INTERNATIONAL DATA SHEET (INTERNATIONAL, ENGLISH)

BERIRAB® P

HUMAN RABIES IMMUNOGLOBULIN

VERSION: 1.0

REVISION DATE: 18-NOV-2014

REASON FOR CHANGE: Deletion of ampoules.

Text Convention:

grey-shaded text: Contains explanatory notes, instructions or definition not to be implemented into any labelling

INTERNATIONAL DATA SHEET

1. NAME OF THE MEDICINAL PRODUCT

Berirab® P
Solution for injection for intramuscular use

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient: Human rabies immunoglobulin

1 ml solution contains:

human protein	100 - 170 mg
thereof immunoglobulins	at least 95 %
with antibodies to rabies virus	at least 150 IU

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for injection for intramuscular use
Berirab P is a clear solution. The colour can vary from colourless to pale-yellow up to light-brown during shelf life.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Post-exposure prophylaxis of rabies infection after

- exposure to scratches, bites or other injuries caused by a suspected rabid animal
- mucous membrane contamination with infectious tissue or saliva of a suspected rabid animal
- contact of mucous membranes or newly skin injury with rabies live attenuated vaccine e.g. vaccination baits.

Human rabies immunoglobulin must always be used in combination with a rabies vaccine.

National and/or WHO guidelines regarding protection against rabies should be observed.

4.2 Posology and method of administration

Posology
Post-exposure prophylaxis consists of a regimen of one dose of immunoglobulin and full courses of rabies vaccination. Rabies immunoglobulin and the first dose of rabies vaccine should be given as soon as possible after exposure. Additional doses of rabies vaccine should be given according to official guidelines or the manufacturer's instruction.

Rabies prophylaxis exclusively with simultaneous vaccination: recommended dose of rabies immunoglobulin is 20 IU Berirab P per kg body weight (bw).

Because of the risk of interference with antibody production related to vaccination, neither the dose should be increased nor repeat rabies immunoglobulin be given even if the onset of the simultaneous prophylaxis is delayed.

Method of administration
Human rabies immunoglobulin should be administered via the intramuscular route.
See section 6.6 "Special precautions for disposal and other handling" for further information regarding method of administration.

Of the total quantity of rabies immunoglobulin, as much as possible should be instilled deeply into and around the wound. The remainder is to be injected i.m. preferably into the vastus lateralis muscle with the patient lying down.

If comparatively large total volumes are required, it is advisable to administer them in divided doses at different sites. This applies in the case of doses above 2 ml for children up to 20 kg bw and doses above 5 ml for persons above 20 kg bw.

In case of simultaneous prophylaxis the immunoglobulin and the vaccine should be administered at contralateral sites of the body.

The immunoprophylaxis should be carried out immediately even in case that suspicion is not clarified if the animal was infected. Wounds should not be primarily sewed. Parts of the body that are possibly contaminated and all wounds are to be cleaned immediately with soap or detergent, washed well with water and treated with 70% alcohol or iodine tincture; this is also true for contamination with vaccine solution from vaccination baits.

In the presence of a coagulation disorder, in the case of which intramuscular injections are contraindicated, Berirab P may be given subcutaneously. Afterwards the injection site should be compressed with a swab.

However, it should be noted that there are no clinical efficacy data to support administration by the subcutaneous route.

4.3 Contraindications

Because of the life-threatening risk due to rabies, there are no contraindications to the administration of rabies immunoglobulin.

4.4 Special warnings and precautions for use

Ensure that Berirab P is not administered into a blood vessel because of the risk of shock.

True hypersensitivity reactions are rare. Berirab P contains a small quantity of IgA. Individuals who are deficient in IgA have the potential for developing IgA antibodies and may have anaphylactic reactions after administration of blood components containing IgA.

Rarely human rabies immunoglobulin can induce a fall in blood pressure with anaphylactic reactions, even in patients who had tolerated previous treatment with human immunoglobulin.
Therapeutic measures depend on the nature and severity of the event. The current medical standards for shock treatment are to be observed.

Patients should be observed for at least 20 minutes after administration of Berirab P. Particularly in cases of inadvertent i.v. injection, patients should be observed for longer term (at least 1 hour) after administration.

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 viral safety.
It is strongly recommended that every time that Berirab P is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.

4.5 Interactions with other medicinal products and other forms of interactions

Vaccinations with live attenuated virus vaccines
Immunoglobulin administration may impair the efficacy of live attenuated virus vaccines such as measles, rubella, mumps and varicella vaccines for a period of up to three months. After administration of Berirab P an interval of at least three months should elapse before vaccination with live attenuated virus vaccines. In the case of measles, this impairment may persist for up to four months. Therefore, patients receiving measles vaccine 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 misleading 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).

4.6 Pregnancy and lactation

The safety of Berirab P for use in human pregnancy has not been established in controlled clinical trials. Long lasting clinical experience with immunoglobulins does indicate that no harmful effects on the course of pregnancy, on the foetus or the neonate are to be expected.

4.7 Effects on ability to drive and use machines

No effects on the ability to drive and use machines have been observed.

4.8 Undesirable effects

In rare cases the following adverse reactions may occur:

- allergic reactions including fall in blood pressure, dyspnoea, cutaneous reactions, in isolated cases reaching as far as anaphylactic shock, even when the patient has shown no hypersensitivity to previous administration of immunoglobulins.
- generalized reactions such as chills, fever, headache, malaise, nausea, vomiting, arthralgia and moderate back pain.
- cardiovascular reactions particularly if the product is inadvertently injected intravascularly.

Local reactions
At the injection site local pain, tenderness or swelling can be observed in rare cases.

For safety with respect to transmissible agents, see section 4.4 “Special warnings and precautions for use”.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions.

4.9 Overdose

Consequences of an overdose are not known. Nevertheless, the dose should never be raised (interference with antibody production related to vaccination, see section 4.2 "Posology and method of administration").

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group*:* immune sera and immunoglobulins, human rabies immunoglobulin, ATC-code: J06B B05
Berirab P contains mainly immunoglobulin G (IgG) with a specifically high content of antibodies against rabies virus.

5.2 Pharmacokinetic properties

Human rabies immunoglobulin for intramuscular administration is bioavailable in the recipient's circulation after a delay of 2 to 3 days.

Human rabies immunoglobulin has a half-life of about 3 to 4 weeks. This half-life may vary from patient to patient.

IgG and IgG-complexes are broken down in cells of the reticuloendothelial system.

5.3 Preclinical safety data

Berirab P contains rabies immunoglobulin as active ingredient which is derived from human plasma and acts like endogenous constituent of plasma. Single dose i.m. application of immunoglobulin to various animal species did not reveal toxic effects.
Preclinical studies with repeated dose applications (chronic toxicity, cancerogenicity and mutagenicity) cannot be reasonably performed in conventional animal models due to the development of antibodies following the application of heterologous human proteins.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

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

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products, diluents or solvents.

6.3 Shelf life

3 years
Berirab P must not be used after the expiry date given on the pack and container.
Once the container has been opened the contents have to be used immediately.

6.4 Special precautions for storage

Berirab P is to be stored at +2 °C to +8 °C (refrigerator). Do not freeze!
Keep container in the outer carton in order to protect its contents from light.

Keep out of the reach and sight of children!

6.5 Nature and contents of container

Immediate containers
SCF syringes of colourless glass (Type I, Ph. Eur.)

Presentations
Pack of 1 prefilled syringe with 2 ml containing at least 300 IU of rabies antibodies
Pack of 1 prefilled syringe with 5 ml containing at least 750 IU of rabies antibodies

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Do not use solutions which are cloudy or contain residues (deposits/particles).
Berirab P is ready for use and should be administered at body temperature.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

CSL Behring GmbH

Emil-von-Behring-Str. 76
35041 Marburg
Germany

8. MARKETING AUTHORISATION NUMBER

– country specific –

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

– country specific –

10. DATE OF REVISION OF THE TEXT

November 2014

HISTORY OF REVISIONS

Version No.	Revision Date	Reason for Change
1.0	18-NOV-2014	Deletion of ampoules