Management of pancreatitis in dogs and the role of PANOQUELL®-CA1 (fuzapladib sodium for injection)

Fuzapladib sodium for injection can help manage clinical signs associated with the acute onset of pancreatitis, a common disorder in canine patients

written by

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Overview of the management of pancreatitis

Pancreatitis is the most common disorder of the exocrine pancreas in dogs. The disease is often characterized by vomiting and cranial abdominal pain, although more subtle clinical signs can occur in some dogs.[1] Therefore, veterinarians should maintain a high index of suspicion for pancreatitis to effectively identify all cases.

Despite its common occurrence, pancreatitis has been a challenge for veterinarians for many years. This has been due to a lack of targeted treatment options for the disease and a subsequent reliance on supportive and symptomatic care. However, in November 2022, the US Food and Drug Administration (FDA) conditionally approved PANOQUELL®-CA1 (fuzapladib sodium for injection) for the management of clinical signs associated with the acute onset of pancreatitis in dogs. This drug opens the door for the targeted management of this challenging disease. PANOQUELL®-CA1 should be used in conjunction with traditional standard of care therapy for acute pancreatitis (example: fluid therapy, antiemetics, pain management, diet).

PANOQUELL®-CA1 overview

Improvement in the clinical signs associated with pancreatitis is based on a significant reduction in the modified canine activity index (MCAI) from day 0 to day 3 in a field effectiveness study.[2] MCAI is a clinical severity scoring system that involves the assessment of several clinical signs of pancreatitis; this includes lethargy/activity, appetite, vomiting, cranial abdominal pain, dehydration, stool consistency, and the presence of blood in stool.[3] Dogs receiving PANOQUELL®-CA1 achieved more rapid clinical improvement compared with dogs that received a vehicle control, which is the current standard of care.

PANOQUELL®-CA1 contains the active ingredient fuzapladib sodium, which has also been licensed under the brand names BRENDA-Z and BRENDA in Japan as of 2018.

The mechanism of action of PANOQUELL®-CA1 is inhibition of leukocyte function–associated antigen-1 (LFA-1). This reduces neutrophil extravasation into the tissues. Depletion of neutrophils has been shown to be beneficial in experimental models of pancreatitis by reducing concentrations of disease biomarkers, tissue damage, and systemic organ dysfunction.[4]

Conditional FDA approval: What does it mean?

Conditional FDA approval means that when it is used according to the label, the FDA considers the drug safe and to have a reasonable expectation of effectiveness. Conditional approval is valid for 1 year and can be extended for up to a total of 5 years. During this period, the company is tasked with collection of additional data for the drug to be considered to receive full FDA approval.[5] It is likely that this data, in addition to collective clinical experience with PANOQUELL®-CA1, will help further guide use of this drug in dogs and patient selection. It is a violation of federal law to use this product other than as directed in the labeling.

How can PANOQUELL®-CA1 be given?

PANOQUELL®-CA1 is administered at a dose of 0.4 mg/kg (0.1 mL/kg) intravenously (IV) once daily for 3 consecutive days.[2] The drug is available as a multiuse vial that remains stable for 28 days in the fridge and can be used for multiple patients. The author has used PANOQUELL®-CA1 in conjunction with standard of care therapy for pancreatitis in several dogs, with anecdotal success.

What contraindications are there for PANOQUELL®-CA1?

As with all drugs, PANOQUELL®-CA1 should not be given to dogs with a known hypersensitivity to its ingredients (eg, fuzapladib sodium).[2] There is also no published data on PANOQUELL®-CA1 in dogs younger than 6 months of age, and its use should therefore be avoided in this patient population.[2]

What are the potential adverse effects?

As with most drugs, adverse effects are possible. The top 3 adverse reactions reported in the field trial for PANOQUELL®-CA1 included anorexia, digestive tract disorders, and respiratory disorders.[2] These abnormalities were also noted in the vehicle control population, albeit with a lower frequency.[2] Other uncommon but severe adverse events included pruritis/urticaria, anaphylaxis, cerebral edema, hypertension, and cardiac arrest.[2] These adverse events could be due to PANOQUELL®-CA1, the primary disease process, or unrelated disease processes.

Foreign market experience has also indicated facial/tongue swelling, collapse, and seizures as potential adverse effects from PANOQUELL®-CA1.

What should be done if an adverse effect has occurred from PANOQUELL®-CA1?

Any suspected adverse effects should be reported to the FDA and Ceva Animal Health. Ceva's product support can be reached at 1-800-999-0297. Further information on reporting adverse effects is provided on the FDA website.

Supportive and symptomatic care

Fluid therapy

Most dogs with pancreatitis are dehydrated on presentation due to vomiting and other factors. Fluid therapy is therefore important to overcome dehydration, correct ongoing losses, and maintain perfusion of the pancreas. The best initial fluid type is likely a balanced isotonic electrolyte solution (eg, Lactated

Ringer's Solution (LRS)), and choice of fluid type should consider the dog's acid-base and electrolyte status. In human medicine, meta-analyses have shown that LRS is preferred over normal saline.[6] Quarter shock doses of IV fluids over 10 to 15 minutes may be needed in dogs with evidence of severe dehydration and hypotension.

Response to fluid therapy should be determined by monitoring perfusion parameters, blood pressure, and/or serum lactate. Once there is improvement and/or normalization of these parameters, fluid rates can be tapered accordingly and fluid prescription recalculated to account for maintenance needs coupled with ongoing losses. Dogs that are hypotensive despite adequate fluid resuscitation may require vasopressor therapy and are likely best handled in an emergency or specialty hospital. Dogs with mild dehydration may not require IV fluids and may be treated with subcutaneous fluids. On www.panoquell.com, there is an electronic dehydration wheel that aids the veterinarian in calculating the mLs/hr if IV fluids are needed. The veterinarian can input the weight, percent dehydrated, and hours to rehydrate. Visit: **www.panoquell.com/dehydration-wheel**.

Pain management and analgesia

Dogs with pancreatitis should be assumed to have some level of abdominal pain or discomfort. Some dogs may be stoic and therefore not show overt signs of abdominal pain; it is the author's belief that these dogs should still receive analgesia, as it can result in resolution of more subtle signs of pain such as inappetence and mild tachycardia. Opioid analgesics are the mainstay of analgesia in dogs with pancreatitis. Nonsteroidal anti-inflammatory drugs (NSAIDs) are considered contraindicated due to the heightened concern for gastrointestinal and renal adverse effects in hypovolemic and dehydrated dogs.[7] The analgesic effect of opioids is mediated through their actions on μ, ɗ, and κ receptors in the central nervous system. Full μ opioid agonists (eg, methadone or fentanyl) are considered the most effective analgesics and should be used in patients with severe abdominal pain. Partial μ opioid agonists (eg, buprenorphine) are often suitable for patients with mild to moderate discomfort. Some clinicians avoid using fentanyl to treat acute pancreatitis due to concerns for disproportionately severe intestinal ileus relative to other opioids; however, evidence is lacking, and the author's experience suggests that dose titration allows for suitable use in most dogs.[7] Other full μ opioid agonists such as hydromorphone are associated with a higher prevalence of vomiting and are generally avoided, although this can be mitigated in healthy surgical patients by premedication with maropitant citrate.[8]

Adjunctive analgesia may be used in dogs with refractory pain or in an attempt to reduce opioid use. Ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist that can be administered as a continuous rate infusion. A second-line adjunctive therapy would be lidocaine. Lidocaine is a local anesthetic that blocks voltage-gated sodium channels. It may have the added benefits of improving gastrointestinal function and reducing inflammation. Alternatively, locoregional anesthetic techniques have been suggested, including epidurals and transversus abdominis plane blocks.[9,10]

Outpatient analgesic options considered by the author include gabapentin, codeine, and amantadine. If there is a sudden relapse of pain during recovery from pancreatitis, repeat abdominal ultrasound and examination for peripancreatic fluid accumulations or thrombi is recommended.

Nutritional support

Historically, it was thought that dogs with pancreatitis should be kept *nil per os* to prevent excess stimulation of the exocrine pancreas. However, this has been debunked, and early enteral nutrition is now encouraged in the management of dogs with pancreatitis.[11] Early enteral nutrition is well tolerated and results in a faster return to voluntary food intake and a reduction in gastrointestinal intolerance, relative to dogs with delayed enteral nutrition.[11, 12] General recommendations for diet formulations for dogs with acute pancreatitis include highly digestible, low-fat diets. Feeding prescriptions should be calculated in terms of patient resting energy requirement (RER). RER can be calculated as [(body weight in kg ^ 0.75) * 70] and reflects the number of daily calories needed to sustain homeostasis and the basal metabolic rate. Typically, a dog should be started at 20% to 30% of their RER, which should be increased by 20% to 30% every 6 to 24 hours. Dogs that have been anorexic for more than 3 to 5 days and are considered to be in a state of malnourishment should have a slower escalation to full RER. Serum electrolyte concentrations should be monitored closely in these patients.

Antinausea medication

Control of vomiting is an important part of the management of pancreatitis. Antiemetics can be used to reduce the incidence of vomiting and to control nausea, which is often associated with reduced voluntary food intake. Maropitant citrate and/or ondansetron are commonly used for this purpose in dogs.

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