

## A Revolution in Feline Diabetes Mellitus Care! Novel Drugs and New Recommendations

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### Sodium-glucose cotransporter 2 (SGLT2) inhibitors

- In 2024, the FDA in the United States approved two SGLT2 inhibitors for the treatment of diabetes mellitus in cats: Bexacat (bexagliflozin tablets, Elanco) and Senvelgo (velagliflozin solution, Boehringer Ingelheim). As of this writing (April 2025), only Senvelgo has been approved in Canada.
- Both drugs are administered once daily, and dose titration is typically not necessary. Since Senvelgo is a solution, it could be titrated if needed, but this should be an uncommon need.
- SGLT2 inhibitors work by limiting renal glucose reabsorption, leading to excretion of excess blood glucose in urine. They do not cause hypoglycemia (even if given to a non-diabetic cat) because they only block one of two receptors in the renal tubules.

### Candidates for treatment with an SGLT2 inhibitor

- Currently, the recommended candidates are **newly diagnosed** diabetic cats that have never been treated with insulin, that are not 'sick' (e.g., no vomiting, diarrhea, lethargy, hypo/anorexia), and do not have serious concurrent diseases.

### Contraindications for treatment with an SGLT2 inhibitor

- Cats with certain concurrent illnesses should not be treated with SGLT2 inhibitors:
  - Hepatic disease
  - Renal disease (IRIS stage 3 or higher) because the drugs have not been evaluated in this type of patient.
  - Current or history of pancreatitis
  - Ketonuria or ketonemia; blood beta-hydroxybutyrate (BHB) >3.6 mmol/L
  - Other serious systemic illnesses
  - Not eating well, lethargic, dehydrated - if the patient can be stabilized, treatment may be possible
- Cats that are currently on insulin or those previously treated with insulin.
  - Cats that were previously treated with insulin may be more likely to develop ketosis or diabetic ketoacidosis (DKA) when treated with SGLT2 inhibitors.
  - The reason is that a percentage of diabetic cats will be insulin dependent. It is not known how many diabetic cats are insulin-dependent but likely the percentage would be very small. Veterinarians are allowed to use drugs off-label as long as we can support the choice. If an owner is struggling to treat a diabetic cat with insulin, changing to Senvelgo may be appropriate (ensure the owner understands the potential risk and document it in the patient's file). As more experience is gained using these drugs in a variety of diabetic cats, it is likely the label recommendations will change.

### Minimum diagnostics before treatment with an SGLT2 inhibitor

- A good medical history, thorough physical examination (with body condition score [BCS], muscle condition score [MCS], weight, blood pressure)

- Complete blood count, serum chemistries, total T4, fructosamine. For some patients, additional testing may include fPLI, cobalamin, and imaging.

#### Dosages and efficacy

- Senvelgo is dosed at 1 mg/kg once daily. Each mL is 15 mg and the bottle is 30 mL (450 mg/bottle). The bottle will last 90 days for a 5 kg cat. It does not require refrigeration once opened and has a six-month shelf life once opened. The bottle comes with a dosing syringe - the dose is measured in the same way Metacam is measured. Senvelgo can be given orally or with a small amount of food.
- Efficacy for Senvelgo is between 80%-90%. Most cats respond to treatment within the first week.

#### Key points for monitoring cats receiving an SGLT2 inhibitor

- Patients should be closely monitored in the initial eight weeks
  - Mild diarrhea is the most common adverse effect; it usually resolves on its own.
  - DKA is the most serious adverse effect; it is most likely to occur within the first 14 days of treatment. It is important to note that cats on these medications may develop euglycemic DKA (eDKA) - they have ketoacidosis with a normal blood glucose.
- Blood glucose curves are not required for monitoring as patients that are well-controlled on these drugs have a very stable blood glucose around the clock, i.e., there is no 'curve.'

#### Plan for monitoring cats receiving an SGLT2 inhibitor

When	What	What to do
2-3 days	<ul style="list-style-type: none"><li>● PE including BCS, MCS, weight</li><li>● Clinical signs</li><li>● BHB (blood) for DKA/eDKA</li><li>● Glycemic control*</li></ul>	Continue medication unless weight loss or BHB is not decreasing
7 days		Same as above
2 weeks		Continue medication unless weight loss or BHB is not decreasing; monitor closely if average BG is $\geq 13.9$ mmol/L and/or fructosamine is elevated
4 weeks		Same as above
Every 3-4 months		Same as above
If the cat is unwell at any time, check for DKA/eDKA.		

BCS, body condition score; BHB, beta-hydroxybutyrate; MCS, muscle condition score; PE, physical exam

\*Glycemic control can be assessed in a variety of ways: spot blood glucose, a blood glucose curve, serum fructosamine, or data from a Freestyle Libre.

- Four appointments are needed by week 4, so it may be best to book these appointments in advance.

- Ongoing monitoring: cats should be re-evaluated every 3-4 months or whenever they show signs of systemic illness. In addition to a physical exam (with BCS, MCS, weight) and medical history, monitoring can include:
  - Blood glucose
  - Serum Fructosamine
  - Serum BHB
  - Serum feline pancreas-specific lipase (fPL)
  - Liver parameters
  - Serum cholesterol and triglycerides
- Cats on an SGLT2 inhibitor have no greater risk of urinary tract infection than cats on insulin. Urine cultures are not needed unless there are clinical signs or hematuria.
- Current recommendations suggest that owners should check urine ketones (with test strips) once monthly and should monitor for polyuria, polydipsia, polyphagia, or any other change.
- Assess for DKA/eDKA if any of the following occur:
  - Hypo/anorexia, lethargy, depression, unintentional weight loss
  - Poor or worsening glycemic control by eight weeks or any time thereafter
  - Increased fructosamine or no decrease from level at diagnosis
  - Increasing BHB
  - Persistent or progressive hypertriglyceridemia and/or hypercholesterolemia
- Treating DKA/eDKA: this is a life-threatening emergency; some patients may be euglycemic or nearly so (blood glucose <15 mmol/L). Stop the oral drug. Treatment is the same for any case of DKA (insulin and 5-10% dextrose). The current recommendation is that recovered cats should be managed with insulin rather than an SGLT2 inhibitor.