regimens are given as a guideline.

The dosage regimen using the subcutaneous route should achieve a sustained level of IgG.
A loading dose of at least 0,2 to 0,5 g/kg (1,3 to 3,1 ml/kg) bodyweight – divided over several days with a maximal daily dose of 0,1 to 0,15 g/kg bodyweight and as indicated by the treating doctor – may be required.
After steady state IgG levels have been attained, maintenance doses are administered at repeated intervals, ideally weekly, to reach a cumulative monthly dose of about 0,4 to 0,8 g/kg (2,5 to 5,0 ml/kg) bodyweight.
Trough levels should be measured in order to adjust the dose and dosage interval.

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 a 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 (1 600 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 product must be inspected visually prior to administration and should not be used if there is any variation of physical appearance.

Method of administration:

Depending on the indication, BERIGLOBIN P should be administered via the subcutaneous or intramuscular route.

Subcutaneous administration:

Subcutaneous infusion should be initiated and monitored by a physician experienced in the treatment of immunodeficiencies and in the guidance of patients for home treatment. The patient 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.
Do not inject intravascularly! Note that there is an increased risk of inadvertent intravascular injection in patients who have repeatedly received intramuscular injections.
The product 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.

Intramuscular administration:

Intramuscular injection must be given by a doctor 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.
Do not inject intravascularly! Note that there is an increased risk of inadvertent intravascular injection in patients who have repeatedly received intramuscular injections.

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

SIDE-EFFECTS AND SPECIAL PRECAUTIONS

In a clinical study with subcutaneous administration in 60 patients the following undesirable effects have been reported.
The following standard categories of frequency are used:

Very common	≥ 1/10
Common	≥ 1/100 and < 1/10
Uncommon	≥ 1/1 000 and < 1/100
Rare	≥ 1/10 000 and < 1/1 000
Very rare	< 1/10 000 (including reported single cases)

Body as a whole – general disorders:

Rare: In single cases: Generalised reactions such as chills, fever, headache, malaise, moderate back pain, syncope, dizziness, rash, bronchospasm. Allergic reactions including fall in blood pressure.

Application site disorders:

Very common: Swelling, soreness, redness, induration, local heat, itching, bruising or rash. The frequency declined very rapidly within the first ten infusions, when patients became used to the subcutaneous form of treatment. (In study patients who were treated with subcutaneous immunoglobulin for years before the trial, injection site reactions were not reported.)

Adverse reactions reported from post marketing surveillance are similar to the reactions which have also been observed during the clinical trials. In addition, the following have also been reported during post marketing surveillance:

Cardiovascular disorders, general:

Uncommon: Cardiovascular reactions particularly if the product has been inadvertently injected intravascularly.

Vascular (extracardiac) disorders:

Uncommon: Vascular disorders associated with subcutaneous substitution therapy: There are reports from patients being treated subcutaneously with high doses of immunoglobulins for substitution therapy (e.g. primary immunodeficiency syndrome) of arterial and venous thromboembolic events including myocardial infarction, stroke, deep venous thrombosis and pulmonary embolism.

Body as a whole – general disorders:

Uncommon: Allergic/anaphylactic reactions including dyspnoea, cutaneous reactions, in isolated cases reaching as far as anaphylactic shock, even when the patient has shown no hypersensitivity to previous administration. Generalised reactions such as nausea, vomiting, arthralgia.

Special precautions:

Do not inject intravascularly! If BERIGLOBIN P is accidentally administered into a blood vessel, patients could develop shock. When administering intramuscularly, it is recommended to ensure by aspiration that no vessel has been penetrated.
The recommended infusion rate stated under "DOSAGE AND DIRECTIONS FOR USE" should be adhered to. Patients should be closely monitored and carefully observed for any adverse event throughout the infusion period.
Certain adverse reactions may occur more frequently in patients who receive human normal immunoglobulin for the first time or, in rare cases, when the product is switched or when treatment has been paused 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, and these patients should be treated with caution.
Rarely, BERIGLOBIN P can induce a fall in blood pressure with anaphylactic reaction, even in patients who had tolerated previous treatment with normal human immunoglobulin.

Potential complications can often be avoided by ensuring that

- patients are not sensitive to BERIGLOBIN P by first injecting the product slowly (see also "DOSAGE AND DIRECTIONS FOR USE");
- patients are carefully monitored for any symptoms throughout the infusion period.

In particular, patients should be monitored during the first infusion and for the first hour thereafter, in order to detect potential adverse reactions in the following situations:

- patients naïve to human normal immunoglobulin,
- patients switched from an alternative product, or
- when there has been a long interval since the previous infusion.

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.

Thromboembolic events associated with subcutaneous substitution therapy:

The subcutaneous use of high doses of immunoglobulins for substitution therapy (e.g. primary immunodeficiency syndrome) have been associated with arterial and venous thromboembolic events including myocardial infarction, stroke, deep venous thrombosis and pulmonary embolism. Caution should be exercised in prescribing BERIGLOBIN P for subcutaneous substitution therapy in such patients with pre-existing risk factors for thrombotic events (such as advanced age, hypertension, diabetes mellitus and a history of vascular disease or thrombotic episodes, patients with acquired or inherited thrombophilic disorders, patients with prolonged periods of immobilisation, severely hypovolemic patients, patients with diseases which increase blood viscosity). These patients should be informed about first symptoms of thromboembolic events including shortness of breath, pain and swelling of a limb, focal neurological deficits and chest pain and should be advised to contact their physician immediately upon onset of symptoms. Such patients should be sufficiently hydrated before use of BERIGLOBIN P.

Important information about some special excipients of BERIGLOBIN P:
This medicine contains up to 110 mg sodium per dose (bodyweight 75 kg) if the maximal daily dose (11,25 g = 70,3 ml) is applied. To be taken into consideration in patients on a controlled sodium diet.

Virus safety:

Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation/removal of viruses. Despite this, when medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or emerging viruses and other pathogens.

The measures taken are considered effective for enveloped viruses such as HIV, HBV and HCV, and for the non-enveloped viruses HAV and parvovirus B19.
There is reassuring clinical experience regarding the lack of hepatitis A or parvovirus B19 transmission with immunoglobulins and it is also assumed that the antibody content makes an important contribution to the virus safety.
In the interest of patients, it is strongly recommended that every time that BERIGLOBIN P is administered to them, the name and batch number of the product is recorded in order to maintain a link between the patient and the batch of the product.

Effects on ability to drive and use machines:

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

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

There are no known symptoms of overdosage.

IDENTIFICATION

Solution for injection for subcutaneous or intramuscular administration.
Beriglobin® P is a clear solution. The colour can vary from colourless to pale-yellow up to light brown during shelf life.

PRESENTATIONS

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.

STORAGE INSTRUCTIONS

Store in a refrigerator at 5 °C ± 3 °C in the outer carton in order to protect from light.
Do not freeze!
KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS

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 BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATES OF REGISTRATION

Actor Pharma (Pty) Ltd[1]
Unit 7, Royal Palm Business Estate
646 Washington Street, Halfway House
Midrand, 1685
Gauteng, South Africa

On behalf of: CSL Behring GmbH, 35041 Marburg, Germany

DATE OF PUBLICATION OF THIS PACKAGE INSERT

The date on the registration certificate of BERIGLOBIN P: 09 September 1992
The date of the most recently revised package insert as approved by Council: 15 October 2012

® – **Beriglobin® P** is a registered trademark of CSL Behring.

[1]Company Registration number: 2008/008787/07

BER/PI/01/05.2018

CSL Behring

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 S4

NS2 (Namibia)

PROPRIETARY NAMES 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)
  - Antibody deficiency (hypogammaglobulinaemia)
  - Common variable immunodeficiency
  - Severe combined immunodeficiency
  - IgG subclass deficiencies with recurrent infections
- Replacement of antibodies in
  - cancer of the 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 long 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 P 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 P.

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 breastfeeding:

- Ask your doctor or pharmacist for advice before taking any medicine if you are pregnant or breastfeeding 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 breastfeeding 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 bodyweight) 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 bodyweight – 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 a 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 (1 600 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 overdosage.
In the event of overdosage, 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 under "PRESENTATION OF BERIGLOBIN P" and "IDENTIFICATION OF BERIGLOBIN P").
- 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.

PRESENTATIONS 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 NUMBERS / REFERENCE NUMBERS

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

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CSL Behring

PASIËNTINLIGTINGSBLAD

Lees hierdie hele blad noukeurig deur voordat u begin om Beriglobin® P te gebruik.
- Hou hierdie blad. U mag dit nodig vind om dit weer te lees.
- Indien u enige verdere vrae het, vra asseblief u dokter of u apteker.
- **Beriglobin® P** is vir u persoonlik voorgeskryf en u moet nie u medisyne met ander mense deel nie. Dit kan hulle skade aandoen, selfs al is hulle simptome dieselfde as u s'n.
- Indien enige van die newe-effekte ernstig word, of indien u enige newe-effekte opmerk wat nie in hierdie blad gelys is nie, vertel asseblief u dokter of apteker.

SKEDULERINGSTATUS S4

NS2 (Namibië)

EIENDOMSNAME EN DOSEERVORM

Beriglobin® P 2 ml.

Oplossing vir inspuiting vir subkutane of intramuskulêre toediening.

Beriglobin® P 5 ml.

Oplossing vir inspuiting vir subkutane of intramuskulêre toediening.

WAT BERIGLOBIN® P BEVAT
1 ml bevat 160 mg menslike normale immunoglobulien.
Die ander bestanddele is: Aminoasynsuur (glisien), HCl en NaOH (in klein hoeveelhede vir pH aanpassings), natriumchloried, water vir inspuitings.

WAARVOOR BERIGLOBIN P GEBRUIK WORD
BERIGLOBIN P word gebruik vir:
- Vervangingsterapie in volwassenes en kinders met oorerflike (primêre) immuniteitsgebreksindroom soos bv.:
  - Aangebore afwesigheid van teenliggame (agammaglobulinemie)
  - Teenliggaam gebrek (hipogammaglobulinemie)
  - Algemene veranderlike immuniteitsgebrek
  - Ernstige gekombineerde immuniteitsgebrek
  - IgG subklas-gebrekke met herhalende infeksies
- Vervanging van teenliggame in
  - kanker van die beenmurg (myeloom) of
  - kwaadaardige siekte van witbloedselle (kroniese limfositiese leukemie). Hierdie siekte lei tot ernstige teenliggaam gebrek (sekondêre hipogammaglobulinemie) en herhalende infeksies.
- Hepatitis A voorkoming
  - in reisigers wat minder as twee weke voor moontlike blootstelling aanmeld, verkieslik in kombinasie met inenting.
    Vir langtermyn hepatitis A voorkoming, word aktiewe immunisasie aanbeveel.
  - in persone wat minder as 2 weke gelede blootgestel is.
- Behandeling van inflammasie van die slymvliese, veroorsaak deur bestralingsterapie (radiogeniese mukositis).

VOORDAT U BERIGLOBIN P GEBRUIK
Die volgende inligting behoort in ag geneem te word deur u en u dokter voordat u BERIGLOBIN P gebruik.

Moet nie BERIGLOBIN P gebruik nie as:
- U allergies (hipersensitief) is vir enige van die bestanddele van die produk.
- Lig asseblief u dokter in as u allergies is vir enige medisyne of kos.
- In 'n bloedvat in.
- In 'n spier indien u ly aan 'n bloedstollingsafwyking.

Neem spesiale voorsorg met BERIGLOBIN P:
- Indien BERIGLOBIN P per ongeluk toegedien is binne-in 'n bloedvat. U kan 'n ernstige allergiese reaksie (anafilaktiese skok) ontwikkel. Hierdie reaksie word gesien as 'n val in bloeddruk en kortasem. U kan ook bloedklonte ontwikkel (trombo-emboliese voorval).
- Indien u vir die eerste keer menslike normale immunoglobulien ontvang.
- Indien u 'n ander produk vir behandeling van dieselfde simptome in die verlede ontvang het.
- Wanneer die behandeling vir langer as agt weke onderbreek was.

Ware hipersensitiwiteitsreaksies is raar. Dit kan voorkom in die baie seldsame gevalle van IgA gebrek met anti-IgA teenliggame. In hierdie geval behoort u met sorg behandel te word.

Selde kan BERIGLOBIN P 'n val in bloeddruk veroorsaak met anafilaktiese reaksie. Hierdie reaksie mag ook voorkom al het u vorige behandelings met menslike normale immunoglobulien verdra.

Trombo-emboliese voorvalle wat verband hou met onderhuidse vervangingsterapie:
Met die onderhuidse gebruik van hoë dosisse immunoglobuliene vir vervangingsterapie (bv. primêre immuniteitsgebreksindroom) is gevalle van bloedklonte gerapporteer (trombo-emboliese voorvalle). Dit kan hartaanvalle (miokardiale infarksie), beroerte, bloedklonte in die bene (diepaartrombose) en bloedklonte in die longare tot gevolg hê (pulmonêre embolisme).

As u enige van die bekende risiko faktore om bloedklonte te ontwikkel het, soos indien
- u oorgewig is,
- u bejaard is,
- u diabetes het,
- u bedlêend was vir 'n geruime tyd,
- u nou of reeds probleme met u bloedvate gehad het (vaskulêre siektes of verstopping van 'n vat),
- u nou of reeds probleme met niere gehad het,
- u hoë bloeddruk het,
- u aan enige siekte ly wat bloedverdikking veroorsaak,
- u ly aan 'n verhoogde geneigdheid vir bloedklontvorming (trombofilie).

Vertel asseblief u dokter of gesondheidsorgdeskundige as een of meer van die bogenoemde gevalle op u van toepassing is, voor hoë-dosis onderhuidse behandeling met BERIGLOBIN P.

Die eerste simptome van bloedklont vorming kan die volgende insluit: kortasem, pyn en swelling van 'n ledemaat, ongevoeligheid of swakheid in 'n arm of been of een kant van u gesig, skielike verwarring, moeilike spraak of verstaan asook bors pyn. Kontak asseblief dadelik u dokter, as u enige van hierdie simptome ondervind. Maak asseblief seker dat u genoegsame water ingeneem het voor hoë-dosis onderhuidse behandeling met BERIGLOBIN P.

Moontlike komplikasies kan dikwels vermy word deur te verseker dat:
- u nie sensitief is vir menslike normale immunoglobulien nie. Die produk behoort aanvanklik stadig ingespuit te word. Die aanbevole infusietempo behoort gevolg te word (sien "HOE OM BERIGLOBIN P TE GEBRUIK").
- u versigtig gemonitor word vir enige simptome gedurende die infusieperiode, veral as
  - u menslike normale immunoglobulien vir die eerste keer ontvang,
  - u verander het vanaf 'n alternatiewe produk, of
  - daar 'n lang tussenpose was sedert die vorige infusie.

In hierdie gevalle behoort u gemonitor te word gedurende die eerste infusie en vir die eerste uur daarna. Alle ander pasiënte behoort waargeneem te word vir ten minste 20 minute na toediening.

As 'n allergiese of anafilaktiese reaksie vermoed word, moet die toediening dadelik gestaak word. In geval van skok moet die huidige mediese standaardbehandeling vir skok toegepas word.

Inligting oor die veiligheid ten opsigte van infeksies:
Wanneer medisyne voorberei word uit menslike bloed of plasma word sekere voorsorgmaatreëls in plek gestel om te verhoed dat infeksies oorgedra word aan pasiënte. Hierdie sluit in:
- Versigtige seleksie van bloed- en plasmaskenkers om seker te maak dat dié wat 'n risiko het om infeksies te dra, uitgesluit word, en
- Die toetsing van elke skenking en plasma samevoegings vir tekens van virusse/infeksies.

Vervaardigers van hierdie produkte sluit ook stappe in gedurende die verwerking van die bloed of plasma wat virusse kan inaktiveer of kan verwyder. Ten spyte van hierdie maatreëls, kan die moontlikheid dat infeksies oorgedra kan word tydens toediening van medisyne wat voorberei is van menslike bloed of plasma, nie heeltemal uitgesluit word nie. Dit geld ook vir enige onbekende of nuwe virusse of ander tipes infeksie.
Die maatreëls wat geneem word, word as voldoende beskou vir omhulde virusse soos menslike immuniteitsgebreksvirus (MIV, die VIGS virus) hepatitis B virus en hepatitis C virus (lewer inflammasie), en vir die nie-omhulde hepatitis A virus en parvovirus B19 (Sticker se siekte). Immunoglobuliene is nog nie geassosieer met hepatitis A of parvovirus B19 infeksies nie, moontlik omdat die teenliggame teen hierdie infeksies, wat in die produk vervat is, beskermend is.

Elke keer as u BERIGLOBIN P gebruik behoort u die volgende in u behandelingsdagboek aan te teken:
- die datum van toediening
- die lotnommer van die produk
- die volume wat ingespuit is.

Die gebruik van BERIGLOBIN P met voedsel en drank:
BERIGLOBIN P kan gebruik word sonder om voedsel en drank in ag te neem.

Swangerskap en borsvoeding:
- Vra u dokter of apteker vir advies voordat u enige medisyne neem indien u swanger is of u baba borsvoed.
- Die veiligheid van BERIGLOBIN P vir gebruik in menslike swangerskap is nog nie vasgestel nie.
- Kliniese ondervinding met immunoglobuliene dui daarop dat daar geen skadelike gevolge op die verloop van swangerskap, of op die fetus en die neonaat te verwagte is nie.
- U dokter sal besluit of dit geskik is vir u om BERIGLOBIN P te ontvang indien u swanger is of u baba borsvoed.

Indien u swanger is of u baba borsvoed terwyl u BERIGLOBIN P gebruik raadpleeg asseblief u dokter, apteker of ander gesondheidsorgdeskundige om advies.

Bestuur en gebruik van masjinerie:
BERIGLOBIN P behoort nie 'n invloed te hê op u vermoë om te bestuur of masjinerie te gebruik nie.

Belangrike inligting omtrent sommige van die bestanddele van BERIGLOBIN P:
BERIGLOBIN P bevat tot soveel as 110 mg natrium per dosis (75 kg liggaamsgewig) as die maksimum daaglikse dosis gegee word (11,25 g = 70,3 ml). Hierdie behoort in aanmerking geneem te word indien u op 'n gekontroleerde natrium dieet is.

Gebruik van ander medisynes saam met BERIGLOBIN P:
- Vra asseblief u dokter of apteker vir advies indien u tans of onlangs enige ander medisyne, insluitend inentings of medisyne wat verkry is sonder voorskrif, gebruik het.
- U moet nie hierdie medisinale produk met ander medisinale produkte, oplosmiddels of verdunningsmiddels meng nie.
- Die resultate van sommige bloedtoetse kan beïnvloed word deur BERIGLOBIN P. As u binnekort enige tipe bloedtoetse moet ondergaan, maak seker dat die dokter wat u behandel weet dat u BERIGLOBIN P ontvang.
- Indien u enige ander medisyne op 'n gereelde grondslag gebruik, insluitend komplementêre of tradisionele medisyne, kan die gelyktydige gebruik van BERIGLOBIN P saam met die hierdie medisynes ongewensde interaksies veroorsaak. Raadpleeg asseblief u dokter, apteker of ander gesondheidsorgdeskundige vir advies.

HOE OM BERIGLOBIN P TE GEBRUIK
Gebruik altyd BERIGLOBIN P presies soos u dokter u ingelig het. U moet u dokter of apteker raadpleeg as u onseker is.

Dosis:
Die dosis en intervalle van infusie hang af van die indikasie.

Vervangingsterapie:
Die produk behoort via die onderhuidse roete toegedien te word.
Gebruik altyd BERIGLOBIN P presies soos u dokter u ingelig het. U moet u dokter of apteker raadpleeg indien u onseker is.
U dokter sal die korrekte dosis vir u uitwerk en u gewig en respons op die behandeling in ag neem.
'n Ladingsdosis van ten minste 1,3 tot 3,1 ml/kg liggaamsgewig – verdeel oor verskeie dae – mag nodig wees. Daaropvolgend kan instandhoudingsdosisse toegedien word (tipies weekliks) om 'n kumulatiewe maandelikse dosis van omtrent 2,5 tot 5,0 ml per kg liggaamsgewig te bereik.

Hepatitis A voorkoming:
Die produk moet via die binnespierse roete toegedien word.
- Korttermyn voorkoming in reisigers wat minder as twee weke voor moontlike blootstelling aanmeld:
  Vir 'n verblyf in endemiese gebiede van minder as drie maande, word 'n dosis van 0,003 tot 0,004 g/kg (0,02 ml/kg) liggaamsgewig binnespiers toegedien, aanbeveel.
  BERIGLOBIN P kan in kombinasie met 'n hepatitis A entstof gegee word, maar op verskillende toedieningsareas van die liggaam.
- Hepatitis A voorkoming in persone wat vir minder as twee weke gelede blootgestel was: 0,003 tot 0,004 g/kg (0,02 ml/kg) liggaamsgewig, binnespiers toegedien.

Behandeling van radiogeniese mukositis:
Die produk moet via die binnespierse roete toegedien word.
Aanvanklik 10 ml (1 600 mg), na 2 dae 5 ml (800 mg) en na nog 2 dae weer 5 ml (800 mg).
Die behandeling kan so dikwels as nodig herhaal word.

Toediening:
BERIGLOBIN P is 'n gereed-vir-gebruik oplossing en behoort teen liggaamstemperatuur toegedien te word.
BERIGLOBIN P is 'n helder oplossing. Die kleur kan wissel van kleurloos tot liggeel of ligbruin.
Moet nie oplossings wat troebel is of wat reste (afsaksels/deeltjies) bevat gebruik nie.
Die oplossing moet teen liggaamstemperatuur toegedien te word.
Afhangende van die indikasie moet menslike normale immunoglobulien via die onderhuidse- of binnespierse roetes toegedien word.
Onderhuidse infusie vir tuisbehandeling behoort begin te word deur 'n dokter wat ervare is in die voorligting van pasiënte vir tuisbehandeling.
U sal ingelig word in die gebruik van 'n spuitaandrywer, infusietegnieke, die hou van 'n behandelingsdagboek en die maatreëls wat gevolg moet word in die geval van ernstige ongewenste gebeurtenisse. Binnespierse inspuiting moet deur 'n dokter of verpleegkundige gegee word.
Moet nie binneaars inspuit nie! Let daarop dat daar 'n vergrootte kans van 'n onopsetlike binneaarse inspuiting is by pasiënte wat herhaaldelike binnespierse inspuitings ontvang het.

Onderhuidse toediening:
Onderhuidse infusie vir tuisbehandeling behoort begin en gemonitor te word deur 'n mediese dokter wat ervare is in die behandeling van immuniteitsgebrekke en in die voorligting van pasiënte vir tuisbehandeling. U sal ingelig word in:
- die gebruik van 'n spuitaandrywer,
- die infusietegnieke,
- die hou van 'n behandelingsdagboek en
- maatreëls wat geneem moet word in die geval van ernstige ongewenste gebeurtenisse.

Die aanbevole infusietempo is 22 ml/uur. In 'n kliniese studie met 53 pasiënte wat geëvalueer is, gedurende die opleidingsfase onder die toesig van 'n mediese dokter, is die infusietempo vermeerder van die aanvanklike 10 ml tot 22 ml/uur.
BERIGLOBIN P behoort verkieslik toegedien te word in die buikwand, dy en/of boudspiere. Nie meer as 15 ml behoort ingespuit te word in 'n enkele toedieningsarea nie. Dosisse groter as 15 ml behoort verdeel te word en in 2 of meer toedieningsareas ingespuit word.
U dokter sal u inlig hoe om ongebruikte produk of afval materiaal weg te gooi.

Binnespierse toediening:
Binnespierse inspuiting moet deur 'n mediese dokter of 'n verpleegkundige gegee word.

BERIGLOBIN P behoort verkieslik in die heupspier toegedien word terwyl die pasiënt lê. Wanneer groot dosisse nodig is, word aanbeveel dat dit in verdeelde hoeveelhede toegedien word. Dit is van toepassing in die geval van dosisse meer as 2 ml vir kinders wat tot en met 20 kg weeg en dosisse meer as 5 ml vir pasiënte wat meer as 20 kg weeg.
Enige ongebruikte produk of afval materiaal behoort weggegooi te word in ooreenstemming met die plaaslike voorskrifte.

Indien u onder die indruk is dat die werking van BERIGLOBIN P te sterk of te swak is, praat met u dokter of apteker.

Indien u meer BERIGLOBIN P gebruik as wat u behoort:
Daar is geen bekende simptome van oordosering nie.
In die geval van oordosering raadpleeg u dokter of apteker. Indien nie een beskikbaar is nie, soek hulp by die naaste hospitaal of gifbeheersentrum.

Indien u vergeet om BERIGLOBIN P te gebruik:
Die gevolge van 'n oorgeslane dosis is nie bekend nie.

Gevolge wanneer behandeling met BERIGLOBIN P gestaak word:
U behoort geen effekte te ervaar wanneer behandeling met BERIGLOBIN P gestaak word nie. Raadpleeg asseblief u dokter of apteker voordat behandeling gestaak word.

MOONTLIKE NEWE-EFFEKTE
Soos alle medisynes kan BERIGLOBIN P newe-effekte hê, alhoewel nie almal hulle kry nie. Raadpleeg asseblief dadelik u dokter of gaan dadelik na die Ongevalle Afdeling by u naaste hospitaal indien enige van die gelyste newe-effekte voorkom, of indien u enige newe-effekte opmerk wat nie in hierdie blaadjie gelys is nie.

Die volgende ongewenste effekte is gerapporteer gedurende 'n kliniese studie met onderhuidse toediening:

Lokale reaksies by die inspuitingsarea:
Baie algemeen, m.a.w. meer as 1 uit 10 behandelde persone: Swelling, seerheid, rooiheid, verharding, lokale warm gevoel, jeuk, kneusing of uitslag. Die gereeldheid van hierdie lokale reaksies het baie vinnig afgeneem binne die eerste tien infusies, toe pasiënte gewoond geraak het aan hierdie vorm van behandeling.

Immuunsisteem versteurings:
In enkele gevalle, m.a.w. minder as 1 uit of 10 000 behandelde persone: Allergiese reaksies insluitend bloeddruk daling.

Algemene reaksies:
In enkele gevalle, m.a.w. minder as 1 uit of 10 000 behandelde persone: bv. Kouekoors, koors, hoofpyn, algemene siek gevoel, matige rugpyn, bewusteloosheid, lighoofdigheid, uitslag, aamborstigheid.

Aanvullend tot die reaksies wat waargeneem is gedurende kliniese studies is die volgende ongewenste reaksies gerapporteer nadat die produk op die mark gesit is:

Immuunsisteem versteurings:
Allergiese/anafilaktiese reaksies insluitend moeilike asemhaling en vel reaksies. In geïsoleerde gevalle kan hierdie reaksies lei tot 'n ernstige allergiese reaksie (anafilaktiese skok). Hierdie kan gebeur selfs al het u vorige toedienings van BERIGLOBIN P of 'n soortgelyke produk goed verdra.

Algemene reaksies:
Algemene reaksies wat die hele liggaam betrek, bv. Naarheid, braking, gewrigspyn.

Hart en vaskulêre versteurings:
Bloedsomloop versteurings veral wanneer die produk per ongeluk in 'n bloedvat ingespuit is.

Met die onderhuidse gebruik van hoë dosisse van immunoglobuliene vir vervangingsterapie (bv. primêre immuniteitsgebreksindroom) en vir vaskulêre siektes: Vorming van ongewenste bloedklonte (arteriële en veneuse trombo-emboliese gebeurtenisse) is gerapporteer. Simptome van hierdie kan insluit:
- ernstige borspyn of drukking op die bors (hartaanval)
- swakheid, verlamming of ongevoeligheid aan die een kant van die liggaam, sigsverlies in een of albei oë, moeilike spraak (beroerte)
- hoes, borspyn, vinnige asemhaling, vinnige hart klop (pulmonêre embolisme)
- swelling, pyn, rooiheid van die been (diepaartrombose)

Nie alle newe-effekte gerapporteer vir hierdie medisyne is ingesluit in hierdie blaadjie nie. Indien u algemene gesondheid verswak terwyl u hierdie medisyne neem, raadpleeg asseblief u doktor, apteker of ander gesondheidsorgdeskundige vir advies.

BERGINGSINSTRUKSIES
Moet nie BERIGLOBIN P gebruik na die vervaldatum wat op die etiket en karton aangebring is nie.
- Bewaar in 'n yskas (+2 °C tot +8 °C) en hou die houer in die buitenste karton om dit teen lig te beskerm. Moet nie vries nie!
- Die produk moet visueel ondersoek word voor toediening en moet nie gebruik word indien daar enige afwyking is in die fisiese voorkoms nie (sien onder "AANBIEDING VAN BERIGLOBIN P" en "IDENTIFIKASIE VAN BERIGLOBIN P"
- Sodra 'n houer oopgemaak is moet die inhoud dadelik gebruik word.
- Hou alle medisyne buite die bereik en sig van kinders.
- Neem alle ongebruikte medisyne terug na u apteker toe.

AANBIEDINGE VAN BERIGLOBIN® P
Beriglobin® P 2 ml: 'n Enkel dosis 2 ml helder glas ampule verpak in 'n karton.
Beriglobin® P 2 ml: 'n Enkel dosis 2 ml voorafgevulde spuit verpak in 'n karton.
Beriglobin® P 5 ml: 'n Enkel dosis 5 ml helder glas ampule verpak in 'n karton.
Beriglobin® P 5 ml: 'n Enkel dosis 5 ml voorafgevulde spuit verpak in 'n karton.

IDENTIFIKASIE VAN BERIGLOBIN® P
Beriglobin® P is 'n helder, kleurlose tot liggeel tot ligbruin oplossing.

REGISTRASIENOMMERS / VERWYSINGSNOMMERS
Beriglobin® P 2 ml:
T/30.2/608
11/30.2/0037 (Namibië)

Beriglobin® P 5 ml:
T/30.2/609
11/30.2/0038 (Namibië)

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DATUM VAN PUBLIKASIE VAN HIERDIE PASIËNT INLIGTINGSBLAD
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® – **Beriglobin® P** is 'n geregistreerde handelsmerk van CSL Behring.

[1]Maatskappyregistrasienommer: 2008/008787/07

BER/PIL/01/05.2018

CSL Behring

SKEDULERINGSTATUS S4

NS2 (Namibië)

EIENDOMSNAME EN DOSEERVORM

Beriglobin® P 2 ml.

Oplossing vir inspuiting vir subkutane of intramuskulêre toediening.

Beriglobin® P 5 ml.

Oplossing vir inspuiting vir subkutane of intramuskulêre toediening.

SAMESTELLING
1 ml bevat:
Menslike proteïen 160,0 mg
waarvan immunoglobulien G ten minste 95 %
Verspreiding van IgG subklasse:
IgG_1 ongeveer 61 %
IgG_2 ongeveer 28 %
IgG_3 ongeveer 5 %
IgG_4 ongeveer 6 %
IgA maks. 1,7 mg/ml
Teenliggame teen hepatitis A virus ten minste 100 IU.

Ander bestanddele:
Aminoasynsuur (glisien); natriumchloried; HCl of NaOH (in klein hoeveelhede vir pH aanpassings); water vir inspuiting.

FARMAKOLOGIESE KLASSIFIKASIE
A.30.1 Biologiese middels – Teenliggame.

FARMAKOLOGIESE WERKING
Farmakodinamiese eienskappe:
Normale menslike immunoglobulien bevat hoofsaaklik immunoglobulien G (IgG) wat 'n breë spektrum teenliggame teen verskeie aansteeklike agente bevat. BERIGLOBIN P bevat die immunoglobulien G teenliggame wat voorkom in die gesonde bevolking. Dit word gewoonlik voorberei vanuit 'n plasmasamestelling van ten minste 1 000 skenkers. Dit het 'n verspreiding van immunoglobulien G subklasse wat nou ooreenstem met die wat in natuurlike menslike plasma voorkom. Genoegsame dosisse van hierdie medisinale produk kan abnormaal lae immunoglobulien G vlakke herstel tot binne die normale grense.

Farmakokinetiese eienskappe:
Met subkutane toediening van normale menslike immunoglobulien, word piekvlakke in die pasiënt se bloedsomloop bereik na ongeveer 2 dae.
Data verkry uit 'n kliniese studie (n = 60) wys dat trogvlakke van omtrent 8 tot 9 g/l (n = 53) in die plasma in stand gehou kan word deur weeklikse dosisse van tussen 0,05 en 0,15 g (0,3 tot 0,9 ml) BERIGLOBIN P per kg liggaamsgewig. Dit is gelykstaande aan 'n maandelikse kumulatiewe dosis van 0,2 tot 0,6 g per kg liggaamsgewig.
Met intramuskulêre toediening is BERIGLOBIN P biobeskikbaar in die pasiënt se bloedsomloop na 'n vertraging van omtrent 2 tot 3 dae.
IgG en IgG-komplekse word afgebreek in die selle van die retikuloëndoteliale sisteem.

INDIKASIES
Vervangingsterapie in volwassenes en kinders in primêre immuunontoereikendheid sindroom soos bv.:
- Aangebore agammaglobulinemie en hipogammaglobulinemie, insluitend die wat deur behandeling veroorsaak is.
- Algemene veranderlike immuunontoereikendheid.
- Ernstige gekombineerde immuunontoereikendheid.
- IgG subklas-ontoereikendheid met herhalende infeksies.

Vervangingsterapie in myeloom of kroniese limfositiese leukemie met ernstige sekondêre hipogammaglobulinemie en herhalende infeksies.

Hepatitis A voorkoming:
- In reisigers wat minder as twee weke voor moontlike blootstelling aanmeld, verkieslik in kombinasie met inenting.
  Vir langtermyn hepatitis A voorkoming word aktiewe immunisasie aanbeveel.
- In persone wat minder as 2 weke gelede blootgestel is.

Behandeling van radiogeniese mukositis

KONTRA-INDIKASIES
Hipersensitiwiteit vir enige van die bestanddele van die produk.
BERIGLOBIN P moet nie intramuskulêr toegedien word in gevalle van afwykings van hemostase nie.

WAARSKUWINGS
Moet nie intravaskulêr inspuit nie!
Indien BERIGLOBIN P per ongeluk in 'n bloedvat toegedien word, kan die pasiënt skok of 'n trombo-emboliese gebeurtenis ontwikkel. Tydens intramuskulêre toediening word dit aanbeveel dat daar deur opsuiging seker gemaak word dat geen vat binnegedring is nie.
Die aanbevole infusie tempo onder "DOSIS EN GEBRUIKSAANWYSINGS" moet gevolg word.

INTERAKSIES
Lewendige verswakte virus entstof:
Immunoglobulien toediening mag die doeltreffendheid van lewende verswakte virus entstowwe soos masels, Duitse masels, pampoentjies en waterpokkies vir 'n periode van ten minste ses weke tot drie maande belemmer.
Na BERIGLOBIN P toediening moet 'n tussenpose van ten minste drie maande verby gaan voor inenting met lewende verswakte virus entstowwe. In die geval van masels kan die belemmering van doeltreffendheid vir een jaar duur, daarom moet pasiënte wat masels inentings ontvang hulle teenliggaamstatus laat nagaan.

Steurings met serologiese toetsing:
Wanneer serologiese toetsuitslae interpreteer word, moet dit in ag geneem word dat die verbygaande verhoging van teenliggame wat passief oorgedra is na immunoglobulien inspuiting, positiewe toetsresultate tot gevolg kan hê.
Passiewe oordrag van teenliggame tot rooibloedsel antigene bv. A, B en D kan sekere serologiese toetse vir rooibloedsel allo-teenliggame (bv. Coombs toets), retikulosiet telling en haptoglobin beïnvloed.

SWANGERSKAP EN LAKTASIE
Daar is geen gekontroleerde kliniese proewe gedoen op die gebruik in menslike swangerskap nie. Daarom moet die toediening van hierdie medisinale produk aan swanger vroue en borsvoedende moeders versigtig oorweeg word.
Langdurige kliniese ondervinding met immunoglobuliene dui daarop dat geen nadelige effekte op die verloop van swangerskap of op die fetus en die pasgebore baba verwag word nie.

DOSIS EN GEBRUIKSAANWYSINGS
Dosis:
Die dosis en tussenposes van infusie hang van die indikasie af.

Vervangingsterapie:
Die produk behoort via die subkutane roete toegedien te word.
Dit mag nodig wees om die dosis te individualiseer vir elke pasiënt afhangende van die farmakokinetiese en kliniese reaksie. Die volgende doseringsregimen is 'n basiese riglyn:
Die doseringsregimen vir subkutane toediening behoort 'n standhoudende vlak van IgG te verkry. 'n Ladingsdosis van ten minste 0,2 tot 0,5 g/kg (1,3 tot 3,1 ml/kg) liggaamsgewig mag nodig wees – verdeel oor 'n paar dae met 'n maksimale daaglikse dosis van 0,1 tot 0,15 g/kg liggaamsgewig en soos voorgeskryf deur die behandelende dokter.
Nadat konstante IgG vlakke verkry is, moet instandhoudingsdosisse toegedien word met herhaalde tussenposes, verkieslik weekliks, om 'n kumulatiewe maandelikse dosis in die orde van 0,4 tot 0,8 g/kg (2,5 tot 5,0 ml/kg) liggaamsgewig te bereik.
Trogvlakke moet bepaal word om die dosis en tussenposes tussen dosisse aan te pas.

Hepatitis A voorkoming:
Die produk moet via die intramuskulêre roete toegedien word.
- Kort-termyn voorkoming in reisigers wat minder as twee weke voor moontlike blootstelling aanmeld:
  Vir 'n verblyf in 'n endemiese gebied van minder as drie maande, word 'n dosis van 0,003 tot 0,004 g/kg (0,02 ml/kg) liggaamsgewig intramuskulêr toegedien aanbeveel.
  BERIGLOBIN P kan in kombinasie met 'n hepatitis A entstof toegedien word, maar op verskillende toedieningsareas van die liggaam.
- Hepatitis A voorkoming in pasiënte wat vir minder as twee weke blootgestel was: 0,003 tot 0,004 g/kg (0,02 ml/kg) liggaamsgewig intramuskulêr toegedien.

Behandeling van radiogeniese mukositis:
Die produk moet via die intramuskulêre roete toegedien word.
Aanvanklik 10 ml (1 600 mg), na 2 dae 5 ml (800 mg) en na nog 2 dae weer 5 ml (800 mg).
Die behandeling kan so dikwels as nodig herhaal word.

Toediening:
BERIGLOBIN P is 'n gereed-vir-gebruik oplossing en behoort teen liggaamstemperatuur toegedien te word.
BERIGLOBIN P is 'n helder oplossing. Die kleur kan wissel van kleurloos tot liggeel tot by ligbruin.
Moet nie oplossings wat troebel is of wat afsaksels/partikels bevat gebruik nie.
Die produk moet met die oog ondersoek word voor toediening en moet nie gebruik word as daar enige afwyking in die fisiese voorkoms is nie.

Metode van toediening:
Afhangende van die indikasie moet BERIGLOBIN P subkutaan of intramuskulêr toegedien word.

Subkutane toediening:
Subkutane infusie moet deur 'n mediese dokter, wat ondervinding het in die behandeling van immuunontoereikendheid en in die voorligting van pasiënte wat tuisbehandeling ondergaan, begin en gemonitor word. Die pasiënt sal ingelig word in die gebruik van 'n spuitaandrywer, die infusiemetodes, die hou van 'n behandelingsdagboek en die maatreëls wat gevolg moet word in die geval van ernstige ongewenste gebeurtenisse. Die aanbevole infusietempo is 22 ml/uur. In 'n kliniese studie met 53 pasiënte wat geevalueer is, gedurende die opleidingsfase onder die toesig van 'n mediese dokter, is die infusietempo vermeerder van aanvanklik 10 ml tot 22 ml/uur.
Moet nie intravaskulêr inspuit nie! Let daarop dat daar 'n vergrote kans van 'n onopsetlike intravaskulêre toediening is by pasiënte wat reeds herhaalde intramuskulêre inspuitings ontvang het.
Die produk moet verkieslik toegedien word in die buikwand, dy en/of boudspier. Nie meer as 15 ml moet ingespuit word in 'n enkele toedieningsarea nie. Dosisse meer as 15 ml moet verdeel word en in 2 of meer toedieningsareas ingespuit word.

Intramuskulêre toediening:
Intramuskulêre inspuiting moet deur 'n mediese dokter of 'n verpleegkundige toegedien word. Die produk moet verkieslik ventrogluteaal toegedien word terwyl die pasiënt lê. Indien groter dosisse benodig word, word aanbeveel dat dit in verdeelde hoeveelhede toegedien word. Hierdie is van toepassing in die geval van dosisse meer as 2 ml vir pasiënte met 'n liggaamsgewig van tot en met 20 kg en dosisse meer as 5 ml vir pasiënte met 'n liggaamsgewig van meer as 20 kg.
Moet nie intravaskulêr inspuit nie! Let daarop dat daar 'n verhoogde kans van 'n onopsetlike intravaskulêre inspuiting is by pasiënte wat herhaaldelike intramuskulêre inspuitings ontvang het.

Enige ongebruikte produk of afval materiaal moet weggegooi word in ooreenstemming met die plaaslike voorskrifte.

NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS
In 'n kliniese studie met subkutane toediening in 60 pasiënte is die volgende ongewenste effekte aangemeld.
Die volgende standaard kategorieë van frekwensies word gebruik:

Baie algemeen	> 1/10
Algemeen	> 1/100 en < 1/10
Buitengewoon	> 1/1 000 en <1/100
Seldsaam	> 1/10 000 en < 1/1 000
Baie seldsaam	< 1/10 000(insluitend aangemelde enkele gevalle)

Liggaam as 'n geheel – algemene steurings:
Seldsaam: In enkele gevalle: Algemene reaksies soos kouekoors, koors, hoofpyn, ongesteldheid, matige rugpyn, sinkopee, duiseligheid, uitslag, brongospasma. Allergiese reaksies insluitend 'n daling in bloeddruk.

Toediening-area steurings:
Baie algemeen: Swelling, gevoeligheid, rooiheid, verharding, lokale hitte, jeuk, kneusing of uitslag.
Die frekwensie het baie vinnig afgeneem binne die eerste tien infusies toe pasiënte gewoond geraak het aan die subkutane behandelingsvorm. (By studiepasiënte wat behandel was met subkutane immunoglobulien vir jare voor die studie begin het, is geen toedieningsarea steurings aangemeld nie.)

Ongewenste reaksies wat na registrasie aangemeld is, is soortgelyk aan die reaksies wat ook gedurende kliniese studies waargeneem is. Daarbenewens is die volgende ook aangemeld na registrasie:

Kardiovaskulêre steurings, algemeen:
Buitengewoon: Kardiovaskulêre steurings veral indien die produk onopsetlik intravaskulêr toegedien was.

Vaskulêre (nie-kardiale) steurings:
Buitengewoon: Vaskulêre versteurings wat verband hou met subkutane vervangingsterapie: Pasiënte wat subkutane behandeling met hoë dosisse immunoglobulien vir vervangingsterapie ontvang het (bv. primêre immuunontoereikendheid sindroom) het aangemeld dat hulle arteriële en veneuse trombo-emboliese gebeurtenisse gehad het insluitend miokardiale infarksie, beroerte, diep veneuse trombose en pulmonêre embolisme.

Liggaam as 'n geheel – algemene steurings:
Buitengewoon: Allergiese/anafilaktiese reaksies insluitend dispnee, velreaksies, in geïsoleerde gevalle kan tot anafilaktiese skok voorkom, selfs wanneer die pasiënt geen hipersensitiwiteit getoon het met vorige toedienings nie. Algemene versteurings soos naarheid, braking en artralgie.

Spesiale voorsorgmaatreëls:
Moet nie intravaskulêr inspuit nie! As BERIGLOBIN P per ongeluk in 'n bloedvat toegedien word kan pasiënte skok ontwikkel. Tydens intramuskulêre toediening word dit aanbeveel dat daar deur opsuiging seker gemaak word dat geen vat binnegedring is nie.
Die aanbevole infusietempo aangegee onder "DOSIS EN GEBRUIKSAANWYSINGS" moet gevolg word. Pasiënte moet goed gemonitor en versigtig waargeneem word vir enige ongewenste gebeurtenis gedurende die infusieperiode.
Sekere ongewenste reaksies kan meer dikwels voorkom in pasiënte wat menslike normale immunoglobulien vir die eerste keer ontvang, of, in seldsame gevalle, wanneer die produk verander word of wanneer die behandeling gestaak was vir meer as agt weke.
Ware hipersensitiwiteitsreaksies kom selde voor. Dit kom net voor in baie seldsame gevalle van IgA ontoereikendheid met anti-IgA teenliggame en hierdie pasiënte moet met versigtigheid behandel word.

In seldsame gevalle kan BERIGLOBIN P 'n daling in bloeddruk met anafilaktiese reaksies veroorsaak, selfs in pasiënte wat vorige toedienings van menslike normale immunoglobulien verdra het.

Moontlike komplikasies kan gewoonlik vermy word deur te verseker dat:
- pasiënte nie 'n sensitiwiteit vir BERIGLOBIN P het nie, deur eers die produk stadig in te spuit (sien ook "DOSIS EN GEBRUIKSAANWYSINGS").
- pasiënte versigtig gemonitor word vir enige simptome gedurende die infusieperiode.

In die besonder behoort pasiënte gedurende die eerste infusie en vir die eerste uur daarna gemonitor word om enige potensiële ongewenste reaksies in die volgende gevalle waar te neem:
- pasiënte wat nog nooit normale menslike immunoglobulien ontvang het nie
- pasiënte wat van 'n alternatiewe produk verander is, of
- pasiënte waar daar 'n lang tussenpose sedert die vorige infusie was.

Alle ander pasiënte behoort ten minste 20 minute waargeneem te word na toediening. Indien daar 'n vermoede is van 'n allergiese of anafilaktiese reaksie moet die toediening onmiddellik gestaak word. In die geval van skok moet die huidige mediese standaardbehandeling vir skok toegepas word.

Trombo-emboliese gebeurtenisse wat verband hou met subkutane vervangingsterapie:
Daar is 'n verband tussen arteriële en veneuse trombo-emboliese gebeurtenisse insluitend miokardiale infarksie, beroerte, diep veneuse trombose en pulmonêre embolisme wanneer hoë dosisse immunoglobulien vir vervangingsterapie (bv. primêre immuunontoereikendheid sindroom) subkutaan toegedien word. BERIGLOBIN P vir subkutane vervangingsterapie moet met versigtigheid voorgeskryf word by pasiënte met vooraf bestaande risiko faktore vir trombotiese gebeurtenisse (soos gevorderde ouderdom, hipertensie, diabetes mellitus en 'n geskiedenis van vaskulêre siekte of trombotiese episodes, pasiënte met verworwe of oorgeërfde trombofiliese afwykings, pasiënte wat vir verlengde tydperke onbeweeglik was, pasiënte met ernstige hipovolemie, pasiënte met siektes wat bloed viskositeit verhoog). Hierdie pasiënte moet eers ingelig word aangaande die eerste simptome van trombo-emboliese gebeurtenisse insluitend kortasem, pyn of swelling van 'n liggaamsdeel, senuweeversteurings in spesifieke liggaamsdele en borspyn en moet aangeraai word om hulle dokter dadelik te kontak sodra enige van die simptome 'n aanvang neem. Sulke pasiënte moet genoegsaam gehidreer word voordat BERIGLOBIN P gebruik word.

Belangrike inligting omtrent sekere bestanddele van BERIGLOBIN P:
Die produk bevat tot soveel as 110 mg natrium per dosis (75 kg liggaamsgewig) as die maksimum daaglikse dosis (11,25 g = 70,3 ml) toegedien word. Die natriuminhoud moet oorweeg word by pasiënte wat op 'n gekontroleerde natrium dieet is.

Virus veiligheid:
Standaard maatreëls vir die voorkoming van infeksies veroorsaak deur die gebruik van medisinale produkte wat uit menslike bloed of plasma voorberei is, sluit in die seleksie van skenkers, toetsing van individuele skenkings en plasma-poele vir spesifieke merkers van infeksie en die insluiting van effektiewe vervaardigingstappe vir die inaktivering/verwydering van virusse. Ten spyte hiervan kan die moontlike oordrag van besmetlike agente nie heeltemal uitgesluit word wanneer medisinale produkte wat voorberei is uit menslike bloed of plasma toegedien word nie. Dit is ook van toepassing op onbekende of nuwe virusse en ander patogene.
Die toegepaste maatreëls word as voldoende beskou vir omhulde virusse soos MIV, HBV en HCV, en vir die nie-omhulde virusse HAV en parvovirus B19.
Uit kliniese ondervinding is dit gerusstellend dat daar geen hepatitis A of parvovirus B19 oordrag was deur immunoglobulien toediening nie en dit word ook aanvaar dat die teenliggaaminhoud 'n belangrike rol speel in die virus veiligheid.
In die belang van pasiënte word dit sterk aanbeveel dat elke keer wanneer BERIGLOBIN P toegedien word, die naam en lotnommer van die produk aangeteken word, sodat daar 'n verband behou kan word tussen die pasiënt en die lot van die produk.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN
Daar is geen bekende simptome van oordosering nie.

IDENTIFIKASIE
Oplossing vir inspuiting vir subkutane of intramuskulêre toediening.
Beriglobin® P is 'n helder oplossing. Die kleur kan varieer van kleurloos tot liggeel tot ligbruin oplossing gedurende die rakleeftyd.

AANBIEDINGE
Beriglobin® P 2 ml: 'n Enkel dosis 2 ml helder glas ampule verpak in 'n karton.
Beriglobin® P 2 ml: 'n Enkel dosis 2 ml voorafgevulde spuit verpak in 'n karton.
Beriglobin® P 5 ml: 'n Enkel dosis 5 ml helder glas ampule verpak in 'n karton.
Beriglobin® P 5 ml: 'n Enkel dosis 5 ml voorafgevulde spuit verpak in 'n karton.

BERGINGSINSTRUKSIES
Berg in 'n yskas teen 5 °C ± 3 °C in die karton om dit te beskerm teen lig.
Moet nie vries nie!
HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMERS
Beriglobin® P 2 ml:
T/30.2/608
11/30.2/0037 (Namibië)

Beriglobin® P 5 ml:
T/30.2/609
11/30.2/0038 (Namibië)

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Die datum van die mees onlangs hersiene voubiljet soos deur die Raad goedgekeur: 15 Oktober 2012.

® – **Beriglobin® P** is 'n geregistreerde handelsmerk van CSL Behring.

[1]Maatskappyregistrasienommer: 2008/008787/07

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