

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

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Leucoreduced allogeneic pooled freeze-dried platelet-rich plasma

For intra-articular injection in horses only

4.0 x 10⁹ equine platelets / vial, freeze-dried

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 leucoreduced, apheresis-derived equine platelet concentrates and apheresis-derived frozen plasma. All horses are blood type AaCa positive and negative for plasma antibodies directed at blood types they are not. Donors are from a closed herd compliant with USDA regulations for production of licensed biologics. Selection of donors and evaluation for infectious disease is compliant 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 10⁹ 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 10⁹ equine platelets per vial. Do not mix this product with other products or solutions. Use this product according to the instructions below.

Rehydration instructions:

- 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°C) until administration for not more than four (4) hours.
- Discard the excess product.

Dosage:

For use in regenerative medicine, 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. 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 Please refer to the references on the VetStem website (www.vetstem.com) for additional published recommendations of dosing.

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 not been tested in animals under 9 months of age.

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. Please see the VetStem website for a complete listing of pathogens tested for each donor (www.vetstem.com).

In a placebo-controlled study of 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. These were attributed to the needle injection effect.

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].

All infections and/or reactions thought by the veterinarian to have been associated with the use of **PrecisePRP™ Equine** should be reported 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.

CLINICAL PHARMACOLOGY:

Platelet-rich plasma has been studied in multiple species with varying use profiles. A thorough review of the platelet-rich plasma literature yielded over 30 references in support of this product 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 (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 attributed to the needle injection procedure.

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 4×10^9 equine platelets at a concentration of 500,000 +/- 100,000 platelets per μL .

Manufactured By:

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1-858-748-2004

REFERENCES:

1. Garbin, L.C., et al., *A safety evaluation of allogeneic freeze-dried platelet-rich plasma or conditioned serum compared to autologous frozen products equivalents in equine healthy joints*. BMC Vet Res, 2022. **18**(1): p. 141.
2. Catarino, J., et al., *Treatment of canine osteoarthritis with allogeneic platelet-rich plasma: review of five cases*. Open Vet J, 2020. **10**(2): p. 226-231.
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).
4. Garbin LC, et al., (2021), *A Critical Overview of the Use of Platelet-Rich Plasma in Equine Medicine Over the Last Decade*. Front. Vet. Sci. 8:641818.
5. McCarrel, T. and L. Fortier, *Temporal growth factor release from platelet-rich plasma, trehalose lyophilized platelets, and bone marrow aspirate and their effect on tendon and ligament gene expression*. J Orthop Res, 2009. **27**(8): p. 1033-42.
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

Revised 21 Jun 2023
6235-0003-001-4251

