Tildren®

(tiludronate disodium)

Bisphosphonate drug for intravenous infusion

Turning heartache into hope.

Providing lasting relief for your horse with Navicular syndrome.

- ✓ *Control clinical signs*
- ✓ *Effective*
- ✓ *Long-lasting*
- ✓ *Safe*

Global Excellence in Animal Health

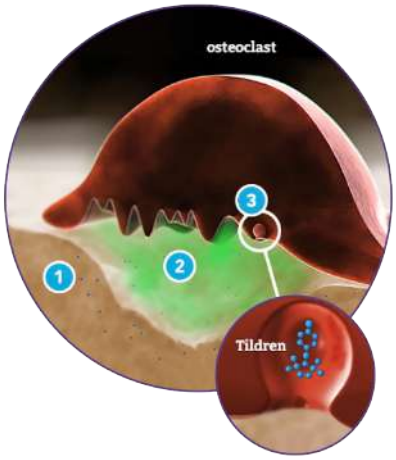
Bimeda®

What Causes Navicular Syndrome?

Navicular syndrome is caused by a disruption in the normal bone remodeling process. Bone absorption by osteoclasts starts outpacing bone rebuilding by osteoblasts, leading to degeneration and lesions of the navicular bone.

Bone Resorption

The primary action of Tildren® is to regulate osteoclasts in the areas of excessive activity. Following IV infusion, Tildren® travels systemically and binds to the mineral matrix of the bone. The acidity of the remodeling environment causes the release of Tildren® from the bone matrix into the resorption space. This leads to improved bone remodeling, decreased mineral loss, and alleviation of pain induced by abnormal osteolysis.



1. Tildren® binds preferentially to the mineral phase of the bone at remodeling sites.
2. Acidification breaks the bond.
3. Tildren® is taken into the osteoclast by endocytosis.

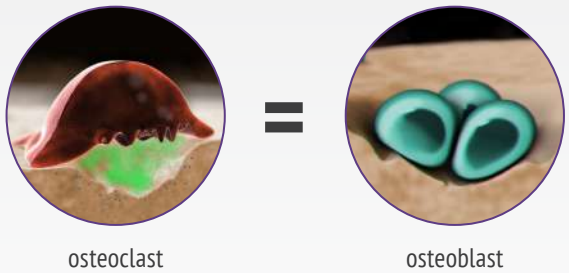
See Tildren® at Work:

In navicular syndrome, excessive mechanical stress results in bone resorption outpacing bone formation.

Tildren® *(tiludronate disodium)* restores balance to the process of bone remodeling by partially inhibiting bone resorption by:

1. Modulating excessive osteoclastic activity
2. Not modifying osteoblastic activity
3. Slowing the rate of bone turnover

By modulating excessive osteoclastic activity, bone remodeling can normalize.



Balance Restored

Tildren restores balance to the process of bone remodeling.

The Proven Effectiveness of Tildren®

The active ingredient in Tildren® is tiludronate disodium, a bisphosphonate that regulates osteoclasts in areas of excessive activity.

1. Tildren® is administered via intravenous infusion over a 90-minute period, quickly binding to the mineral matrix of the bone.
2. The acidity of the remodeling environment releases Tildren® from the bone matrix, where it is then taken into the osteoclast.
3. Once inside, Tildren® inhibits the bone re-absorption process and kills off excess osteoclasts.

Safe and Long-lasting Relief

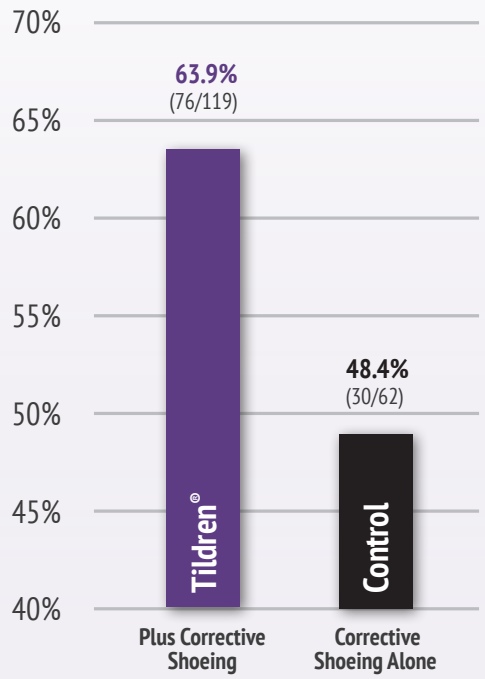
A single 500 mg vial treats horses up to 1,210 lb.

Controlled administration – Reconstituted with 0.9% sodium chloride solution and administered through intravenous infusion over the course of 90 minutes.

Safe – Limited and transient side effects when used according to label.

Long-lasting relief – A single treatment lasts up to six months.

Success at Two Months Post-Treatment



In conjunction with corrective shoeing, Tildren® has been proven to be more effective in controlling the clinical signs of navicular syndrome than corrective shoeing alone.[1]

[1] When given at 1mg/kg IV and evaluated 2 months post-treatment. Freedom of Information Summary, NADA #141-420. Approved February 13, 2014.

Premium Navicular Care

Tildren® has an unmatched track record when it comes to controlling clinical signs of navicular syndrome and relieving osteolytic pain.

- Tiludronate disodium has been in use in markets beyond the US since 2004.
- Many published clinical studies support the safety and efficacy of Tildren® and tiludronate.[1]
- More than 250,000 doses of Tildren® sold worldwide.

Tildren® is most effective when used in conjunction with corrective farriery and a controlled exercise program for a **multimodal approach to navicular syndrome**.

Tildren®
(tiludronate disodium)

FOR USE IN HORSES ONLY

WARNINGS - Do not use in horses intended for human consumption. NSAIDs should not be used concurrently with Tildren®. Concurrent use of NSAIDs with Tildren® may increase the risk of renal toxicity and acute renal failure.

HUMAN WARNINGS - Not for use in humans. Keep this and all drugs out of the reach of children. Consult a physician in case of accidental human exposure.

CAUTION - Federal law restricts this drug to use by or on the order of a licensed veterinarian.

INDICATION - Tildren® is indicated for the control of clinical signs associated with navicular syndrome in horses. Navicular syndrome is the most common cause of chronic forelimb lameness in performance horses. It is a degenerative process instigated by mechanical forces.

CONTRAINDICATIONS - Do not use in horses with known hypersensitivity to tiludronate disodium or to mannitol. Do not use in horses with impaired renal function or with a history of renal disease. Bisphosphonates are excreted by the kidney; therefore, conditions causing renal impairment may increase plasma bisphosphonate concentrations resulting in an increased risk for adverse reactions.

PRECAUTIONS - Approximately 30-45% of horses administered Tildren® will demonstrate transient signs consistent with abdominal pain (colic). Horses should be observed closely for 4 hours post-infusion for the development of clinical signs consistent with colic or other adverse reactions. Colic signs can last approximately 90 minutes and may be intermittent in nature. Hand walking the horse may improve or resolve the colic signs in many cases.If a horse requires medical therapy, non-NSAID treatment should be administered due to the risk for renal toxicity. Avoid NSAID use.

Horses should be well hydrated prior to administration of Tildren® due to the potential nephrotoxic effects of Tildren®.

Tildren® 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).

Horses with HYPP (heterozygous or homozygous) may be at an increased risk for adverse reactions, including colic signs, hyperkalemic episodes, and death.The safe use of Tildren® has not been evaluated in horses less than 4 years of age.

Bisphosphonates should not be used in pregnant or lactating mares, or mares intended for breeding. Bisphosphonates have been shown to cause fetal developmental abnormalities in laboratory animals.

DOSAGE AND ADMINISTRATION - A single dose of Tildren® should be administered as an intravenous infusion at a dose of 1 mg/kg (0.45 mg/lb). The infusion should be administered slowly and evenly over 90 minutes to minimize the risk of adverse reactions. Maximum effect may not occur until 2 months post-treatment.

For **ADMINISTRATION INSTRUCTIONS** (preparation of the reconstituted solution (20mg/mL) and preparation of the solution for infusion) and for complete product information, please read the insert contained within the product packaging.

STORAGE - Sterile powder (not reconstituted): Store at controlled room temperature 68°F-77°F (20°C-25°C). After preparation, the infusion should be administered either within 2 hours of preparation, or it can be stored for up to 24 hours under refrigeration at 36°F-46° F (2°C-8°C) and protected from light.

HOW SUPPLIED - Tildren® is supplied in a 30mL glass vial as a white, sterile lyophilized powder containing 500mg tiludronic acid (as tiludronate disodium) packaged in a folding carton. For technical assistance or to report suspected adverse reactions, call 1-888-524-6332.

INFORMATION FOR OWNERS - Prior to Tildren® administration, owners should be advised of the potential for adverse reactions in the hours or days following treatment. Adverse reactions within 4 hours post dosing may include signs of colic (manifested as pawing, stretching, getting up and down, sweating, rolling, looking at flanks, kicking at belly, frequent gas, and pacing). Owners should be instructed to contact their veterinarian immediately if any adverse reactions are observed. Owners should be advised to consult with their veterinarian prior to the administration of an NSAID following Tildren® administration.

Made in Canada

Patent information: U.S. patent 6,057,306

To learn more about Tildren® visit **www.Tildren.us**

Discover more of Bimeda's wide range of equine health products and pharmaceuticals at **www.BimedaUS.com**

Do not use in horses with impaired renal function or with a history of renal disease. NSAIDs should not be used concurrently with Tildren®. Concurrent use of NSAIDs with Tildren® may increase the risk of renal toxicity and acute renal failure. Horses should be observed closely for 4 hours post-infusion for the development of clinical signs consistent with colic or other adverse reactions.

Caution should be used when administering Tildren® to horses with conditions affecting mineral or electrolyte homeostasis (e.g. HYPP, hypocalcemia) and conditions which may be exacerbated by hypocalcemia (e.g. cardiac disease). The safe use of Tildren® has not been evaluated in horses less than 4 years of age, in pregnant or lactating mares, or in breeding horses. See package insert for full prescribing information.

[1] www.BimedaUS.com

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