RLP
APPROVED

Product Name: Beransa 5 mg Solution for Injection for Dogs
APVMA Approval No: 89658/125697

Label Name:	Beransa 5 mg Solution for Injection for Dogs

Signal Headings:	PRESCRIPTION ANIMAL REMEDY KEEP OUT OF REACH OF CHILDREN FOR ANIMAL TREATMENT ONLY READ SAFETY DIRECTIONS

Constituent Statements:	Each 1 mL vial contains 5 mg bedinvetmab

Claims:	For use by or under direction of a registered veterinarian. For the alleviation of pain associated with osteoarthritis in dogs.

Net Contents:	1 x 1 mL vial 2 x 1 mL vials 6 x 1 mL vials

Directions for Use:	

Restraints:	

Contraindications:	This product must not be used in dogs intended for breeding. This product must not be used in pregnant or lactating dogs as Nerve Growth Factor (NGF) plays a key role in foetal nervous system development. This product must not be used in dogs under 12 months of age. This product must not be used in dogs with hypersensitivity to bedinvetmab.

Precautions:	This product may induce transient or persistent anti-drug antibodies. The induction of such antibodies is uncommon and may have no effect or may result in a decrease in efficacy in animals that responded to treatment previously. If no or limited response is observed within one month after initial dosing, an improvement in response may be observed after administration of a second dose one month later.

	However, if the animal does not show a better response after the second dose, the veterinarian should consider alternative treatments.

Side Effects:	Mild reactions at the injection site (e.g. swelling and heat) may uncommonly be observed. Hypersensitivity-type reactions have been reported very rarely. In case of such reactions, appropriate symptomatic treatment should be administered.

Dosage and Administration:	Avoid excessive shaking or foaming of the solution. Use the contents immediately after broaching the vial. Discard any unused portion. This product does not contain a preservative. Remove the vial(s) from the carton at the time of monthly treatment, aseptically withdraw all liquid from the vial using a needle and syringe and inject the contents subcutaneously. The product should appear clear to slightly opalescent without any visible particles. The recommended minimum dose of BERANSA is 0.5 – 1.0 mg/kg bodyweight , administered subcutaneously, once a month. For dogs weighing between 5 kg and 60 kg, administer the entire contents of one vial (1 mL) of the appropriate strength. For dogs weighing more than 60 kg, the contents of more than one vial are required to constitute a single dose. In those cases, withdraw the entire contents from each required vial into one syringe and administer as a single injection. For dogs weighing less than 5kg, using a 5 mg/mL vial, aseptically withdraw 0.1 mL/kg and administer subcutaneously. Discard any unused portion. The dose range of 0.5 – 1 mg/kg can be achieved using the suggested dosing regime in the table below: Duration of treatment should be based on the individual response of each animal. If a positive response is not observed, consider alternative treatments.

General Directions:	BERANSA (bedinvetmab) is a canine therapeutic monoclonal antibody (mAb) that neutralises Nerve Growth Factor (NGF). The inhibition of NGF-mediated cell signalling has been demonstrated to provide relief from pain associated with osteoarthritis (OA). Bedinvetmab binds NGF with high affinity, is a potent inhibitor of NGF activity and does not recruit complement. In a laboratory study over a 2-week period in young, healthy dogs without osteoarthritis, BERANSA had no adverse effect when administered concomitantly with carprofen, a non-steroidal anti-inflammatory drug (NSAID). There are no safety data on the concurrent long-term use of NSAIDs and BERANSA in dogs. In clinical trials in humans, rapidly progressing osteoarthritis (RPOA) has been reported in a small number of patients receiving humanised anti-NGF monoclonal antibody therapy. The incidence of these events increased with high doses and in human patients receiving long-term (> 90 days) NSAIDs concomitantly with an anti-NGF monoclonal antibody. In patients receiving intermittent concomitant treatment with NSAIDs (fewer than 90 days per year), the incidence of RPOA was not increased. Dogs have no reported equivalent of human RPOA.

No drug interactions were observed in field studies where BERANSA was administered concomitantly with other veterinary medicinal products such as parasiticides, nutritional supplements, antimicrobials, topical antiseptics with or without corticosteroids, antihistamines and vaccines.

If a vaccine is to be administered at the same time as treatment with BERANSA, the vaccine should be administered at a different site to BERANSA, to reduce any potential impact on immunogenicity of the vaccine.

BERANSA should not be mixed in the syringe with other veterinary medicinal products.

Mode of Action
Bedinvetmab, is a canine monoclonal antibody that binds to Nerve Growth Factor (NGF), reduces NGF binding to the tropomyosin receptor kinase A (TrkA) receptor, and decreases TrkA signal transduction in cell types involved in pain. Bedinvetmab binds selectively and with high affinity to NGF. It does not bind to other neurotrophins.

NGF has been found to be elevated in the osteoarthritic joints of dogs. Following a noxious stimulus, inflammatory processes lead to the production and release of NGF by tissues of the joint. Elevated NGF binds to TrkA receptors found on peripheral nerves, immune cells, endothelial cells, synoviocytes, and chondrocytes to induce peripheral sensitisation, neurogenic inflammation, and increased pain perception. NGF binding to TrkA receptors located on immune cells elicits the release of additional pro-inflammatory mediators, including NGF itself. These inflammatory mediators lead to further peripheral sensitisation involved in pain perception. Bedinvetmab binds to NGF and prevents NGF/TrkA cellular signalling.

Pharmacokinetics
In a 6-month laboratory study of healthy, adult Beagles administered bedinvetmab every 28 days at doses ranging from 1-10 mg/kg, AUC and CMAX increased nearly in proportion to dose and steady state was achieved after approximately 2 doses. In a laboratory pharmacokinetic study at the label dose (0.5-1.0 mg/kg), peak serum drug levels were observed at 2-7 days (CMAX = 6.10 µg/mL, TMAX = 5.6 days) after subcutaneous dosing, the bioavailability was approximately 84%, the elimination half-life was approximately 12 days, and the mean AUC0-∞ was 141 µg x d/mL.

In a field effectiveness study at the label dose in dogs with osteoarthritis, the terminal half-life averaged 16 days. Steady state was achieved after 2 doses.

Bedinvetmab, like endogenous proteins, is expected to be degraded into small peptides and amino acids via normal catabolic pathways. Bedinvetmab is not metabolised by cytochrome P450 enzymes; therefore, interactions with concomitant medications that are substrates, inducers, or inhibitors of cytochrome P450 enzymes are unlikely.

Efficacy
In field studies lasting up to 3 months, treatment of dogs with osteoarthritis was demonstrated to have a favourable effect on the reduction of pain assessed by the Canine Brief Pain Inventory (CBPI). CBPI is an assessment by the animal owner of an individual dog's response to pain treatment as assessed by pain severity (scale of 0 to 10, where 0 = no pain and 10 = extreme pain), interference of pain with the dog's typical activities (scale of 0 to 10, where 0 = no interference and 10 = completely interferes) and quality of life. In the pivotal EU multi-centre field study, 43.5% of the BERANSA-treated dogs and 16.9% of the placebo-treated dogs demonstrated treatment success, defined as a reduction of ≥1 in pain severity score (PSS) and ≥2 in pain interference score (PIS), on day 28 after the first dose. An onset of efficacy was demonstrated at 7 days post administration, with treatment success demonstrated in 17.8% of the BERANSA-treated dogs and 3.8% of the placebo-treated dogs. Treatment with bedinvetmab has demonstrated a positive effect on all three components of the CBPI. Data from an uncontrolled follow-up study lasting up to 9 months indicated sustained efficacy of treatment.

Duration of treatment should be based on the individual response of each animal. If a positive response is not observed, consider alternative treatments.

	Immunogenicity In field studies of dogs with osteoarthritis receiving BERANSA once monthly, the appearance of anti-bedinvetmab antibodies was very infrequent. None of the dogs exhibited any adverse clinical signs considered to be associated with binding antibodies to bedinvetmab. Safety No adverse reactions, except mild reactions at the injection site, were observed in a laboratory overdose study when BERANSA was administered for 7 consecutive monthly doses at 10 times the maximum recommended dose. In case of adverse clinical signs after an overdose the dog should be treated symptomatically. Immunomodulation Across multiple studies, BERANSA recipients did not show increases in incidence, severity, duration, or responsiveness to treatment/management of background or incidental diseases. It was concluded that there was no adverse immunomodulation in dogs and that responsiveness to vaccine antigens was normal.

Withholding Periods:	

Trade Advice:	

Safety Directions:	Pregnant women, women trying to conceive, and breastfeeding women should take extreme care to avoid accidental self-injection or needle stick injuries. Consult a medical practitioner if such an injection occurs. Wash hands after use.

First Aid Instructions:	If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 131126.

First Aid Warnings:	

Additional User Safety:	Take care to avoid self-injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or label to the Medical Practitioner. For pregnant women, women trying to conceive, and breastfeeding women, the importance of Nerve Growth Factor in ensuring normal foetal nervous system development is well-established and laboratory studies conducted on non-human primates with human anti-NGF antibodies have shown evidence of reproductive and developmental toxicity. Pregnant women, women trying to conceive, and breastfeeding women should take extreme care to avoid accidental self-injection or needle stick injuries. Consult a medical practitioner if such an injection occurs. Hypersensitivity reactions, including anaphylaxis, could potentially occur in the case of accidental self-injection. Repeated self-administration may increase the risk of hypersensitivity reactions. Wash hands after use.

Environmental Statements:	

Disposal:	Dispose of empty containers by wrapping with paper and putting in garbage. Discarded needles should immediately be placed in a designated and appropriately labelled ‘sharps’ container.

Storage:	Store between 2 °C and 8 °C (refrigerate, do not freeze). Store in the original package. Protect from light. Avoid excessive shaking.

Beransa Solution for Injection for Dogs
Dosage and Administration

	BERANSA strength (mg) to be administered				
Bodyweight (kg)	5	10	15	20	30
5.0 - 10.0	1 vial				
10.1 - 20.0		1 vial			
20.1 - 30.0			1 vial		
30.1 - 40.0				1 vial	
40.1 - 60.0					1 vial
60.1 - 80.0				2 vials	
80.1 - 100.0				1 vial	1 vial
100.1 - 120.00					2 vials