

# INFORMATION FOR PRESCRIBERS & INSTRUCTIONS FOR USE REGENESIS VET™ R.I.A.D™

## SYSTEM DESCRIPTION

Regenes Vet™ Recombinant Inflammatory Antagonist Diluent™ (R.I.A.D™) is a targeted cytokine therapy product developed through a proprietary, provisionally-patented system of processing autologous blood. Through this, a natural (non-doping) product is derived that leverages off the body's ability to heal itself. Please note, Regenes Vet™ R.I.A.D™ is the first product of its kind worldwide and is fundamentally different to other commercially available orthobiologic products such as IRAP, PRP, Platelet Lysate, Stem Cells etc. Medical Device law restricts the use of Regenes Vet™ R.I.A.D™ to licensed veterinarians only.

Although autologous blood products are generally considered very safe, with any medical procedure, there is always the risk of side effects. As with many treatments, Regenes Vet™ R.I.A.D™ can illicit an immune response within the horse's body and as such, although uncommon, minor side effects can occur. It is for this reason that it is imperative that your vet is involved in the administration of any and all treatments such that should any side effects occur, they can be appropriately managed. There are however various steps that can be taken to reduce the chance of side effects occurring which are outlined later in this document.

## INDICATIONS FOR USE

The Regenes Vet™ R.I.A.D™ processing kit is intended to be used for the easy and fast preparation of a unique systemic autologous blood product treatment from a sample of blood collected at the patients point of care. The end product is intended to help with injury healing and overall recovery through targeting a 4-6 very specific anti-inflammatory cytokines that are instrumental in the healing, recovery and longevity cascades.

## CONTRAINDICATIONS

- DO NOT ADMINISTER REGENESIS VET™ R.I.A.D™ WITHIN 21 DAYS OF AN AFRICAN HORSE SICKNESS (AHS) VACCINE OR WITHIN 14 DAYS OF ANY OTHER VACCINE.
- TO BE ADMINISTERED BY A LICENSED VETERINARIAN ONLY.
- Do not administer Regenes Vet™ R.I.A.D™ to horses with a known hypersensitivity to anticoagulants.
- Do not exceed the recommended speed/rate of administration.
- Do not administer Regenes Vet™ R.I.A.D™ to horses that have or are suspected to have an underlying infection and/or virus.
- Do not administer Regenes Vet™ R.I.A.D™ to horses with conditions affecting mineral or electrolyte balance (Hyperkalemic periodic paralysis, hypocalcemia etc.).
- Do not administer Regenes Vet™ R.I.A.D™ to horses with conditions that may be aggravated by hypocalcemia (e.g. cardiac disease).
- Take caution when using Regenes Vet™ R.I.A.D™ in a horse with impaired renal function or with a history of renal disease.
- Do not administer Regenes Vet™ R.I.A.D™ to horses that have Hyperkalemic periodic paralysis (HYPP) or suspected HYPP.
- Do not administer Regenes Vet™ R.I.A.D™ to horses that are or are suspected to be Hypocalcaemic.
- Do not administer Regenes Vet™ R.I.A.D™ to horses that are or are suspected to be Hyperkalemic.
- Take caution when administering Regenes Vet™ R.I.A.D™ to horses that have underlying pathology (e.g. a tying-up predisposition).
- Do not administer a Regenes Vet™ R.I.A.D™ treatment that has or may have been defrosted and refrozen. A compromised cold chain may affect the quality and sterility of the product.
- Regenes Vet™ R.I.A.D™ should be used with caution in horses receiving concurrent administration of other drugs that may reduce serum calcium (such as tetracyclines) or whose toxicity may exacerbate a reduction in serum calcium (such as aminoglycosides).
- The safety of Regenes Vet™ R.I.A.D™ has not been established in pregnant or lactating mares.
- The safety of Regenes Vet™ R.I.A.D™ has not been established when administered concurrently with other medications

## POSSIBLE SIDE EFFECTS & ADVERSE EVENTS

Although uncommon, adverse reactions can happen following the administration of Regenes Vet™ R.I.A.D™. Retrospective blood tests indicate that in majority of adverse events (>70%) the presence of a subclinical underlying virus and/or infection in the horse's body was detected.

The administration of Regenes Vet™ R.I.A.D™ may affect the plasma concentrations of various electrolytes such as potassium,

calcium and magnesium. This can happen immediately following treatment or up to several hours post treatment. For this reason, caution should be used when administering Regenes Vet™ R.I.A.D™ to horses with conditions affecting electrolyte balance (Hypocalcemia, Hyperkalemia, hyperkalemic periodic paralysis etc.). Resultantly, Adverse events can happen following intravenous and intramuscular administration. Typically, adverse events occur within 10-30 minutes following intravenous injection, whilst adverse events following intramuscular injections may take slightly longer for clinical signs to develop. For this reason it is strongly recommended that horses receiving Regenes Vet™ R.I.A.D™ for the first time, or horses that have proven to be sensitive to the product via intravenous administration, are premedicated with Buscopan prior to treatment. Horses should also be hand-walked for 15-20 minutes immediately following the administration Regenes Vet™ R.I.A.D™.

Horses may demonstrate transient signs consistent with abdominal discomfort/ cramping following the IV administration of Regenes Vet™ R.I.A.D™. This is believed to be due to a mild hypocalcaemic effect. Clinical signs usually occur shortly after the administration of Regenes Vet™ R.I.A.D™ and may be associated with a mild abdominal cramping. Horses should be observed closely for 2-4 hours post treatment for the development of any of the abovementioned signs or other adverse reactions. Should any cramping or colic-like symptoms occur, they are usually mild in nature and resolve sporadically. More-often than not, hand-walking the horse for 15-20 minutes may improve or resolve such symptoms. Should a horse require medical treatment for any side effect or reaction, non-NSAID treatments should be administered where possible due to the potential interference of NSAIDs with the cyclooxygenase of platelets and their related growth factors. Please contact your vet immediately should your horse develop any abnormal clinical signs or behaviour.

Although uncommon, side effects following intramuscular injection have also been reported. These include but are not limited to; injection site swelling/hematoma, muscle fasciculation's, sweating, increased respiratory rate and heart rate, lethargy, mild ataxia and in rare cases tying-up-like reactions.

It is imperative that horses are closely monitored after the administration of Regenes Vet™ R.I.A.D™ for at least 2 hours. Should any side effects occur, they usually are very mild and can be resolved with proactive management such as hand walking or treated by your veterinarian if necessary. Side effects that are not detected from unmonitored horses may get progressively worse if left unnoticed. Should you notice any abnormal behaviour following the administration of Regenes Vet™ R.I.A.D™, please contact your vet immediately.

Avoiding injecting too close to a vaccine, slower injection rates and having a horse that is well-hydrated and free from underlying issues seem to significantly reduce the incidence of adverse reactions. Please familiarize yourself with the measures outlined above that can be taken prior to and following the administration of Regenes Vet™ R.I.A.D™ to reduce the chance of an adverse event.

## REPORTING OF ADVERSE EVENTS

To report suspected adverse events please contact Novita Biotechnology™ on info@novita-biotech.com or info@regenesvet.com.

## HOW SUPPLIED

Regenes Vet™ R.I.A.D™ processing kit is supplied as a sterile, disposable kit.

COMPONENT	QTY. IN KIT	STERILISATION METHOD
Disposable Blister tray unit	1	Ethylene oxide
R.I.A.D Glass Processing tubes	6	Gamma radiation
R.I.A.D Final treatment glass vials	2	Steam
Final treatment Freezer packet	1	Ethylene oxide
Alcohol swabs	4	Ethylene oxide or Gamma Radiation
Instructions for use	1	Non-sterile

**NOTE:** The contents of the Disposable kit are for single use only.

## WARNINGS

- Failure to use this device as directed by the instructions for use may result in device failure or compromised safety.
- Inspect the kit prior to use. If the package is open or damaged then the sterility of some products may be compromised.
- Do not use the kit after the expiration date.
- Do not reuse, re-sterilize or reprocess any of the kit components as this could lead to failure and/or contamination of the device. This in turn could lead to patient illness or injury.

- Do not use processing tubes if the liquid above or below the gel separation filter become discoloured or form precipitates.
- Excessive centrifugation speed (over 1900 RCF) may result in tube breakage, exposure to blood and possible injury.
- Use aseptic technique as applicable.
- Discard all disposable kit components using acceptable disposal method for blood-contaminated products.

## PRECAUTIONS

- The Regenes Vet™ R.I.A.D™ kit should be stored upright at all times to avoid leaking of the filter.
- Any and all Regenes Vet™ R.I.A.D™ products should be processed in a centrifuge that is operated on a level and stable surface.
- The end product should be stored in the provided pre-sterilized glass vials. It should not be stored in the provided processing tubes. Should additional pre-sterilized vials be required, they can be purchased directly from the company.
- Do not process materials other than whole blood.
- All glass has the potential for breakage. Precautionary measures should therefore be taken during handling of any and all glass components.
- All processing tubes should be filled gently and slowly. Forcefully depressing the syringe plunger without simultaneously removing air from the tube may create positive pressure in the tube causing the stopper and specimen to fly out with explosive force.

## INSTRUCTIONS FOR USE

**CAUTION:** Medical Device law restricts this device to sale by or on the order of a properly licensed veterinarian.

**CAUTION:** Use aseptic technique as applicable.

## PRIOR TO PROCESSING REGENESIS VET™ R.I.A.D™

- Ensure horse has not received NSAIDs for at least 3 days prior to the processing of Regenes Vet™ R.I.A.D™. NSAIDs interfere with the cyclooxygenase of platelets that the related growth factors are harvested from and as such NSAIDs may affect the quality of the end product.
- Take caution when processing Regenes Vet™ R.I.A.D™ if the horse has or is suspected to have an underlying infection and/or virus as this may contaminate treatments spun for later use.
- Horses temperatures should always be checked prior to the processing of Regenes Vet™ R.I.A.D™.
- Ensure that there are no unwanted drugs in the horse's system when the product is processed as trace amounts may be present in processed treatments which could have unwanted doping-related consequences.
- Regenes Vet™ R.I.A.D™ must only be used on the same horse from which blood was drawn.

## PREPARING FOR BLOOD COLLECTION

- Select a 60mL syringe (or 3 x 20mL syringe) with an 18G needle.
- Wear gloves at all times.
- Aseptic technique should be followed throughout the processing procedure.
- Prepare the skin of the horse for blood collection;
  - Use 2 separate swabs with surgical spirit to wipe the skin twice at the blood collection site.
  - If the horse has long hair clip the blood collection area and swipe with surgical spirit twice after.
- Approximately 20 mL of blood is required for one Regenes Vet™ R.I.A.D™ treatment.
- For one treatment 20mL of blood needs to be drawn. For three treatments draw 60mL of blood.

## PREPARING REGENESIS VET™ R.I.A.D™ PROCESSING TUBES

- Take the 60mL syringe with the blood and replace the 18G needle with a 21G needle.
- Take a Regenes Vet™ R.I.A.D™ processing tube and press the needle through the cap.
- Let the syringe empty and press the syringe slightly till the moment the pressure gets to the point that further emptying is not possible. Tubes should be filled until there is approximately 1cm left between the blood level in the tube and the bottom of the tube cap.
- Due to the nature of the product, limited vacuum exists inside the tube. Therefore, all processing tubes should be filled gently

and slowly. Forcefully depressing the syringe plunger without simultaneously removing air from the tube may create positive pressure in the tube causing the stopper and specimen to fly out with explosive force.

- Remove the syringe and with the needle and fill the next tube.
- When a syringe only partly fills the collection tube, remove the empty syringe with needle and use a full syringe with blood to fill up the tube.
- After filling the tubes, gently invert the tubes 8-10 times up and down.
- Before centrifugation, clean the cap of the tubes with an alcohol swab or surgical spirits.
- The tube needs to be processed within 30-45 minutes of collection.

#### USING THE CENTRIFUGE

- The use of the DigiSystem Centrifuge provided by Regenesis Vet™ is advised.
- Make sure the centrifuge is placed on a level and firm surface.
- Place the tubes in the centrifuge. Always 'in balance' or opposite each other.
- Close the lid.
- Set the centrifuge on 12 minutes on 2400rpm (setting 8-8.5) for Digi System centrifuge.
- The RCF & RPM speed for other centrifuges can be calculated as follows:

$$\text{RPM Speed Setting} = \sqrt{\frac{(\text{RCF}) \times (100\,000)}{(1.12)(r)}}$$

Where "r" (expressed in centimetres) is the length from the centre post of the centrifuge to the bottom of the tube, when the tube is in the horizontal position and the RCF is the desired centrifugal force.

RCF = G force = 1 600 (this is the desired centrifugal force for the Regenesis Vet™ system, should you use a different centrifuge please calculate the necessary RPM for your machine based off a target RCF of 1600).

- CAUTION:** If the glass processing tubes that have cracks or chips in them are used or if tubes are spun at excessive speeds, the processing tubes may break causing the release of sample and/or droplets into the centrifuge bowl.

Centrifuge carriers and inserts should be of the same size and specific to the tubes used. Carriers that are too large or too small for the tube may result in breakage. Tubes should always be 'in balance' in the centrifuge to minimize the possibility of glass breakage. Ensure that the centrifuge comes to a complete stop before attempting to remove any of the processing tubes. Once the centrifuge head has stopped, examine carefully for the presence of any broken tubes. Should any broken tubes be present, do not remove them by hand. Broken tubes should be removed with mechanical devices such as forceps.

#### PREPARING REGENESIS VET™ R.I.A.D™ TREATMENT

- Empty the Regenesis Vet™ R.I.A.D™ collection tube by turning the tube upside down and retract the product using a 20mL syringe with 21G needle.
- Empty the syringe in the presterilized glass product vial.
- Every Regenesis Vet™ R.I.A.D™ treatment vial should contain at least 15 mL of product.
- Label the vial with the correct patient details, date and number of sequence.
- Deep freeze Regenesis Vet™ R.I.A.D™ within 2 hours of processing.
- Each full treatment kit contains 6 processing tubes and 2 glass vials and assumes the first treatment will be given immediately after processing. Should all 3 treatments need to be frozen, the final treatment can be stored and frozen in an unused 20mL syringe or an additional 20mL R.I.A.D™ vial.
- Regenesis Vet™ R.I.A.D™ can be kept for 24 months if kept frozen.
- Frozen Regenesis Vet™ R.I.A.D™ should be defrosted at room temperature for approximately 60 minutes before use. Do not administer the product until it is at room temperature.

#### DOSING & ADMINISTRATION

##### PRIOR TO ADMINISTERING REGENESIS VET™ R.I.A.D™

- It is strongly advised that horses receiving Regenesis Vet™ R.I.A.D™ for the first time, or horses that have proven to be sensitive to the product via intravenous administration, are premedicated with Buscopan.
- Ensure the horse is well hydrated prior to receiving Regenesis Vet™ R.I.A.D™ and has unrestricted access to water.

- Horses temperatures should always be checked prior to your vet administering Regenesis Vet™ R.I.A.D™.
- Where possible, Regenesis Vet™ R.I.A.D™ should be administered before the horse is exercised. Do not exercise the horse for at least 60 minutes after the administration of Regenesis Vet™ R.I.A.D™.
- Ideally, Regenesis Vet™ should NOT be administered within 4 hours following exercise due to the possibility of increased Potassium levels following exercise.
- Do NOT administer Regenesis Vet™ R.I.A.D™ if your horse has or is suspected to have an underlying infection or virus.
- Do not administer Regenesis Vet™ R.I.A.D™ to horses with conditions affecting mineral or electrolyte balance.
- Take caution when administering Regenesis Vet™ R.I.A.D™ to horses with diarrhea as this could affect their electrolyte balance.
- DO NOT ADMINISTER REGENESIS VET™ R.I.A.D™ WITHIN 21 DAYS OF AN AFRICAN HORSE SICKNESS (AHS) VACCINE OR WITHIN 14 DAYS OF ANY OTHER VACCINE.

##### DURING THE ADMINISTRATION OF REGENESIS VET™ R.I.A.D™

- Ensure the horse is calm and well hydrated.
- Each Regenesis Vet™ R.I.A.D™ treatment should be 15-20mL in volume.
- Normal sterility standards should be adhered to when administering Regenesis Vet™ R.I.A.D™.
- Please familiarize yourself with the full list of warnings and contraindications in the prescribing information before proceeding with treatment.
- Intravenous administration
  - Regenesis Vet™ R.I.A.D™ should be administered very slowly and evenly at a rate no faster than 1mL/4 seconds via intravenous route of administration.
  - PLEASE NOTE: Faster injection rates increase the risk of an adverse event.
- Intramuscular administration
  - Regenesis Vet™ R.I.A.D™ should be administered very slowly and evenly at a rate no faster than 1mL/2 seconds via intramuscular route of administration.
  - The full treatment can be split evenly and injected at 2 different injection sites.
- DO NOT ADMINISTER REGENESIS VET™ R.I.A.D™ WITHIN 21 DAYS OF AN AFRICAN HORSE SICKNESS (AHS) VACCINE OR WITHIN 14 DAYS OF ANY OTHER VACCINE.
- TO BE ADMINISTERED BY A LICENSED VETERINARIAN ONLY.

##### FOLLOWING THE ADMINISTRATION OF REGENESIS VET™ R.I.A.D™

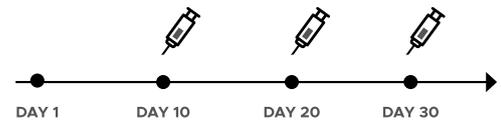
- Horses should be hand walked for 15-20 immediately following the administration of Regenesis Vet™ R.I.A.D™.
- Horses should be observed closely for at least 2 hours after the administration of Regenesis Vet™ R.I.A.D™ for signs of abdominal discomfort or abnormal behaviour.
- Contact your veterinarian if your horse displays any abnormal clinical signs following the administration of Regenesis Vet™ R.I.A.D™ or if you suspect your horse may be having an adverse reaction.
- Do not exercise the horse for at least 60 minutes after the administration of Regenesis Vet™ R.I.A.D™.
- If your horse appears uncomfortable, nervous, or experiences abdominal cramping post-treatment, hand walk the horse for 15-20 minutes. If signs do not resolve contact your veterinarian.
- Should a horse require medical treatment for any side effect or reaction following the administration of Regenesis Vet™ R.I.A.D™, non-NSAID treatments should be administered as far possible due to the interference of NSAIDs with the cyclooxygenase of platelets and their related growth factors.
- Please note Regenesis Vet™ R.I.A.D™ is not something that has an immediate effect. Improvement is most commonly reported from 7-10 days following the administration of Regenesis Vet™ R.I.A.D™.
- Please avoid the administration of NSAIDs as far as possible for at least 3 days following the administration of Regenesis Vet™ R.I.A.D™ as it may interfere with the efficacy of the product.

#### RECOMMENDED FREQUENCY OF DOSING

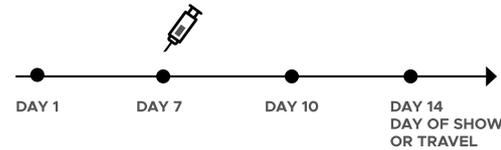
**MAINTENANCE:** 1 x injection on a monthly basis



**INJURY:** 1 x injection every 10 days for 3 injections



**PRE-SHOW TRAVEL:** 7-10 days before show or travel



#### AFRICAN HORSE SICKNESS VACCINE



#### TRANSPORT & STORAGE

- The Regenesis Vet™ R.I.A.D™ kit should be stored at room temperature (18-25°C) out of direct sunlight.
- Self-life is 2 years from the date of manufacture.
- Due to the temperature sensitivity of the product, kits that are not stored as directed may be compromised and therefore not work as desired.
- The disposable Regenesis Vet™ R.I.A.D™ processing kit should be stored in its original unopened packaging.

#### Final product storage

- Do NOT defrost and refreeze. Interruption of the cold chain can compromise the quality and sterility of the product.
- Product should be used within 24 months of processing date.

#### Explanation of Symbols on packaging:

	Lot number
	Expiry date
	Manufacturer
	Sterile
	Sterile using irradiation
	Sterilized using ethylene oxide
	Consult instructions for use
	Do not reuse
	Caution
	Do not use if package is damaged
	Store at room temperature out of direct sunlight
	Caution: Medical device law restricts this device to sale by or on the order of a properly licensed practitioner

#### REPORTING OF ADVERSE EVENTS

To report suspected adverse events please contact Novita Biotechnology on [info@novita-biotech.com](mailto:info@novita-biotech.com) or [info@regenesisvet.com](mailto:info@regenesisvet.com).

#### TERMS & CONDITIONS OF TRADE

Regenesis Vet™ is a product of Novita Biotechnology (Pty) Ltd. Novita Biotechnology's Terms & Conditions of Trade applies to all Regenesis Vet™ products and treatments. Terms & Conditions of trade available at [www.novita-biotech.com](http://www.novita-biotech.com) & [www.regenesisvet.com](http://www.regenesisvet.com).

#### MANUFACTURED FOR:

Novita Biotechnology (Pty) Ltd, 28 Brommaert Avenue, Cape Town, 7806, South Africa | SAHPRA: 00001494MD

South African Provisional Patent Number: 2021/07349 | [www.novita-biotech.com](http://www.novita-biotech.com) | [www.regenesisvet.com](http://www.regenesisvet.com)

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