Calcineurin Inhibitors as Steroid-Sparing Agents

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In the Literature

Banovic F, Robson D, Linek M, Olivry T. Therapeutic effectiveness of calcineurin inhibitors in canine vesicular cutaneous lupus erythematosus. *Vet Dermatol.* 2017;28(5):493-e115.

FROM THE PAGE ...

Vesicular cutaneous lupus erythematosus (VCLE) is a form of cutaneous lupus erythematosus that is seen mainly in collies and Shetland sheepdogs. VCLE has a distinctive clinical appearance, with lesions consisting of annular to serpiginous ulcerations primarily on the ventral abdomen, groin, and axillae, although mucocutaneous junctions and the concave aspect of the pinnae are commonly affected as well. As with many other autoimmune skin diseases, the treatment of choice has historically involved immunosuppressive doses of oral glucocorticoids. Although glucocorticoids are usually effective at inducing remission, side effects are common, and the long-term prognosis is guarded. As such, there is a need for safer long-term treatment options for VCLE. Calcineurin inhibitors (eg, cyclosporine, tacrolimus) are frequently used

Loxicom® (meloxicam)

1.5 mg/mL Oral Suspension

Non-steroidal anti-inflammatory drug for oral use in dogs only

Warning: Repeated use of meloxicam in cats has been associated with acute renal failure and death. Do not administer additional injectable or oral meloxicam to cats. See Contraindications, Warnings, and Precautions for detailed information.

Brief Summary: Before using Loxicom Oral Suspension, consult the product insert, a summary of which follows.

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

Description: Meloxicam is a non-steroidal anti-inflammatory drug (NSAID) of the oxicam class.

Indications: Loxicom Oral Suspension is indicated for the control of pain and inflammation associated with osteoarthritis in dogs.

Contraindications: Dogs with known hypersensitivity to meloxicam should not receive Loxicom Oral Suspension.
Do not use Loxicom Oral Suspension in cats. Acute renal failure and death have been associated with the use of meloxicam in cats.

Warnings: Not for use in humans. Keep this and all medications out of reach of children. Consult a physician in case of accidental ingestion by humans. **For oral use in dogs only.** As with any NSAID all dogs should undergo a thorough history and physical examination before the initiation of NSAID therapy. Appropriate laboratory testing to establish hematological and serum biochemical baseline data is recommended prior to and periodically during administration.
To report suspected adverse reactions, to obtain a Material Safety Data Sheet, or for technical assistance, call Norbrook at 1-866-591-5777.

Precautions: The safe use of Loxicom Oral Suspension in dogs younger than 6 months of age, dogs used for breeding, or in pregnant or lactating dogs has not been evaluated. As a class, cyclo-oxygenase inhibitory NSAIDs may be associated with gastrointestinal, renal and hepatic toxicity. Sensitivity to drug-associated adverse events varies with the individual patient.
Patients at greatest risk for renal toxicity are those that are dehydrated, on concomitant diuretic therapy, or those with existing renal, cardiovascular, and/or hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be carefully approached. NSAIDs may inhibit the prostaglandins that maintain normal homeostatic function. Such anti-prostaglandin effects may result in clinically significant disease in patients with underlying or pre-existing disease that has not been previously diagnosed. Since NSAIDs possess the potential to induce gastrointestinal ulcerations and/or perforations, concomitant use with other anti-inflammatory drugs, such as NSAIDs or corticosteroids, should be avoided or closely monitored. The use of concomitantly protein-bound drugs with Loxicom Oral Suspension has not been studied in dogs. Commonly used protein-bound drugs include cardiac, anticonvulsant and behavioral medications. The influence of concomitant drugs that may inhibit metabolism of Loxicom Oral Suspension has not been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy.

Adverse Reactions: Field safety was evaluated in 306 dogs. Based on the results of two studies, GI abnormalities (vomiting, soft stools, diarrhea, and inappetance) were the most common adverse reactions associated with the administration of meloxicam. Of the dogs that took meloxicam (n=157), forty experienced vomiting, nineteen experienced diarrhea/soft stool, five experienced inappetance, and one each experienced bloody stool, bleeding gums after dental procedure, lethargy/swollen carpus, and epiphora. Of the dogs that took the placebo (n=149), twenty-three experienced vomiting, eleven experienced diarrhea/soft stool, and one experienced inappetance.
In foreign suspected adverse drug reaction (SADR) reporting over a 9 year period, incidences of adverse reactions related to meloxicam administration included: auto-immune hemolytic anemia (1 dog), thrombocytopenia (1 dog), polyarthritis (1 dog), nursing puppy lethargy (1 dog), and pyoderma (1 dog).

Effectiveness: The effectiveness of meloxicam was demonstrated in two field studies involving a total of 277 dogs representing various breeds, between six months and sixteen years of age, all diagnosed with osteoarthritis. Both of the placebo-controlled, masked studies were conducted for 14 days. All dogs received 0.2 mg/kg on day 1. All dogs were maintained on 0.1 mg/kg oral meloxicam from days 2 through 14 of both studies. Parameters evaluated by veterinarians included lameness, weight-bearing, pain on palpation, and overall improvement. Parameters assessed by owners included mobility, ability to rise, limping, and overall improvement. In the first field study (n=109), dogs showed clinical improvement with statistical significance after 14 days of meloxicam treatment for all parameters. In the second field study (n=48), dogs receiving meloxicam showed a clinical improvement after 14 days of therapy for all parameters; however, statistical significance was demonstrated only for the overall investigator evaluation on day 7, and for the owner evaluation on day 14.

How Supplied:
Loxicom Oral Suspension 1.5 mg/mL: 10, 32 and 100 mL bottles with small and large dosing syringes.

Storage: Store at controlled room temperature 68-77°F (20-25°C).
Excursions permitted between 59°F and 86°F (15°C and 30°C). Brief exposure to temperature up to 104° F (40°C) may be tolerated provided the mean kinetic temperature does not exceed 77°F (25°C); however such exposure should be minimized.

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as steroid-sparing agents in dogs with autoimmune skin diseases, but there is a lack of published data examining the outcomes of these treatments.

In this study, the authors analyzed the outcomes of 11 dogs with VCLE that were treated with oral modified cyclosporine (5-10 mg/kg q24h). Initial therapies included systemic and topical antimicrobials (6 and 2 dogs, respectively) and oral corticosteroids (9 dogs); these treatments resulted in clinical improvement for several dogs, but none achieved clinical remission. After initiation of treatment with oral modified cyclosporine, complete remission was noted in 8 of the 11 dogs within 35 to 70 days. Complete remission was achieved in 2 additional dogs when the cyclosporine dosage was increased and topical tacrolimus was added. Relapse was often seen when cyclosporine doses were tapered. Three dogs were euthanized, but clinical remission was maintained in the remaining 8 dogs with oral cyclosporine and, occasionally, topical tacrolimus or pimecrolimus.

… TO YOUR PATIENTS

Key pearls to put into practice:

1. Cyclosporine appears to be a safer long-term treatment option for VCLE than glucocorticoids alone.

2. Once clinical remission has been achieved, clinicians should attempt to gradually taper medications to the lowest effective dose. Topical calcineurin inhibitors (eg, tacrolimus, pimecrolimus) can be used to further reduce the need for oral cyclosporine. Although these topical products are initially expensive, one tube usually lasts several months, as only a small amount is used for each dose.

3. In dogs with immune-mediated skin disease, avoiding excess sun exposure is recommended. UV light has been known to exacerbate skin lesions in humans with CLE,[1] and anecdotal information supports this effect in dogs.

Reference

1. Kim A, Chong BF. Photosensitivity in cutaneous lupus erythematosus. *Photodermatol Photoimmunol Photomed*. 2013;29(1):4-11.

See page 44 for product information summary.