PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

KamRAB™

Rabies Immunoglobulin (Human)

Solution for intramuscular injection (150 IU/mL)

2.0 mL vials and 10.0 mL vials

Passive, Transient Post-Exposure Agent For Prophylaxis Of Rabies

Manufactured by:
Kamada Ltd.
2 Holzman St, Science Park,
P.O. Box 4081, Rehovot 7670402, Israel

Imported by:
Imported by/Importé par:
Quality & Compliance Services Inc.,
Mississauga, ON L5N 5R1
for/pour
Valneva Canada Inc.,
Kirkland, QC H9H 5B9

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

KamRAB is a human rabies immunoglobulin (HRIG) indicated for passive, transient post-exposure prophylaxis (PEP) of rabies infection, when given immediately after contact with a rabid or possibly rabid animal. KamRAB should be administered concurrently with a full course of rabies vaccine.

- Do not administer additional (repeat) doses of KamRAB once vaccine treatment has been initiated, since this may interfere with the immune response to the rabies vaccine.
- Do not administer KamRAB to patients with a history of a complete pre-exposure or post-exposure vaccination regimen and confirmed adequate rabies antibody titer.

1.1. Pediatrics

Pediatrics (<18 years): The safety and effectiveness of KamRAB in the pediatric population have not been established.

1.2. Geriatrics

Geriatrics (> 65 years of age): Clinical studies of KamRAB did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently from younger subjects. Clinical experience with HRIG products has not identified differences in effectiveness between elderly and younger patients.

2. CONTRAINDICATIONS

None.

3. DOSAGE AND ADMINISTRATION

3.1. Dosing Considerations

- **For wound infiltration and intramuscular use. Do not administer intravenously.**

Local Treatment of Wounds prior to KamRAB Administration

The World Health Organization (WHO) and National Advisory Committee on Immunization (NACI) have outlined recommendations for passive and active immunization after exposure to an animal suspected of having rabies. Immediate and thorough cleansing of all bite wounds and scratches with soap and water is an important component of post-exposure prophylaxis (PEP). A virucidal agent (e.g., povidone-iodine solution) should be used to irrigate the wounds.

Tetanus prophylaxis and measures to control bacterial infection should be given if medically indicated.

3.2. Recommended Dose and Dosage Adjustment

Post-exposure prophylaxis consists of a single dose of KamRAB and a full course of rabies vaccine. The recommended dose of KamRAB is 20 IU/kg body weight, given at the time of the first vaccine dose. KamRAB and the first dose of rabies vaccine should be given as soon as possible after exposure, as delays are potentially lethal. However, should a delay occur, KamRAB should be administered at any time up to and including seven days after the first dose of vaccine. The rabies vaccine should be given according to the manufacturer's instructions.

No more than the recommended dose of KamRAB should be given because KamRAB partially suppresses active antibody production following vaccination. For the same reason, additional doses of KamRAB should not be given, even if the antibody response to vaccination is delayed.

3.3. Administration

- **When the bite site is known and infiltration at the bite site is feasible**:

    - Infiltrate as much of the dose as possible into and around any detectable bite wounds. Inject any remaining volume intramuscularly into the upper arm deltoid region or, in small children, into the anterolateral aspect of the thigh. Administer the remaining KamRAB at site(s) distant from the site of the rabies vaccine.

- Avoid administration into the gluteal region, where absorbance is unpredictable (unless the exposure site is in the gluteal region):
- When the bite site is unknown or indeterminate (undetectable) or if infiltration is difficult at the bite site (e.g., lips, fingers, knee), administer the full KamRAB dose by the intramuscular route at a site distant from the site of rabies vaccination.
- If a large intramuscular volume is required (>2 mL for children or >5 mL for adults), administer the total volume in divided doses at different sites.
- If intramuscular administration is contraindicated (e.g., in patients with uncorrectable bleeding disorders), administer KamRAB subcutaneously. However, note that there are

no clinical efficacy data to support administration of KamRAB by the subcutaneous route.
- Do not mix with the rabies vaccine or administer in the same syringe with the rabies vaccine.
- Do not administer into the same anatomical site(s) as rabies vaccine.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. If either of these conditions exists, DO NOT use KamRAB; discard the vial.

Further Information on Rabies Post-Exposure Prophylaxis:

Consult public health officials if questions arise about the need for rabies prophylaxis.

3.4. Reconstitution

Reconstitution is not required. KamRAB is supplied in single-use vials containing ready-to-use solution.

3.5. Missed Dose

Not applicable.

4. OVERDOSAGE

For management of a suspected drug overdose, contact your regional poison control centre.

5. DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intramuscular	Single-use vials containing 2 mL or 10 mL of ready-to-use human rabies immunoglobulin (HRIG) solution with a potency of 150 IU/mL	Glycine, Water for Injection, Sodium Hydroxide

6. DESCRIPTION

KamRAB is a sterile, non-pyrogenic aqueous solution of anti-rabies immunoglobulin (≥95% protein as IgG). The product is stabilized with 0.3 M glycine and has a pH of 5.5 ± 0.5. It does not contain preservatives and the vial stopper is not made with natural rubber latex. KamRAB is a clear to opalescent liquid.

7. WARNINGS AND PRECAUTIONS

General

Transmissible Infectious Agents

KamRAB is derived from human plasma; therefore, the potential exists that KamRAB administration may transmit infectious agents such as viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent, and theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

- The risk of transmitting an infectious agent has been minimized by:
    - Screening plasma donors for prior exposure to certain viruses
    - Testing for certain viral infections
    - Inactivating and removing certain viruses during the manufacturing process [**see Pharmaceutical Information**].

Despite these measures, KamRAB administration can still potentially transmit infectious diseases. There is also the possibility that unknown infectious agents may be present in KamRAB.

Hematologic

Thrombosis

- Patients at increased risk of thrombosis or thrombotic complications should be monitored

for at least 24 hours after KamRAB administration.

- Patients at increased risk of thrombosis include patients with acquired or hereditary hypercoagulable states, prolonged immobilization, in-dwelling vascular catheters, advanced age, estrogen use, a history of venous or arterial thrombosis, cardiovascular risk factors (including history of atherosclerosis and/or impaired cardiac output), and hyperviscosity syndromes (including cryoglobulinemias, fasting chylomicronemia and/or high triglyceride levels, and monoclonal gammopathies).

- Consider measurement of baseline blood viscosity in patients at risk for hyperviscosity.

The risk of thrombosis or thrombotic complications has been minimized by the manufacturing process that allows the removal of thrombogenic activity.

Hemolysis

- Hemolysis may occur in patients receiving immunoglobulin products, particularly those who are determined to be at increased risk. Patients at increased risk include those with non-O blood group types, those with underlying associated inflammatory conditions, and those receiving high cumulative doses of immunoglobulins over the course of several days.

- Clinical symptoms and signs of hemolysis include fever, chills and dark urine. If any of these occur, perform appropriate laboratory testing and administer medical therapy as indicated.

Immune

Previous Rabies Vaccination

Patients who can document previous complete rabies pre-exposure prophylaxis or complete post-exposure prophylaxis should only receive a booster rabies vaccine without KamRAB, because KamRAB may interfere with the anamnestic response to the vaccine.

Live Attenuated Virus Vaccines

KAMRAB administration may interfere with the development of an immune response to live attenuated virus vaccines.

- Avoid immunization with measles vaccine within 4 months after KamRAB administration.
- Avoid immunization with other live attenuated virus vaccines within 3 months after KamRAB administration.

Monitoring and Laboratory Tests

Interference with Serologic Testing

- A transient rise of the various passively transferred antibodies in the patient's blood may result in misleading positive results of serologic tests after KamRAB administration.

- Passive transmission of antibodies to erythrocyte antigens, e.g., A, B, and D, may interfere with serologic tests for red cell antibodies such as the antiglobulin test (Coombs' test).

Sensitivity/Resistance

Anaphylactic Shock

- KamRAB should not be injected into a blood vessel because of the risk of severe allergic or hypersensitivity reactions, including anaphylactic shock. KamRAB can induce a fall in blood pressure associated with an anaphylactic reaction, even in patients who tolerated previous treatment with human immunoglobulin.

- Discontinue KamRAB injection immediately if there is an allergic or anaphylactic type reaction. In case of shock, implement standard medical treatment. Epinephrine should be available for treatment of acute anaphylactic symptoms.

Hypersensitivity

- Patients with a history of prior systemic allergic reactions following administration of human immunoglobulin preparations should be monitored for hypersensitivity.

- KamRAB contains a small quantity of IgA. Patients who are deficient in IgA have the potential to develop IgA antibodies and may have anaphylactic reactions following administration of blood components containing IgA. The healthcare provider should assess the risks of this reaction against the benefits of administering KamRAB.

Skin (Local) Reactions at Vaccination Sites

Injection site pain was observed in some patients administered KamRAB [see ADVERSE REACTIONS]

7.1. Special Populations

7.1.1. Pregnant Women

KamRAB has not been studied in pregnant women. Therefore, the risk of major birth defects and miscarriage in pregnant women who are exposed to KamRAB is unknown. Animal developmental or reproduction toxicity studies have not been conducted with KamRAB. It is not known whether KamRAB can cause harm to the fetus when administered to a pregnant woman or whether KamRAB can affect reproductive capacity. It is reported that major birth defects (ie major congenital anomalies) in Canada occur in approximately 3–5% of newborn infants and in 8% to 10% of stillbirths, and miscarriage occurs in 15-20% of clinically recognized pregnancies.

7.1.2. Breast-feeding

There is no information regarding the presence of KamRAB in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for KamRAB and any potential adverse effects on the breastfed infant from KamRAB or from the underlying maternal condition.

7.1.3. Pediatrics

Pediatrics (<18 years): The safety and effectiveness of KamRAB in the pediatric population have not been established.

7.1.4. Geriatrics

Clinical studies of KamRAB did not include sufficient numbers of subjects aged 65 years and

over to determine whether they respond differently from younger subjects. Clinical experience with HRIG products has not identified differences in effectiveness between elderly and younger patients.

8. ADVERSE REACTIONS

8.1. Adverse Reaction Overview

Because clinical trials are conducted under very specific conditions, the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

8.2. Clinical Trial Adverse Reactions

KamRAB was evaluated in three single-center, controlled clinical trials. Subjects in the clinical studies of KamRAB were healthy adults, primarily white and ranged in age from 18 to 72 years. A total of 160 subjects were treated in these three studies, including 91 subjects who received single intramuscular doses of KamRAB (20 IU/kg) with or without rabies vaccine.

The table below summarizes adverse events (assessed by the investigator as related or unrelated to study treatment) occurring in >3% of subjects in the clinical trials of KamRAB. The most frequent adverse events in the KamRAB group (>6%) were injection site pain, headache, muscle pain, and upper respiratory tract infection.

Table 2: Adverse Events Occurring in >3% of Subjects in All Studies Combined

	KamRAB N = 91	**Comparator HRIG N = 84**	**Saline Placebo + Vaccine N = 8**
Injection site pain	30 (33)	26 (31)	2 (25)
Headache	14 (15)	11 (13)	3 (38)
Muscle pain	8 (9)	6 (7)	0 (0)
Upper respiratory tract infection	8 (9)	8 (10)	0 (0)
Joint pain	5 (6)	0 (0)	1 (13)
Dizziness	5 (6)	3 (4)	0 (0)
Fatigue	5 (6)	2 (2)	0 (0)
Abdominal pain	4 (4)	1 (1)	0 (0)
Blood in urine	4 (4)	2 (2)	0 (0)

	KamRAB N = 91	Comparator HRIG N = 84	Saline Placebo + Vaccine N = 8
Nausea	4 (4)	3 (4)	0 (0)
Feeling faint	4 (4)	1 (1)	0 (0)
Bruising	3 (3)	1 (1)	0 (0)
Sunburn	3 (3)	0 (0)	0 (0)
White blood cells in urine	3 (3)	4 (5)	0 (0)

Data are presented as number of subjects (% of subjects)

8.3. Less Common Clinical Trial Adverse Reactions

Less common adverse events were joint pain, dizziness, fatigue, abdominal pain, blood in urine, nausea, feeling faint, bruising, sunburn, and white blood cells in urine.

9. DRUG INTERACTIONS

9.1. Overview

Concomitant Vaccine Administration

- Do not administer additional (repeat) doses of KamRAB once vaccination has been initiated, since additional doses of KamRAB may interfere with the immune response to the vaccine.

- Do not administer KamRAB into the same anatomical site(s) as rabies vaccine.

KamRAB contains other antibodies that may interfere with the response to live vaccines such as measles, mumps, polio or rubella. Avoid immunization with live virus vaccines within 3 months after KamRAB administration, or in the case of measles vaccine, within 4 months after KamRAB administration.

10. ACTION AND CLINICAL PHARMACOLOGY

10.1. Mechanism of Action

Rabies is a zoonotic disease caused by RNA viruses in the family Rhabdoviridae, genus Lyssavirus. Virus is typically present in the saliva of rabid mammals and is transmitted primarily through a bite. KamRAB is infiltrated into the inoculation site (i.e., at the beginning of anti-rabies PEP) to previously unvaccinated persons, to provide immediate passive rabies virus neutralizing antibody protection until the patient's immune system responds to vaccination by actively producing antibodies.

10.2. Pharmacodynamics

A protective threshold for rabies virus neutralizing activity (RVNA) has never been established. However, the WHO has generally accepted a RVNA of at least 0.5 IU/mL measured 14 days after initiation of PEP as protective. By comparison, the ACIP recommends complete neutralization of rabies virus at a 1:5 serum dilution by a rapid fluorescent focus inhibition test (RFFIT) from 1 to 2 weeks after prophylaxis; this corresponds to RVNA ~0.1-0.2 IU/mL. In support of these recommendations, there has been almost no documented clinical disease when the current rabies PEP regimen is administered appropriately.

KamRAB has the potential to attenuate the patient's immune response to rabies vaccine. This was evaluated in a double-blind, randomized study where 16 healthy subjects were administered either KamRAB (20 IU/kg IM) or saline placebo followed by three doses of a rabies vaccine. Lower RVNA levels were seen in the KamRAB + vaccine group compared to the placebo + vaccine group at all time-points beginning on Day 14, confirming that KamRAB interferes with the host immune response to rabies vaccine.

10.3. Pharmacokinetics

A randomized, single-dose, two-period, two-treatment, two-sequence, double-blind, crossover study assessed the pharmacokinetics of KamRAB. Twenty-six healthy volunteer subjects were randomized to receive a single IM injection of 20 IU/kg HRIG on two separate occasions (KamRAB or Comparator HRIG). Subjects received the second treatment (A or B) following the 42-day test period and a 21-day washout period. Single dose IM injection of KamRAB resulted in maximum plasma RVNA levels of 0.25 IU/mL. The median Tmax was 7 days (range: 3 – 14 days). The elimination half-life was approximately 17.9 days.

Additionally, a prospective, randomized, double-blind, non-inferiority, study evaluated the pharmacokinetics, safety and effectiveness of simulated post-exposure prophylaxis with KamRAB with co-administration of active rabies vaccine in 118 healthy subjects. Subjects were randomized into two treatment groups (59 per treatment group) to receive intramuscular KamRAB or comparator HRIG at a dose of 20 IU/kg on Day 0, and rabies vaccine on Days 0, 3, 7, 14 and 28. The geometric mean of the peak plasma RVNA was 39.9 IU/mL and 36.2 IU/mL for KamRAB and comparator HRIG respectively. For both treatment groups, the median T_{max}

was 14 days (range: 14 – 49 days). The half-lives were 48.6 hours and 52.7 hours for KamRAB and comparator HRIG respectively (Table 3).

A plot of plasma rabies virus neutralizing antibody titer concentration versus time (Figure 1) demonstrated that, in both treatment groups, plasma rabies virus neutralizing antibody concentrations declined in a biphasic manner after the absorption phase was complete.

Figure 1: Plasma HRIG Concentrations [Mean (±SD)] at Scheduled PK Sampling Days (Semi-log Scale), Phase 2/3 Study, Pharmacokinetic Analysis

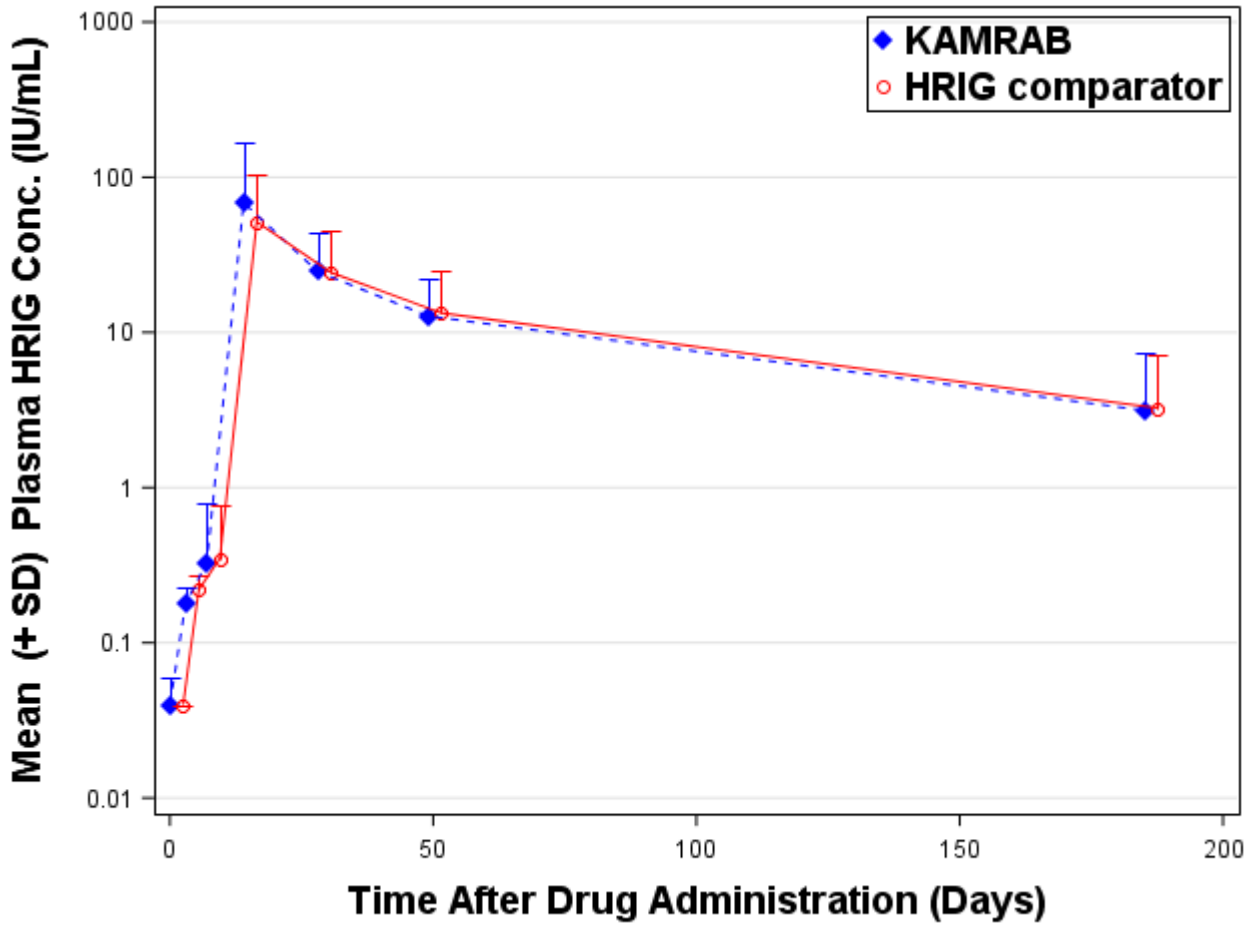

Table 3: Pharmacokinetic Comparison of PK Parameters for Plasma HRIG concentration, Phase 2/3 Study, Pharmacokinetic Analysis

PK Parameter Units	Statistic	Kamada-HRIG[1]	Comparator HRIG[1]
C_{max}	N	59	58

PK Parameter Units	Statistic	Kamada-HRIG[1]	Comparator HRIG[1]
	Median	51.7	35.7
	Geometric mean (SD)	39.9 (3.11)	36.2 (2.64)
$AUC_{0\text{-last}}$ (Days*IU/mL)	N	59	58
	Median	1595	1447
	Geometric mean (SD)	1313 (2.93)	1480 (2.24)
$AUC_{0\text{-Inf}}$ (Days*IU/mL)	N	43	44
	Median	1574	1635
	Geometric mean (SD)	1603 (2.27)	1657 (2.17)

11. STORAGE, STABILITY AND DISPOSAL

- Store KamRAB at 2-8 °C (36-46 °F). Do not freeze.
- Keep vial in carton until use.
- KamRAB may be stored at room temperatures not exceeding 25 °C (77 °F) for up to one month.
- Use within one month after removal from refrigeration, Do not return to refrigeration.
- Do not use after the expiration date printed on the label.

PART II: SCIENTIFIC INFORMATION

12. PHARMACEUTICAL INFORMATION

Drug Substance

KamRAB Rabies Immunoglobulin (Human) is a sterile solution containing anti-rabies immunoglobulins (≥95% protein as IgG) for intramuscular injection with a nominal potency of 150 IU/mL.

Product Characteristics

KamRAB is prepared from human plasma from donors hyper-immunized with rabies vaccine. Individual plasma units are tested using FDA-licensed serologic assays for hepatitis B surface antigen (HBsAg) and for antibodies to hepatitis C virus (HCV) and human immunodeficiency virus types 1 and 2 (HIV-1/2), as well as by FDA-licensed Nucleic Acid Testing (NAT) for hepatitis B virus (HBV), HCV and HIV-1. Each plasma unit must be non-reactive (negative) in all tests. Plasma is also tested by in-process NAT procedures for HAV and parvovirus B19. Each plasma unit must be non-reactive to HAV, while the limit in the manufacturing pool is set not to exceed 104 IU per mL for parvovirus B19.

Viral Inactivation

To reduce the risk of viral transmission further, the manufacturing process for KamRAB includes three steps specifically designed to remove or inactivate viruses. The first of these is solvent/detergent (S/D) treatment with a mixture of tri-(n-butyl) phosphate (TnBP) and Octynoxol 9, which inactivates enveloped viral agents such as HIV, HBV and HCV. The second and third are heat-treatment (pasteurization) steps, which can inactivate both enveloped and non–enveloped viruses, and a nanofiltration (NF) step which removes viruses on the basis of size. The effectiveness of the S/D treatment, pasteurization and nanofiltration procedures for reducing viral content has been assessed using a series of viruses with a range of physico-chemical characteristics. The results of the viral challenge studies are summarized in the following table.

Table 4: Log_{10} Virus Reduction during Manufacture of KamRAB

Process Step	Enveloped Viruses				Non-enveloped Viruses	
	HIV-1	BVDV	PRV	WNV	EMCV	PPV
S/D treatment	>4.99	>5.70	>4.38	>5.46	Not tested	Not tested

Process Step	Enveloped Viruses				Non-enveloped Viruses	
	HIV-1	**BVDV**	**PRV**	**WNV**	**EMCV**	**PPV**
Heat treatment	>6.21	>5.67	Not tested	>6.33	3.30	Not tested
Nanofiltration	Not tested	Not tested	>6.58	Not tested	>7.66	3.41
Global Log_{10} Reduction Factor	**>11.20**	**>11.37**	**>10.96**	**>11.79**	**>10.96**	**3.41**

Abbreviations: BVDV: bovine viral diarrhea virus; EMCV: encephalomyocarditis virus; HIV-1: human immunodeficiency virus 1; HRIG: human rabies immunoglobulin; PPV: Porcine parvovirus; PRV: Pseudorabies virus; S/D: solvent/detergent; WNV: West Nile Virus

13. CLINICAL TRIALS

13.1. Trial Design and Study Demographics

Table 5 - Summary of patient demographics for clinical trials in <specific indication>

Study #	Trial design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
003	Prospective, randomized, double-blind, non-inferiority, pharmacokinetic, safety and effectiveness study of simulated post-exposure prophylaxis	20 IU/kg KamRAB or comparator HRIG at a dose of 20 IU/kg on Day 0, and rabies vaccine on Days 0, 3, 7, 14 and 28	118 subjects (59 per treatment group)	KamRAB 43.3 (18-69) Comparator 46.3 (20-72)	M & F

13.2. Study Results

The efficacy of KamRAB administered concurrently with rabies vaccine was studied in a single-center, randomized, comparator HRIG-controlled clinical study. Study subjects were healthy adults 18 to 72 years of age who were without significant acute or chronic illness. A total of 118 subjects (59 per treatment group) received intramuscular KamRAB or comparator HRIG at a dose of 20 IU/kg on Day 0, and rabies vaccine on Days 0, 3, 7, 14 and 28. The mean age of study subjects was 45 years; subjects were, predominantly white (93%), and 64% were women. The efficacy variable was RVNA, as assessed by RFFIT, on Day 14. Efficacy analyses were performed on the As-Treated Population, which comprised the 116 study subjects who received KamRAB or comparator HRIG and at least 3 of the 5 doses of rabies vaccine before Day 14.

Efficacy, considered when RVNA titer is 0.5 IU/mL or higher on Day 14 (as established by the WHO), was met by 56/57 subjects (98.2%) in the KamRAB group and 59/59 subjects in the comparator HRIG group. The lower limit of the 90% CI was greater than the pre-specified non-inferiority margin of -10%; thus, KamRAB was non-inferior to comparator HRIG.

Table 6: Subjects with Geometric Mean RVNA ≥0.5 IU/mL on Day 14 (As-Treated Population)

	KamRAB with Rabies Vaccine (N=57)	Comparator HRIG with Rabies Vaccine (N=59)
Rabies virus neutralizing antibody titer ≥0.5 IU/mL, n (%)	56 (98.2)	59 (100)
Exact 95% CI for proportion (%)	(90.6, 100)	(93.9, 100)
Difference (Pa-Pb)[a] (%)	-1.8	
Exact 90% CI for difference[b] (%)	(-8.1, 3.0)	

[a] 'Pa' and 'Pb' are the proportion of participants with IgG antibody titer ≥0.5 IU/mL on Day 14 in Groups A and B, respectively. Group A = KamRAB +Rabies Vaccine, Group B = Control HyperRAB®+Rabies Vaccine.
[b] based on Farrington-Manning score statistic.
Abbreviations: CI: confidence interval; HRIG: human rabies immunoglobulin; IU: international units; mL: milliliter

Additional efficacy analyses included pharmacokinetics **[see Action Clinical Pharmacology, 11.3 Pharmacokinetics**].

14. NON-CLINICAL TOXICOLOGY

Intramuscular administration of a single dose of KamRAB to rats at 60 and 120 IU/kg (3-fold and 6-fold higher than the recommended human dose of 20 IU/kg), did not result in any signs of toxicity.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

Rabies Immunoglobulin (Human)

Read this carefully before you start taking **KamRAB**. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **KamRAB**.

What is KamRAB used for?

- KamRAB is used to treat rabies infection. It is a single dose treatment used along with a full course of rabies vaccine

How does KamRAB work?

KamRAB contains antibodies that inactivate the rabies virus. It is administered as soon as possible after a person is bitten by an animal suspected of being infected with rabies and is injected directly into and around the wound as a single dose.

Any person who might have been exposed to rabies and has never been vaccinated against rabies should receive KamRAB as well as a series of rabies vaccinations. KamRAB provides immediate protection against the rabies virus until the person to develop antibodies of his/ her own against the rabies virus.

What are the ingredients in KamRAB?

Medicinal ingredients: Anti-rabies immunoglobulin (human antibodies to rabies)

Non-medicinal ingredients: glycine, water for injection and sodium hydroxide

KamRAB is available in the following dosage forms:

Single-use vials containing 2 mL or 10 mL of ready-to-use solution with a potency of 150 IU/mL.

To help avoid side effects and ensure proper use, talk to your healthcare professional

before you recieve KamRAB. Talk about any health conditions or problems you may have, including if you:

- Have any bleeding disorders or take medication for bleeding disorders
- Have an inflammatory condition
- Are receiving high doses of other immunoglobulins.
- Have previously received vaccinations for rabies
- Have previously had allergic reactions after being injected with other immunoglobulins
- Have any immune deficiencies which cause you to be deficient in certain antibodies
- Are pregnant or breast feeding

Other warnings you should know about:

KamRAB is made from human plasma; therefore, the potential exists that KamRAB administration may transmit infectious disease such as viruses, both known and unknown, and other diseases such as the Creutzfeldt-Jakob disease (CJD) agent. The risk of getting an infectious disease from KamRAB administration is very small and is minimized by screening human plasma donors for prior exposure to certain viruses, testing donors for certain viral infections and by designated viral inactivation and removal certain viruses during the manufacturing of KamRAB; however, there is the possibility that KamRAB administration could transmit infectious diseases.

KamRAB administration may interfere with other vaccines. It is important to avoid immunization with measles vaccines within 4 months after KamRAB administration and avoid immunization with other live vaccines for 3 months after KamRAB administration.

KamRAB should not be mixed with the rabies vaccine or injected in the same syringe with the rabies vaccine.

KamRAB should not be administered into the same injection site on the body where rabies vaccine was injected.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with KamRAB:

- Administration of other vaccines

Treatment with KamRAB:

KamRAB should be administered by a healthcare professional provider only.

KamRAB is administered following suspected exposure to a rabid animal, at the time of the first rabies vaccine dose.

If the bite wound is visible, KamRAB should be injected into and around the bite wound, and any remaining product should be injected intramuscularly in the arm or the thigh.

If the bite would is not visible, or if injection at the bite wound is difficult, KamRAB should be injected intramuscularly on a part of the body that is far away from the site of any rabies vaccinations.

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Usual dose:

The recommended dose of KamRAB is 20 IU/kg body weight.

Overdose:

Overdose of KamRAB is unlikely. If it does happen, your doctor will treat any symptoms that follow.

If you think you have been administered too much KamRAB, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using KamRAB?

The most frequent side effects occurring with KamRAB included pain at the site of injection, headache, muscle pain, and upper respiratory tract infection. Less common side effects

included joint pain, dizziness, fatigue, abdominal pain, blood in the urine, nausea, feeling faint, bruising, and sunburn.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
RARE Serious allergic reactions, with symptoms such as swelling of the face and throat, difficulty breathing, and rash		✓	✓
fever, chills and dark urine		✓	✓

These are not all the possible side effects you may feel when taking KamRAB. If you experience any side effects not listed here, contact your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Reporting Suspected Side Effects

For the general public: Should you experience a side effect following immunization, please report it to your doctor, nurse, or pharmacist.

Should you require information related to the management of the side effect, please contact your healthcare provider. The Public Health Agency of Canada, Health Canada and Valneva Canada Inc. cannot provide medical advice.

For healthcare professionals: If a patient experiences a side effect following immunization, please complete the Adverse Events Following Immunization (AEFI) Form appropriate for your province/territory (http://www.phac-aspc.gc.ca/im/aefi-essi-form-eng.php) and send it to your local Health Unit.

Keep out of reach and sight of children.

If you want more information about KamRAB

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website; the manufacturer's website www.valneva.ca, or by calling 1-855-356-0831

This leaflet was prepared by Kamada Ltd.

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