

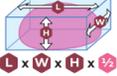


For intratumoral injection in dogs only
Antineoplastic
Single use vial



- Determine the Tumor Volume using the modified ellipsoid formula to account for the tumor shape (cube volume x 1/2) as below:

$$\frac{\text{Length (cm)}}{\text{cm}} \times \frac{\text{Width (cm)}}{\text{cm}} \times \frac{\text{Height (cm)}}{\text{cm}} \times \frac{1}{2} = \text{Tumor Volume cm}^3$$



- Confirm the Tumor Volume does not exceed 10 cm³.
- Do not use STELFONTA if Tumor Volume is >10 cm³.

STEP 2. Calculate the mL of STELFONTA to inject:

$$\frac{\text{Tumor Volume (cm}^3\text{)}}{\text{Dose (0.5 mL/cm}^3\text{)}} = \text{mL of STELFONTA to be injected}$$

- Confirm the dose of STELFONTA does not exceed 0.25 mL/kg body weight and do not use if the calculated dose exceeds this.
- Do not exceed 5 mL per dog, regardless of tumor volume or body weight.
- The minimum dose of STELFONTA is 0.1 mL, regardless of tumor volume or body weight. If the calculated dose is < 0.1 mL, administer 0.1 mL.
- Confirm the calculated dose of STELFONTA using the online dosing calculator at www.stelfonta.com/calculator (or scan the QR code above).



Administration of STELFONTA:

Sedation may be necessary to safely and accurately administer STELFONTA to decrease the chance of accidental self-injection. Wear gloves, eye protection, and lab coat or gown in the preparation and administration of STELFONTA. Care should be taken to restrict injections to the tumor only. STELFONTA should not be injected into the margins, beyond the periphery, or deep to the tumor.

- Shave the tumor site. Avoid manipulation of the tumor.
- Draw the calculated volume of STELFONTA into a sterile Luer-lock syringe with a 23 gauge needle.
- Identify an appropriate injection point on the edge of the tumor. See Figure 1. Insertion of the needle depends on the tumor's location, form, and appearance. If a tumor protrudes above the surface of the skin, insert the needle at an oblique angle of approximately 45°.
- Insert and embed the needle in the tumor through a single injection site and draw the syringe plunger back slightly to ensure STELFONTA is not injected into a blood vessel. While applying even pressure on the syringe plunger, move the needle back and forth in a fanning manner to inject STELFONTA into the tumor. See Figure 1. The drug should fully perfuse the entire tumor.
- When the total dose of STELFONTA has been administered, pause to allow tissue dispersion before removing the needle from the tumor. Pull back on the syringe plunger to create a small negative pressure before removing the needle to minimize leakage from the injection site.
- After the needle is withdrawn, apply light pressure for 30 seconds over the needle exit hole using a gloved finger. If leakage does occur, rinse injection site with saline to wash STELFONTA from the skin surface. Do not re-administer.
- To minimize risk of accidental self-injection, do not recap the needle. Dispose of the needle and syringe.

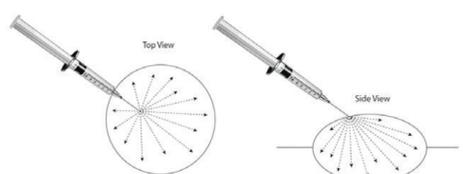


Figure 1: Dispersion of STELFONTA throughout the tumor.

CONTRAINDICATIONS

Do not inject STELFONTA into subcutaneous mast cell tumors located above the elbow or hock (e.g. on the body, head, or neck). This may result in accumulation of necrotic debris in the subcutaneous space increasing the risk of systemic adverse reactions, including death, from mast cell degranulation (see **Adverse Reactions**).

WARNINGS

Human Safety Warnings

NOT FOR USE IN HUMANS. KEEP THIS AND ALL MEDICATIONS OUT OF REACH OF CHILDREN.

Caution is required during treatment to avoid accidental self-injection. Dogs undergoing treatment with STELFONTA should be adequately restrained and sedation used if necessary. Use a Luer-lock syringe to administer STELFONTA. Do not recap the needle. Accidental self-injection may result in local inflammatory reactions, including swelling, redness and severe wound formation. In case of accidental self-injection, immediately rinse the area with water, seek medical advice immediately, and show the package insert to the physician.

Wear personal protective equipment consisting of disposable gloves, protective eye wear, and a lab coat or gown when handling STELFONTA. STELFONTA is an irritant and accidental exposure to skin, eye, or by ingestion should be avoided. In case of dermal or ocular exposure, repeatedly wash the exposed skin or eye with water. If wearing contacts, rinse their eyes first then remove contacts and continue to rinse with water. If symptoms such as local signs of redness and swelling occur, or if there has been ingestion, seek the advice of a physician and show them the package insert.

Limited data is available on the potential teratogenic effects of STELFONTA. Therefore, STELFONTA should not be administered by women who are pregnant or planning to become pregnant.

People with known hypersensitivity to tigilanol tiglate or to any of the excipients should avoid contact with STELFONTA.

Animal Safety Warnings

Dogs should be monitored during and for 5-7 days after intra-tumoral treatment with STELFONTA for signs of systemic mast cell degranulation such as vomiting, diarrhea, lethargy, anorexia/hyporexia, altered breathing, hypotension, urticaria, edema at or away from the treated site, or bruising at or away from the treated site. If signs are observed, appropriate treatment should be started immediately.

Always administer the concomitant medications (prednisone or prednisolone, diphenhydramine, and famotidine), as directed in the Dosage and Administration section, with STELFONTA in order to decrease the potential for severe systemic adverse reactions, including death, from mast cell degranulation (see **Adverse Reactions**).

Treatment with STELFONTA causes tumor necrosis which is part of the mechanism of action of the drug. Bruising, heat, pain, and swelling may begin at the site within 2 hours of treatment. By day 7 after treatment, wound formation including full thickness dermal necrosis with exudate, peripheral tissue edema, erythema, skin discoloration, tissue sloughing, and necrotic eschar may occur.

STELFONTA can induce a substantial local inflammatory reaction which may result in severe pain and swelling, bruising, cellulitis, extensive wound formation, and severe tissue sloughing extending away from the treated site. Consider administering analgesic medications prior to, during, and after treatment with STELFONTA in addition to the use of corticosteroids and both H1 and H2 receptor blocking agents.

Amputation of an extremity has been reported in some cases (see **Post-Approval Experience**).

Some dogs require wound care and pain management for an extended period.

Do not inject STELFONTA into normal subcutaneous tissue or adjacent tissues (e.g., beyond tumor margins) because severe edema, erythema, and necrosis of the injected tissue may occur.

PRECAUTIONS

STELFONTA is not intended for the treatment of metastatic mast cell tumors.

The safe and effective use of STELFONTA has not been evaluated in dogs with a mast cell tumor volume >10 cm³.

Use STELFONTA with caution in tumors located within mucocutaneous regions (e.g., eyelids, vulva, prepuce, and anus) as tumor necrosis could cause a change in morphology of the mucocutaneous region resulting in loss of functional integrity.

Use STELFONTA with caution in mast cell tumors with significant ulceration as leakage of the drug from the ulcerated area may occur following treatment potentially reducing effectiveness.

Some discharge from the site following treatment is expected. Wear disposable gloves to clean the site with warm water as necessary.

After treatment with STELFONTA, dogs may require additional care of the treated site to aid in the healing process, especially if there is extensive wound formation (see **Animal Safety Warnings and Post-Approval Experience**).

Tongue lesions have been reported (see **Post-Approval Experience**). Do not allow the dog to lick the site for the first few days after treatment. Discourage excessive licking for the remainder of the healing period.

An Elizabethan collar or a non-constricting dry gauze bandage may be needed to prevent the dog from self-traumatizing the treated site.

After treatment with STELFONTA, separation from other household animals may be necessary to prevent grooming and trauma to the treated site.

STELFONTA has not been evaluated in dogs with signs of systemic disease due to the mast cell tumor(s).

The safe and effective use of STELFONTA has not been evaluated for simultaneous treatment of more than one mast cell tumor.

The safe use of STELFONTA has not been evaluated in dogs with concurrent diseases that may result in delayed wound healing.

The safe use of STELFONTA under conditions of use has not been evaluated in dogs younger than 3.5 years old.

The safe use of STELFONTA has not been evaluated in dogs that are pregnant, lactating, or intended for breeding.

ADVERSE REACTIONS

Human Exposure

There was one human exposure during the field study where the veterinarian had a needle stick injury to the thumb at completion of tumor treatment and was injected with an unknown amount of STELFONTA. The incident resulted in pain and necrosis of the center of the thumb at the point of needle stick. The wound healed over a period of three months. See Pictures 1 and 2 below.

A separate needle stick injury was reported with a maximum potential dose of 0.1 mL tigilanol tiglate into the distal extremity of the left index finger, resulting in a localized burning sensation, local inflammation, bruising, muscular pain up the left arm, and localized tissue necrosis. Muscular pain resolved in the first 12-24 hours and the wound healed in 8 weeks. There have been other needle stick injuries reported, with at least one injection into a thumb, with minimal (stinging, pain, and swelling) to no adverse events associated with these accidental self-injections.

Picture 1. Thirteen days after self-injection



Picture 2. Seventy-four days after self-injection



Field Study

In a well-controlled, multi-center, randomized, double-masked field study evaluating the effectiveness and safety of STELFONTA for the treatment of cutaneous and subcutaneous mast cell tumors in dogs, 117 dogs treated with STELFONTA and 42 dogs receiving sham treatment (untreated control) were evaluated for safety. Eighty-one dogs were treated with STELFONTA on Day 0. Thirty-six previously untreated control dogs were treated with STELFONTA on Day 30. In addition, 18 dogs treated with STELFONTA on Day 0 had the same tumor re-treated with STELFONTA on Day 30 due to incomplete response. The most common adverse reactions included wound formation, injection site pain, lameness in the treated limb, vomiting, diarrhea, and hypoalbuminemia. Wound formation, vomiting, and diarrhea were mainly observed within the first 7 to 10 days after treatment. Injection site pain and lameness in the treated leg were mainly observed within the first 2 days after treatment. Hypoalbuminemia was mainly observed within the first 28 days after treatment. All dogs received concomitant medications as noted in the Effectiveness section. The adverse reactions during the study are summarized in Table 1 below.

Table 1: Adverse Reactions During the Field Study

Adverse Reaction	STELFONTA 1 st Treatment (n = 117)	STELFONTA 2 nd Treatment (n = 18)	UNTREATED CONTROL (n = 42)
Wound formation	110 (94.0%)	12 (66.7%)	3 (7.1%)
Injection site pain	61 (52.1%)	7 (38.9%)	1 (2.4%)
Lameness in treated limb	29 (24.8%)	2 (11.1%)	1 (2.4%)
Vomiting	24 (20.5%)	3 (16.7%)	4 (9.5%)
Diarrhea	24 (20.5%)	3 (16.7%)	2 (4.8%)
Hypoalbuminemia ^a	21 (18.0%)	2 (11.1%)	1 (2.4%)
Injection site bruising/erythema/edema/irritation	20 (17.1%)	3 (16.7%)	1 (2.4%)
Anorexia	14 (12.0%)	2 (11.1%)	3 (7.1%)
Regional lymph node swelling/enlargement	13 (11.1%)	1 (5.6%)	1 (2.4%)
Tachycardia	12 (10.3%)	0 (0.0%)	1 (2.4%)
Weight loss	12 (10.3%)	3 (16.7%)	5 (11.9%)
Cystitis	10 (8.6%)	1 (5.6%)	2 (4.8%)
Dermatitis	9 (7.7%)	1 (5.6%)	1 (2.4%)
Personality/behavior change	8 (6.8%)	0 (0.0%)	2 (4.8%)
Infection at injection site	8 (6.8%)	0 (0.0%)	0 (0.0%)
Tachypnea	7 (6.0%)	2 (11.1%)	1 (2.4%)
Pruritus	6 (5.1%)	3 (16.7%)	2 (4.8%)
Lethargy/Depression	6 (5.1%)	1 (5.6%)	1 (2.4%)
Pyrexia	3 (2.6%)	2 (11.1%)	0 (0.0%)

^aThere was a statistically significant decrease in albumin and albumin/globulin ratios at Day 7 in the STELFONTA group compared to the control group. The hypoalbuminemia ranged from 2.0 to 2.6 g/dL (reference range 2.7-3.9 g/dL). Note: If an animal experienced the same adverse reaction more than once, only the highest grade was tabulated.

Adverse reactions were graded using the Veterinary Co-operative Oncology Group – Common Terminology Criteria for Adverse Events (VCOG-CTCAE).¹ Most adverse reactions were Grade 1 (mild) or 2 (moderate). Grade 3 (severe) and 4 (life-threatening) adverse reactions in dogs treated with STELFONTA included: lameness in the treated limb (6 dogs), injection site pain (4 dogs), wound formation (3 dogs), lethargy/depression (3 dogs), anorexia (2 dogs), infection at injection site (1 dog), pruritus (1 dog), and tachycardia (1 dog).

Adverse reactions associated with use of the required concomitant corticosteroids were similarly reported in STELFONTA and untreated control dogs and included elevated alkaline phosphatase, polyuria, and polydipsia.

Wound Formation

Tumor observations were conducted at 2, 4, 8, and 24 hours and 4 days after treatment. The 81 dogs treated with STELFONTA on Day 0 were reported most frequently with swelling, bruising, pain and heat at all tumor observation timepoints. The following were reported at 24 hours post treatment:

- Swelling: 97.5% (79/81 dogs)
- Pain: 69.1% (56/81 dogs)
- Bruising: 91.4% (74/81 dogs)
- Heat: 53.1% (43/81 dogs)

At 24 hours post treatment, intact skin was reported in 71.6% (58/81 dogs) of STELFONTA treated dogs. On Day 4 intact skin was reported in 17.3% (14/81 dogs) of STELFONTA treated dogs. On Day 4, the following observations were reported with the highest frequency:

- Necrosis: 55.6% (45/81 dogs)
- Exudate: 37.0% (30/81 dogs)
- Crater pockets: 37.0% (30/81 dogs)
- Eschar: 28.4% (23/81 dogs)
- Ulceration: 11.1% (9/81 dogs)

A wound healing assessment was performed on the effectiveness dataset which included 80 dogs in the STELFONTA group and 38 dogs in the untreated control group. Wounds developed in 92.5% (74/80) of STELFONTA treated dogs and 2.6% (1/38) of untreated control dogs by Day 7. On Day 28, the presence of wounds was 40% (32/80) in the STELFONTA group and 2.6% (1/38) in the untreated control group. On Day 42 and Day 84, the presence of wounds was 27.1% (16/59) and 1.8% (1/57), respectively, in the STELFONTA group.

Exudate from the treated site including serous, serosanguinous, sanguineous, seropurulent, and purulent discharges were seen mainly on Day 7 and to a lesser extent on Day 14. Sloughing of the treated site was observed from Day 7 to Day 42, with decreasing frequency after Day 7.

CLIENT INFORMATION SHEET



This Client Information Sheet contains important information about STELFONTA®. Before your dog is treated, you should carefully read this information and discuss the following with your veterinarian:

- How STELFONTA works.
- All parts of your dog's treatment plan. **It is very important to follow the treatment plan exactly as directed.**
- The risks and benefits of STELFONTA, including the potential for serious side effects.

This sheet is provided only as a summary and does not take the place of instructions from your veterinarian. Talk with your veterinarian if you do not understand any of this information or if you want to know more about STELFONTA.

What is STELFONTA?

- STELFONTA is a drug used to treat mast cell tumors, a common form of cancer that affects dogs.
- The active ingredient in STELFONTA is tigilanol tiglate, a substance that works by:
 - » Breaking down the tumor cell walls
 - » Disrupting blood vessels in the tumor
 - » Destroying the tumor and forming a 'pocket' or wound where the tumor was.

What should I tell my veterinarian before my dog is treated with STELFONTA?

- Tell your veterinarian about all other medications your dog is taking, including prescription drugs, over the counter drugs, flea and tick medications, heartworm and deworming medications, and vitamins and supplements (including herbal or homeopathic products).
- Tell your veterinarian about your dog's previous or current medical conditions, including any infection.
- Tell your veterinarian if your dog is pregnant, is nursing puppies, or is intended for breeding purposes.

How is STELFONTA given to my dog?

- Your veterinarian will inject your dog's tumor with STELFONTA. The injection will be given at the veterinary clinic. Your dog may need to be sedated during the procedure.

What additional medications need to be given to my dog before, on, and after the day of treatment with STELFONTA?

- To help prevent the potential for severe side effects that can occur, your veterinarian will prescribe three medications:
 - » You must start to give your dog the corticosteroid two days before the STELFONTA treatment day and continue for a total of 10 days.
 - » You will start giving your dog the H1 and H2 blockers on the STELFONTA treatment day and continue for a total of 8 days.
- Your veterinarian will fill out the medication schedule included in this Client Information Sheet for you to follow, so that you can give your dog the medications correctly.
- If you are unable to give your dog the medications as directed, talk to your veterinarian about other options. **Do not skip these medications.**

How will STELFONTA affect my dog?

- STELFONTA is used to treat a mast cell tumor on your dog.
- It can be difficult to predict how your dog's tumor will respond to STELFONTA.
- A wound will form where STELFONTA was administered. It is difficult to predict the size and severity of the wound formed. In some cases, an extensive wound that is deeper and/or larger than the original treatment site may develop, which may lead to unexpected complications.
- Tumors treated with STELFONTA typically go through a 4- to 6-week tumor breakdown and healing process.
- The healing process may take longer in some dogs.
- During the tumor breakdown and healing process, your dog may require additional care of the treated tumor site to aid in the healing process.

See the diagrams for more information.

LESS THAN 4 HOURS AFTER STELFONTA TREATMENT:

Start of Tumor Breakdown

Within the first few hours following treatment with STELFONTA, the cells in the tumor and tumor blood vessels will begin to break down. You will be able to see a change in the color of the tumor. At the same time there is usually swelling at the treated tumor site.

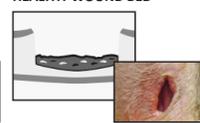
1-7 DAYS AFTER STELFONTA TREATMENT: Continued Tumor Breakdown

The treated tumor site will become blackened. The skin over the surface of the tumor may breakdown and fluid may leak from the tumor. Swelling of the treated tumor site may continue causing some discomfort to your dog through this stage. Your veterinarian can prescribe pain medication to help your dog through this period if needed. As the tumor breaks down there will be a 'pocket' or wound where the tumor once was. A healthy wound bed will be seen, reddish in color, which will allow healthy new skin to grow.

24 HRS POST-TREATMENT: TUMOR BREAKDOWN EVIDENT



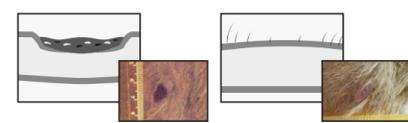
DAY 7: TUMOR BREAKDOWN WITH FORMATION OF HEALTHY WOUND BED



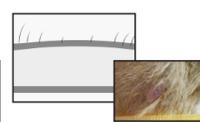
7 - 42 DAYS AFTER STELFONTA TREATMENT: Wound Resolution

Healthy new skin will grow and close over the pocket or wound where the tumor once was. In many dogs, the hair will regrow, and skin will return to its original color.

DAY 14 AFTER STELFONTA TREATMENT: TUMOR SITE



DAY 28 AFTER STELFONTA TREATMENT: TREATED TUMOR SITE HEALED



Some dogs experience extensive wounds after STELFONTA treatment that take longer to heal, as in the case below.



What are some possible side effects of STELFONTA?

- STELFONTA may cause side effects, even at the prescribed dose. These side effects include, but are not limited to:
 - » During the first days after treatment, you may see bruising or swelling around the treated tumor site. The swelling may cause your dog some discomfort and pain for several days after treatment. Your dog may seem tired during this time and may eat less.
 - » In some cases, extensive swelling, severe pain, large amounts of discharge, odor, infection, or wound formation extending into the area surrounding the tumor site may develop, delaying wound healing and requiring additional management of the wound. If any of these occur, contact your veterinarian who will assess if your dog requires additional treatments during this time (e.g., pain medications, bandages, an Elizabethan collar, antibiotics). **(see reverse side)**

