PrecisePRP™ Equine
Equine leucoreduced allogeneic pooled freeze-dried platelet-rich plasma
VetStem, Inc.

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For intra-articular injection in horses only

4.0 x 10^9 equine platelets / vial, freeze-dried
< 1500 white blood cells / µL

Single patient use vial for rehydration to 8 mL with sterile water

A freeze-dried species-specific source of concentrated platelets in plasma

CAUTION:

Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION:

PrecisePRP™ Equine is a leucoreduced allogeneic, pooled freeze-dried, platelet-rich plasma product from up to 18 equine donors. The biological source material for this product is in-date, apheresis-derived equine platelet concentrates leucoreduced to less than 1500 white blood cells per µL and apheresis-derived frozen plasma. All horses are blood type AaCa positive and negative for plasma antibodies (A,C,K,P,Q,U, and D) . Donors are from a closed herd compliant with USDA regulations for production of licensed biologics. Donors are selected and evaluated for infectious disease in accordance with FDA CVM Guidance #254. Supplied in a 50 mL glass vial, this product is a sterile, nonpyrogenic white-to-tan powder. Once rehydrated with 8 mL of sterile water for injection, this product is a gold translucent fluid with 4.0 x 10^9 platelets per vial and less than 1500 white blood cells per µL.

INDICATION:

PrecisePRP™ Equine is intended to provide a species-specific source of concentrated platelets in plasma for intra-articular administration.

DOSAGE AND ADMINISTRATION:

PrecisePRP™ Equine is for intra-articular administration only. One vial provides 8 mL of leucoreduced allogeneic pooled freeze-dried platelet-rich plasma with a total of approximately 4 x 10^9 equine platelets per vial and less than 1500 white blood cells per µL. Do not mix this product with other products or solutions. Use this product according to the instructions below.

Rehydration instructions (Perform Aseptically):

- Draw 8 milliliters of sterile water into a sterile syringe and needle.
- Apply the supplied vented administration clave to the **PrecisePRP™ Equine** vial and firmly seat it on the crimped seal.
- Disengage the needle and, using sterile technique, attach the syringe to the clave hub.
- Slowly add the sterile water down the side of the vial lumen to avoid foaming and immerse the cake in the rehydrating fluid.
- Gently mix the fluid and the lyophilized powder by swirling the vial to rehydrate.
- Draw into a syringe using the bidirectional clave.
- Engage a needle greater than or equal to 22 gauge for administration.
- Store at room temperature (18-25℃) until administration for not more than four (4) hours.
- Discard the excess product.

Dosage:
Dosage is lesion dependent and determined by the practitioner at the time of use. Each microliter of **PrecisePRP™ Equine** contains 500,000 +/- 100,000 platelets and less than 1500 white blood cells. The dose given may be adjusted based on the size of the joint to be injected. As a general rule, the dosage per joint should be 2-4 mL

CONTRAINDICATIONS:

Do not use in horses with known hypersensitivity to **PrecisePRP™ Equine**.

WARNINGS:

For use in horses only. Not for use in humans. Keep out of reach of children. Rehydrated **PrecisePRP™ Equine** should be used within 4 hours of rehydration.

PRECAUTIONS:

PrecisePRP™ Equine has only been tested in mature adult horses.

PrecisePRP™ Equine has not been evaluated in breeding, pregnant, or lactating horses.

PrecisePRP™ Equine is not intended for intravenous administration.

PrecisePRP™ Equine has not been tested in donkeys or mules.

ADVERSE REACTIONS:

PrecisePRP™ Equine is made using platelets and plasma from up to 18 Equine donors and, as with all blood products, has a risk of infectious disease. Donor maintenance includes routine screening for pathogens by PCR and ELISA testing.

In a placebo-controlled study of 12 adult horses, **PrecisePRP™ Equine** was tested at the label dose of 4 mL per joint in two consecutive joint injections two weeks apart. The horses were monitored for treatment-related effects on gait, daily health observations, temperature, pulse, respiration, clinical pathology, injection sites, veterinary physical exams and the reported adverse events by treatment group are reported in **Table 1**.

Table 1. Adverse events reported in the placebo-controlled safety study

Adverse Event	PrecisePRP™ Equine (N=6)	Saline Placebo (N=6)
Mild transient lameness post-injection	1	4
Colic	0	1

The mild lameness reported resolved within 1 day in the **PrecisePRP™** group and within 1-2 days in the Placebo group.

Published safety data exists for both canine and equine allogeneic platelet-rich plasma. Clinical case reports, systemic literature reviews, preclinical safety analysis, and comparative studies with autologous platelet-rich plasma and mesenchymal stem cells are available for the horse and dog. In the safety evaluation of equine platelet-rich plasma published by Garbin[1], a pooled allogeneic freeze-dried platelet-rich plasma was evaluated with autologous frozen products for safety and found to be statistically unremarkable from autologous products relating to inflammation and lameness post injection. In an Italian clinical trial in canine patients, no adverse events associated with immunogenicity were noted utilizing a pooled allogeneic platelet-rich plasma[2].

Report any suspected adverse reactions associated with the use of **PrecisePRP™ Equine** to VetStem Customer Service by calling 858-748-2004. For additional information about adverse drug experience reporting animal drugs, contact FDA at 1-888-FDA-VETS or visit http://www.fda.gov/animalveterinary/safetyhealth.

INFORMATION FOR HORSE OWNERS:

Owners of patients should be made aware of the use of allogeneic blood products and their possible side effects. Adverse reactions may include joint pain for several days following injection, transient inflammation and swelling in the injected joint, and joint infections and transmission of disease agents from donor animals.

CLINICAL PHARMACOLOGY:

Platelet-rich plasma has been studied in multiple species with varying use profiles. A thorough review of the literature yielded over 30 references in support of platelet-rich plasma and its use as a topical, intraarticular and/or intralesional therapy published since 2008. Meta-analysis in human clinical trials as well as multiple study reviews in canine and equine suggest that the most common concern for platelet-rich plasma effectiveness is associated with a lack of uniformity and standardization[3, 4]. Important components of platelet-rich plasma have been debated; however, total platelet dose, growth factor content, and leucocyte count appear to be common factors for most authors when relating in vitro characterization and effectiveness outcomes[5]. Review of the veterinary literature was used to support both potential indications as well as dose and administration.

Platelets are provided to supply the growth factors and cytokines located in the alpha granules. After administration, the growth factors and cytokines are released into the area of injection and provide anti-inflammatory cytokines and repair signaling. Platelets also release factors that attract mesenchymal stem cells, leucocytes, and other mononuclear immune cells to assist in the repair process. It has been reported that platelet-rich plasma injected reduces pain signaling.

Recently, the discussion of platelet phenotypes and their relationships to platelet function, circulation, and membrane characteristic have led to the exploration of new methods for platelet concentrate storage, including storage at 4-8°C. Current published uses of platelet-rich plasma in the canine and equine support that it can be used intra-articularly, intralesionally, or topically and should be activated to allow the release of dense and alpha granules. Cold-stored platelets have been characterized as moderately activated as compared to room temperature-stored platelets. Recent in vitro characterization of the cold-stored platelets supports that their phenotype is most consistent with the desired function of platelet-rich plasma[6]. Manipulating the storage parameter for platelet concentrates prior to pooling and lyophilization allows platelet lyophilization without cryopreservatives (VetStem pilot data, 2022).

SAFETY:

PrecisePRP™ Equine was studied in a randomized, masked, placebo-controlled target animal safety study of 12 (adult horses) at the label dose of 4 mL in comparison to a blinded control group injected with 4 mL of placebo saline. The horses were injected in one radiocarpal joint and one tarsocrural joint, with the injections being two weeks apart. Horses were followed for seven days after each injection and monitored for clinical and laboratory safety of the **PrecisePRP™ Equine** injections. This study was conducted with a formal IACUC approval and was conducted at an independent veterinary school testing facility.

There were no treatment-related adverse reactions reported. The study included evaluations of daily health, temperature, pulse, respiration, clinical pathology, injection sites reactions (heat, swelling, passive flexion pain and joint circumference), veterinary physical exams, and lameness evaluations. A single adverse event in the placebo group was reported as colic, which resolved within one day. The above adverse event **Table 1** shows that four control horses and one treated horse had mild transient lameness.

STORAGE CONDITIONS:

Store the lyophilized **PrecisePRP™ Equine** at room temperature (18-25°C). Current expiration dating is two years from manufacturing date. Use the rehydrated **PrecisePRP™ Equine** within 4 hours of rehydration.

HOW SUPPLIED:

PrecisePRP™ Equine is supplied as a freeze-dried product in a 50 mL vial. Each vial contains approximately 4 x 10^9 equine platelets at a concentration of 500,000 +/- 100,000 platelets per µL and less than 1500 white blood cells per µL.

Manufactured By:

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1-858-748-2004

REFERENCES:

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3. Everts, P.A., et al., *Modifying Orthobiological PRP Therapies Are Imperative for the Advancement of Treatment Outcomes in Musculoskeletal Pathologies.* Biomedicines, 2022. **10**(11).
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6. Zhao, H.Q., et al., *Cold-stored platelets are effective in an in vitro model of massive transfusion protocol assessed by rotational thromboelastometry.* Transfusion, 2022. **62 Suppl 1**: p. S53-S62.

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Patent Pending

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