SUMMARY OF PRODUCT CHARACTERISTICS

NAME OF THE MEDICINAL PRODUCT:

Rabies Antiserum 1000 I.U. I.H.S. (5mL, Liquid vial)

COMPOSITION:

Each vial contains;

Equine rabies immunoglobulin fragments not less than 1000 I.U.

Preservative	:	Cresol B.P. ≤ 0.25%v/v
Excipient	:	Sodium chloride B.P.
Stabilizer	:	Glycine B.P.
Vehicle	:	Water for injection B.P.

PHARMACEUTICAL DOSAGE FORM:

Solution for injection.

THERAPEUTIC INDICATIONS:

Rabies Antiserum is indicated in rabies post-exposure prophylaxis in subjects suspected to have been exposed to the rabies virus, particularly in case of severe exposure (see Dosage & Administration).

According to the recommendations of the WHO expert consultation on rabies, Rabies Antiserum must always be used in association with a rabies vaccine. The only exception is for patients already immunised with a rabies vaccine and who are able to produce documentation confirming vaccination with a cell-culture vaccine (i.e. full pre-exposure vaccination within the previous year, subsequent booster injection within the 5 previous years or full post-exposure prophylaxis). These people may receive the vaccine alone.

Administration must always be performed under medical supervision (according to local recommendations).

The drug can be safe with the use of antibiotics and tetanus toxoid.

POSOLOGY AND METHOD OF ADMINISTRATION:

Treatment must be adapted according to the type of contact (see table) and the subject's immune status.

The table is a guide for post-exposure prophylaxis based on WHO report TRS 1012, 2018.

Recommended post-exposure prophylaxis according to type of exposure.

Category of exposure	**Type of exposure to a domestic or wild animal suspected or confirmed to be rabid or animal unavailable for testing**	**Recommended post-exposure prophylaxis**
I	Touching or feeding animals, licks on intact skin (no exposure)	None, if reliable case history is available[a]
II	Nibbling of uncovered skin Minor scratches or abrasions without bleeding (exposure).	Administer vaccine immediately Stop treatment if animal remains healthy throughout an observation period of 10 days[b] or is proven to be negative for rabies by a reliable laboratory using appropriate diagnostic techniques. Treat as category III if bat exposure involved.
III	Single or multiple transdermal[c] bites or scratches, contamination of mucous membrane or broken skin with saliva from animal licks, exposures due to direct contact with bats (severe exposure).	Administer rabies vaccine immediately, and rabies immunoglobulin, preferably as soon as possible after initiation of postexposure prophylaxis. Rabies immunoglobulin can be injected up to 7 days after administration of first vaccine dose.

		Stop treatment if animal remains healthy throughout an observation period of 10 days or is proven to be negative for rabies by a reliable laboratory using appropriate diagnostic techniques.

[a] If an apparently healthy dog or cat in or from a low-risk area is placed under observation, treatment may be delayed.

[b] This observation period applies only to dogs and cats. Except for threatened or endangered species, other domestic and wild animals suspected of being rabid should be euthanized and their tissues examined for the presence of rabies antigen by appropriate laboratory techniques.

[c] Bites especially on the head, neck, face, hands and genitals are category III exposures because of the rich innervation of these areas.

For post-exposure prevention of rabies, treatment associating the equine rabies immunoglobulin with the rabies vaccine is recommended, although experience indicates that vaccine alone could be sufficient for minor exposure (category II).

Prompt and local treatment of all bite or scratch wounds is very important and must be performed immediately following the bite or the scratch.

First-aid recommendations include immediate and thorough flushing out and washing of the wound for 15 minutes with water and soap, detergent, povidone iodine or any other substance with a proven destructive action on the rabies virus. If no soap or antiviral agents are available, the wound should be thoroughly and extensively washed with water.

Rabies Antiserum should be injected as soon as possible after exposure.
The recommended dose is 40 IU/kg of body weight in adults and children.
The dose calculation is based on a product concentration of 200-IU/mL in the vial.
In the case of multiple wounds, the volume of the calculated dose of the equine rabies immunoglobulin may not be sufficient to infiltrate all wounds. In these circumstances, the recommended dose of Rabies Antiserum may be diluted with physiological saline to obtain a sufficient volume to be able to infiltrate all wounds.

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

Administration: Infiltration around and into the wounds.

The entire immunoglobulin dose, or as much as anatomically possible (but avoiding possible compartment syndrome), should be infiltrated carefully into or as close as possible to the wound(s) or exposure sites.

If, however, there is a high likelihood that there are additional small wounds (e.g. if a child does not report all wounds), exposure was to bats or exposure was other than through a bite, injection of the remaining RIG volume intramuscularly as close as possible to the presumed exposure site, to the degree that is anatomically feasible, is indicated.

RIG is administered only once, preferably at or as soon as possible after initiation of post-exposure vaccination. It is not indicated beyond the seventh day after the first dose of rabies vaccine, regardless of whether the doses were received on days 3 and 7, because an active antibody response to the rabies vaccine has already started, and this would represent a waste of RIG.

Use of the same syringe or mixing rabies vaccine and RIG are not advised. For severe and multiple wounds, which require more immunoglobulin than the maximum dose, the product may be diluted with sterile normal saline to a volume sufficient for effective, safe infiltration of all wounds.

Pediatric dose:

The recommended dose is 40 IU/kg of body weight.

CONTRAINDICATIONS:

Given the lethal risk associated with rabies, there are no contraindications to the administration of the rabies immunoglobulin.

WARNINGS AND PRECAUTIONS:

Do not administer the product via the intravenous route (risk of shock).

In the event of a history of known allergy to equine proteins, the use of the human rabies immunoglobulin should be preferred.

Rabies Antiserum used alone is not a rabies treatment. Multiple injections in the wound must be avoided.

Rabies Antiserum must not be administered with the same syringe as the one used to inject the rabies vaccine, or administered at the same anatomical site as the rabies vaccine.

In view of the heterologous nature of the equine rabies immunoglobulin, the risk of undesirable effects such as anaphylactic shock should always be assessed: In order to detect any persons pre-sensitised to heterologous proteins, patients should be thoroughly interviewed about their history of allergy, with particular emphasis on any prior injections of heterologous proteins which may have induced reactions. Allergies induced by contact with animals, especially horses, or food allergies should also be investigated.

This risk should be considered as rare, given the high level of purification of Rabies Antiserum.
Administration of the equine rabies immunoglobulin should be performed under strict medical supervision, in order to prevent any possible anaphylactic shock (see Adverse Reactions). If allergic or anaphylactic reactions occur, the injection should be stopped immediately. In case of shock, treatment of shock should be implemented.
In case of unavailability of the human rabies immunoglobulin, administration of the equine rabies immunoglobulin should be done.
Treatment should be complemented with a tetanus treatment if necessary and an antibiotic therapy in order to prevent infections other than rabies.

Use in pregnancy:

In view of the fatal risks connected with rabies, pregnancy does not constitute a contraindication to the initiation of post-exposure treatment for rabies.
The safety of this product during pregnancy has not been established during clinical studies in humans but it has been used during pregnancy.
However, if a choice is possible, preference should be given to the use of human rabies immunoglobulins.

Caution for Usage

Special precautions for use and other handling: Any unused product or waste material should be disposed of in accordance with local requirements.

Incompatibilities: In the absence of compatibility studies, this medicinal product should not be mixed with other medicinal products.
Use of the same syringe or mixing rabies vaccine and RIG are not advised.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION:

As a general rule, corticosteroids should be avoided, as they may attenuate the immune response.

PREGNANCY AND LACTATION:

Pregnancy

In view of the fatal risks connected with rabies, pregnancy does not constitute a contraindication to the initiation of post-exposure treatment for rabies.

The safety of this product during pregnancy has not been established during clinical studies in humans but it has been used during pregnancy.
However, if a choice is possible, preference should be given to the use of human rabies immunoglobulins.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:

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

SIDE/ADVERSE/UNDESIRABLE EFFECTS:

Post marketing data: *General disorders and administration site conditions:* Very rare undesirable effects: Immediate or delayed allergic type reactions occur after the use of heterologous (non-human) proteins.

The immediate reactions observed are anaphylactoid reactions with hypotension, dyspnoea (breathing problems), rash or urticaria. In very rare cases, more severe reactions such as Quincke's oedema or anaphylactic shock may occur.

Delayed serum sickness-like reactions (illness due to an allergic reaction) or angioneurotic oedema reported after the administration of heterologous (non-human) proteins may occur about six days after the beginning of treatment. These consist of an inflammatory reaction due to activation of the complement and the formation of immune complexes (type III hypersensitivity reaction), occasionally accompanied by clinical symptoms such as fever, pruritus, erythema (rash) or urticaria, adenopathy, and arthralgia.

OVERDOSE:

If the recommended dosage is not strictly followed (overdosage), there is a risk of immunosuppressive interference with the rabies vaccine.

PHARMACOLOGICAL PROPERTIES:

Mechanism of action:

Pharmacotherapeutic Group: Immunoglobulins-Specific immunoglobulins. **ATC Code:** J06BB05.

Pharmacology: ***Pharmacodynamics:*** *Mechanism of Action:* Rabies Antiserum contains $F(ab')_2$ fragments of equine rabies immunoglobulin, which have the property to neutralise the rabies virus at the exposure site and before it reaches nerve endings. ***Pharmacokinetics:*** Local infiltration is crucial since the serum concentration of virus neutralising

antibodies achieved after intramuscular administration is low, or even negligible. A pharmacokinetic study performed in healthy volunteers confirmed that the absorption rate of equine rabies immunoglobulins was slow after intramuscular administration. Serum concentrations usually reach their peak (C_{max} = 8.86 ± 6.65 µg/mL) in 10.80 ± 2.48 hours. ***Toxicology:*** *Preclinical Safety Data:* The results of acute toxicity studies in animals (mice and rats) have demonstrated the absence of toxicological signs. There is no associated embryo-foetal toxicity with Rabies Antiserum. The lack of mutagenicity was confirmed using an Ames test.

SHELF-LIFE:

2-Years (Stored at 2-8°C)

STORAGE CONDITION:

Store between +2°C and +8°C (in a refrigerator). Do not freeze. Protect from light.

PRESENTATION:

Solution for injection (vial) 5 mL x 1's, 10's.

DISPOSABLE:

Left over product and used vials should be discarded as Biomedical waste.

Manufacturer:

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Sy. No. 117, Thimmapur (V), Kothur (M),
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