ClinicalNotes

Considerations in the Management of Osteoarthritis

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Osteoarthritis (OA) is a common condition in dogs, with 1 study showing ≈40% of dogs 8 months to 4 years of age having radiographic signs consistent with OA in ≥1 joint.[1] Of those dogs with radiographic signs of OA, ≈60% had clinical signs of joint pain apparent on veterinary examination.[1]

These statistics not only highlight how common OA is, but they also stand in contrast with the traditional view of OA as an age-related disease of geriatric pets. Instead, OA commonly begins early in life, often being triggered by developmental joint disease or joint trauma.[2] Additional risk factors such as diet, obesity, genetics, and breed can all influence the development and progression of OA.[2]

Osteoarthritis: A Progressive Clinical Disease

OA is a global disease process affecting the entire joint, with articular cartilage damage being just one part of the issue.[3] Inflammation and crosstalk between the many different tissues within the joint (ie, joint capsule, synovium, synovial fluid, cartilage, subchondral bone) drive this process and result in the development of pain, continued inflammation, and clinical disease.[3]

OA is a progressive, cyclic disease that generally worsens over time, with joint pain and inflammation leading to decreased activity, periarticular fibrosis, loss of range of motion, weight gain, and muscle atrophy.[3] These changes then lead to further reduction in activity, further muscle atrophy and weight gain, additional inflammatory mediators, and increasing joint pain and inflammation, where the cycle begins again.

Prompt diagnosis and aggressive treatment are critical to trying to slow the progression of disease and interrupt this cycle, as early intervention may help delay or even prevent joint failure.[3] Dogs at high risk for developing OA should be identified early on, and for dogs that are already demonstrating clinical signs of OA, identifying their stage of disease is necessary to begin appropriate management.

Osteoarthritis Staging

Staging of OA provides an objective patient assessment that can help in guiding therapy choices and monitoring disease progression. The Canine OsteoArthritis Staging Tool (COAST) is a widely recognized tool that can offer significant benefits for veterinarians, clients, and patients. The COAST tool incorporates both owner assessments and veterinarian clinical assessments to stage both preclinical dogs, "at risk" dogs, and dogs with clinical signs of OA.[4] Dogs are assigned a COAST stage from 0 to 4 based on veterinarian and owner assessments (see ***Table***).

TABLE: Coast Stages[4]

Preclinical	0	Clinically normal, no OA risk factors
	1	Clinically normal but OA risk factors present (eg, young, overweight golden retriever)
Clinical	2	Mild OA (eg, 5-year-old Labrador retriever with a history of intermittent lameness)
	3	Moderate OA (eg, 8-year-old, large-breed dog with hip dysplasia)
	4	Severe OA (eg, 12-year-old dog with severe hip and stifle OA)

Using the COAST staging tool allows for standardized scoring of OA severity, in turn allowing veterinarians and pet owners to determine a pet's baseline and track progress over time.

Osteoarthritis Management Strategies

Once an individual patient's COAST stage has been identified, it is important to work with the owner to define the goals of treatment. Each patient should be considered as an individual, and unique treatment priorities should be discussed with the owner. Common treatment goals include improving quality of life and decreasing pain, but owners may have additional goals that are specific to their individual pet or lifestyle. For example, they may prioritize being able to participate in a specific activity with their dog to help maintain the human–animal bond. Open discussion with clients is essential to identifying these desirable and reasonable treatment goals. In addition, the practitioner's preferred strategy for managing OA should be identified; ideally, this should include modulating, minimizing, and/or eliminating inflammation.[3]

Successfully managing OA requires a multimodal approach and understanding when the various strategies should be incorporated. OA cannot and should not be addressed through a single medication or treatment. Instead, multiple interventions are required for successful management and can include a combination of lifestyle and nutritional modifications, NSAIDs, biologics, and adjunct therapies, all of which can offer benefits based on the individual patient's needs and owner preferences.

Lifestyle & Nutritional Modifications

Lifestyle modifications are a key step in the multimodal management of OA. All dogs with OA, whether in stage 1 or stage 4, can benefit from lifestyle modifications. Weight optimization is essential, considering the role that obesity plays in many cases of OA, and is best achieved after controlling pain and gradually increasing exercise.[5]

All dogs with OA can benefit from daily activity, which can be broken into daily playtime and daily exercise. Daily playtime is the time spent when the dog is running, jumping, chasing, etc; however, the duration and frequency of daily playtime should be limited, with a stronger focus being on daily exercise. A daily exercise plan should be customized to the dog's overall health and degree of osteoarthritis. For example, a goal should be to work up to two 20-minute walks daily, as activity of this length and frequency can aid in weight management and help maintain limb function. This plan should be developed through collaboration with the owner to ensure it is practical and reasonable for both the patient and the owner. Nutritional interventions can also provide benefits to the OA patient.

Administering eicosapentaenoic acid (EPA) and/or docosahexaenoic acid (DHA), providing a minimum daily dose of 100 mg/kg of DHA/EPA, or providing a diet supplemented with these ingredients can be considered in all COAST stages of OA,[2] as these ingredients have been shown to offer benefits in the adjunctive treatment of dogs with OA.[6]

NSAIDs

For dogs with clinical signs of OA (COAST stage 2 or higher), additional treatments beyond lifestyle modifications are recommended to control pain and inflammation.[2,7]

NSAIDs are the best tool available for the management of inflammation and are thus considered a first-line treatment in dogs with stage 2 or greater OA.[2,3] An NSAID should be administered daily for 1 to 4 months, after which time tapering or reducing the dose frequency can be considered based on patient response and NSAID tolerability as assessed during regular rechecks.[3] Long-term NSAID use has been shown to be effective and safe in dogs,[8] and some patients, particularly those in COAST stage 3 to 4, may benefit from long-term daily NSAID administration.[2,3]

When it comes to choosing an NSAID, using one that targets prostaglandin E_2 receptor 4 (EP4 receptor antagonist) can be advantageous, as these have been shown to effectively control OA without blocking production of prostaglandins.[9] Conversely, cyclooxygenase-inhibiting NSAIDs are less targeted and work by inhibiting the production of a variety of prostanoids. Galliprant™ (grapiprant tablets) specifically targets the EP4 receptor, which

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SELECT IMPORTANT SAFETY INFORMATION

If Galliprant is used long-term, appropriate monitoring is recommended. Concomitant use of Galliprant with other anti-inflammatory drugs, such as COX-inhibiting NSAIDs or corticosteroids, should be avoided. See important safety information on page 5.

COAST = Canine OsteoArthritis Staging Tool

is the primary mediator of prostaglandin E_2-induced inflammation, nerve sensitization, and pain.[9] Because grapiprant blocks a single downstream receptor rather than decreasing production of prostaglandins, it helps to preserve homeostatic function and reduce the impact on organ health.[9,10]

Since Galliprant™ (grapiprant tablets) received FDA approval, >25 million dogs in the United States have been treated with grapiprant. Adverse events, including vomiting and diarrhea, occurred in <1 in 10,000 reports (very rare based on Council for International Organizations of Medical Sciences classification), according to unpublished adverse event reporting data. Many of these signs occurred in <1 in 100,000 reports.[11,12]

Monoclonal Antibodies

Anti-nerve growth factor monoclonal antibody (anti-NGF mAb) is another therapeutic consideration for dogs with OA. This treatment works by blocking the activity of NGF, which contributes to neurogenic pain in OA.[13,14] Bedinvetmab, an available anti-NGF mAb, is labeled for the control of pain associated with OA.[15] Patient selection and the recommended timing of anti-NGF initiation may be clinician-dependent, with varying expert views.[2,7] A recent unpublished study in a canine model of acute synovitis revealed that grapipiprant and bedinvetmab provided the same degree of pain control, as measured by force plate gait analysis; however, grapiprant was associated with greater reductions in joint swelling.[16] This observed difference in anti-inflammatory activity is consistent with the differing mechanism of action and corresponding FDA-approved indications for each drug.

Adjunct Therapies

Although lifestyle changes and pharmaceutical therapies are a strong foundational starting point in the management of pain and inflammation in many dogs with OA, periodic flare-ups may still occur. These flare-ups do not indicate that the current treatment protocol is not working. Instead, the patient's current treatment regimen should be continued and adjunct treatments considered to help manage the flare-up. Adjunct treatment options include oral analgesics (eg, amantadine, gabapentin), intra-articular injections (eg, hyaluronic acid, corticosteroids, platelet-rich plasma), physical rehabilitation, and shockwave therapy. These adjunct treatments may be used on a short-term basis until the clinical signs of OA have abated, or a longer course of treatment may be necessary depending on patient response.

Client Communication

Managing OA requires effective and frequent client communication, and regular recheck examinations are essential to determine whether prescribed treatments are proving to be safe and effective for a given patient. The importance of regular follow-up should be emphasized when educating owners of dogs with OA; if a dog experiences an OA flare-up, follow-up examination can allow for patient assessment and the discussion of additional measures to alleviate pain and improve the dog's quality of life.

Owners must also understand that, when used according to a veterinarian's directions, long-term NSAID use in dogs has been shown to be a safe and effective means of preventing ongoing inflammation and reducing the frequency of OA flare-ups. In addition, owners must understand that flare-ups will occur in dogs with OA, despite effective management. A flare-up does not mean that the current treatment is not working; it simply means the dog needs an adjunct treatment (on a temporary or long-term basis). Owners should be educated on how to recognize flare-ups, and the veterinary team should discuss treatment options with them so they feel prepared for that eventuality. Finally, it should be reiterated that OA management is stepwise; treatment begins with lifestyle modifications, and other treatments are layered in depending on the patient's needs.

Conclusion

Osteoarthritis is a common sequela of developmental disease, joint injury, and/or obesity. Once early signs of OA arise, this condition is likely to gradually progress over time. Prompt diagnosis can allow for early interventions, and COAST can help facilitate both early diagnosis and accurate patient monitoring. The veterinary team should work with clients to develop a multimodal treatment plan at the first signs of OA. With regular rechecks and effective client communication, these interventions can help prolong quality of life in dogs with OA. ●

For references, please visit
cliniciansbrief.com/article/clinical-notes-considerations-management-osteoarthritis

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Galliprant®
(grapiprant tablets)

For oral use in dogs only

20 mg, 60 mg and 100 mg flavored tablets

A prostaglandin E_2 (PGE_2) EP4 receptor antagonist; a non-cyclooxygenase inhibiting, non-steroidal anti-inflammatory drug

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

Before using Galliprant, please consult the product insert, a summary of which follows:

Indication:
GALLIPRANT (grapiprant tablets) is indicated for the control of pain and inflammation associated with osteoarthritis in dogs.

Dosage and Administration:
Always provide "Information for Dog Owners" Sheet with prescription.
Use the lowest effective dose for the shortest duration consistent with individual response.

The dose of GALLIPRANT (grapiprant tablets) is 0.9 mg/lb (2 mg/kg) once daily.

Only the 20 mg and 60 mg tablets of GALLIPRANT are scored.
The dosage should be calculated in half tablet increments.
Dogs less than 8 lbs. (3.6 kgs) cannot be accurately dosed.

Dosing Chart

Dose	Weight in pounds	Weight in kilograms	20 mg tablet	60 mg tablet	100 mg tablet
0.9 mg/lb (2 mg/kg) once daily	8-15	3.6-6.8	0.5		
	15.1-30	6.9-13.6	1		
	30.1-45	13.7-20.4		0.5	
	45.1-75	20.5-34		1	
	75.1-150	34.1-68			1

The 100 mg tablet is not scored and should not be broken in half.
Breaking the 100 mg tablet in half will not guarantee that half of the active ingredient is contained within each half of the tablet. For dogs larger than 150 lbs (68 kgs), use a combination of tablet and half tablets to achieve the appropriate dose.

See product insert for complete dosing and administration information.

Contraindications:
GALLIPRANT should not be used in dogs that have a hypersensitivity to grapiprant.

Warnings:
Not for use in humans. Keep this and all medications out of reach of children and pets. Consult a physician in case of accidental ingestion by humans.
For use in dogs only. Store GALLIPRANT out of reach of dogs and other pets in a secured location in order to prevent accidental ingestion or overdose.

Precautions:
The safe use of GALLIPRANT has not been evaluated in dogs younger than 9 months of age and less than 8 lbs (3.6 kg), dogs used for breeding, or in pregnant or lactating dogs.

Adverse reactions in dogs receiving GALLIPRANT may include vomiting, diarrhea, decreased appetite, mucoid, watery or bloody stools, and decreases in serum albumin and total protein.

If GALLIPRANT is used long term appropriate monitoring is recommended.

Concurrent use with other anti-inflammatory drugs has not been studied. Concomitant use of GALLIPRANT with other anti-inflammatory drugs, such as COX-inhibiting NSAIDs or corticosteroids, should be avoided. If additional pain medication is needed after a daily dose of GALLIPRANT, a non-NSAID/ non-corticosteroid class of analgesic may be necessary.

The concomitant use of protein-bound drugs with GALLIPRANT has not been studied. Commonly used protein-bound drugs include cardiac, anticonvulsant and behavioral medications.

Drug compatibility should be monitored in patients requiring adjunctive therapy. Consider appropriate washout times when switching from one anti-inflammatory to another or when switching from corticosteroids or COX-inhibiting NSAIDs to GALLIPRANT use.

The use of GALLIPRANT in dogs with cardiac disease has not been studied.

It is not known whether dogs with a history of hypersensitivity to sulfonamide drugs will exhibit hypersensitivity to GALLIPRANT. GALLIPRANT is a methylbenzenesulfonamide.

Adverse Reactions:
In a controlled field study, 285 dogs were evaluated for safety when given either GALLIPRANT or a vehicle control (tablet minus grapiprant) at a dose of 2 mg/kg (0.9 mg/lb) once daily for 28 days. GALLIPRANT-treated dogs ranged in age from 2 yrs to 16.75 years. The following adverse reactions were observed:

Table 1. Adverse reactions reported in the field study.

Adverse reaction*	GALLIPRANT (grapiprant tablets) N = 141	Vehicle control (tablets minus grapiprant) N = 144
Vomiting	24	9
Diarrhea, soft stool	17	13
Anorexia, inappetence	9	7
Lethargy	6	2
Buccal ulcer	1	0
Immune mediated hemolytic anemia	1	0

*Dogs may have experienced more than one type or occurrence during the study.

GALLIPRANT was used safely during the field studies with other concurrent therapies, including antibiotics, parasiticides and vaccinations.

To report suspected adverse drug events and/or to obtain a copy of the Safety Data Sheet (SDS) or for technical assistance, call 1-888-545-5973.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVeterinary/SafetyHealth

Information for Dog Owners:
Owners should be advised of the potential for adverse reactions and be informed of the clinical signs associated with drug intolerance. Adverse reactions may include vomiting, diarrhea, decreased appetite, and decreasing albumin and total protein. Appetite and stools should be monitored and owners should be advised to consult with their veterinarian if appetite decreases or stools become abnormal.

Effectiveness:
Two hundred and eighty five (285) client-owned dogs were enrolled in the study and evaluated for field safety. GALLIPRANT-treated dogs ranging in age from 2 to 16.75 years and weighing between 4.1 and 59.6 kgs (9 – 131 lbs) with radiographic and clinical signs of osteoarthritis were enrolled in a placebo-controlled, masked field study. Dogs had a 7-day washout from NSAID or other current OA therapy. Two hundred and sixty two (262) of the 285 dogs were included in the effectiveness evaluation. Dogs were assessed for improvements in pain and function by the owners using the Canine Brief Pain Inventory (CBPI) scoring system.[7] A statistically significant difference in the proportion of treatment successes in the GALLIPRANT group (63/131 or 48.1%) was observed compared to the vehicle control group (41/131 or 31.3%). GALLIPRANT demonstrated statistically significant differences in owner assessed pain and function. The results of the field study demonstrate that GALLIPRANT, administered at 2 mg/kg (0.9 mg/pound) once daily for 28 days, was effective for the control of pain and inflammation associated with osteoarthritis.

Storage Conditions:
Store at or below 86° F (30° C)

How Supplied:
20 mg, 60 mg and 100 mg flavored tablets in 7, 30 and 90 count bottles

Approved by FDA under NADA # 141-455

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