<Date>

Senvelgo® (velagliflozin) 15 mg/ml oral solution for cats: Known risk of diabetic ketoacidosis (DKA) in cats with diabetes mellitus associated with the use of the product

Dear Veterinarian,

Boehringer Ingelheim Vetmedica GmbH in agreement with the European Medicines Agency and <National Competent Authority> would like to communicate important information about the safe use of Senvelgo®, including those situations that may require immediate intervention.

The reason for this letter is to highlight correct use of the product to minimise serious consequences (including diabetic ketoacidosis (DKA) and fatalities) which have been reported from post-marketing pharmacovigilance data.

Key messages:

1. Senvelgo® 15 mg/ml oral solution for cats contains velagliflozin, an SGLT-2 inhibitor in veterinary medicine, and is indicated to reduce hyperglycaemia in non-insulin dependent diabetic cats; therefore, not all diabetic cats may be suitable for treatment with Senvelgo®, especially those currently being managed with insulin. Careful patient selection is important.
2. Serious consequences (including diabetic ketoacidosis (DKA) and fatalities) have been reported from post-marketing pharmacovigilance data, including cases where unsuitable cats were switched from insulin therapy to Senvelgo®.
3. Most of these DKA cases occurred between 0-4 days after starting treatment. This highlights the importance of checking for ketones after initiating treatment, daily for the first 7 days and then every 1-3 days for the following week. In addition, screening for the presence of ketone bodies should ideally also be performed on plasma within this first 2-week period.
4. Prior to initiating treatment with Senvelgo®, screening for DKA must be performed as DKA is a potentially fatal metabolic complication of diabetes mellitus.
5. Insulin pre-treated diabetic cats are at higher risk of developing DKA and ketonuria, compared to newly diagnosed patients.
6. Veterinarians should inform cat owners of the risk of DKA and seek to ensure that cat owners are able to carefully monitor their cats for potential development of DKA; immediate veterinary consultation is necessary if ketones are detected or clinical signs of DKA are observed.
7. For the first two weeks of treatment, it is important to closely monitor cats for potential development of DKA and whenever the cat shows clinical signs of illness whilst being treated.
8. Immediate discontinuation of treatment in the event of confirmed or suspected DKA or diabetic ketonuria, appropriate investigation, and immediate initiation of appropriate therapy (e.g. insulin therapy) is required. Cat owners should be advised to contact their veterinarian in this respect.

9. DKA, under SGLT-2 inhibition, may occur with normal blood glucose concentrations (euglycaemic ketoacidosis). However, the immediate initiation of insulin treatment is still needed to stop the progression of ketoacidosis.

Background information

Senvelgo® 15 mg/ml oral solution for cats, was first authorised in the European Union (EU) in November 2023. It contains velagliflozin, a sodium-dependent glucose co-transporter 2 (SGLT-2) inhibitor and represents a new active substance for use in veterinary medicine.

Senvelgo® is indicated for the reduction of hyperglycaemia in cats with non-insulin dependent diabetes mellitus. A SGLT-2 inhibitor works differently to insulin and reduces blood glucose by preventing renal glucose re-absorption and is only suitable for use in cats that are still able to produce sufficient amounts of endogenous insulin. Therefore, the use of SGLT-2 inhibitors is not recommended for all diabetic cats. Patient selection is consequently highly important. There is currently no test available to differentiate between insulin-dependent and non-insulin dependent diabetic cats, and thus patient selection requires clinical judgement. Treatment should not be initiated or resumed, if ketonuria or blood ketone bodies at concentrations indicative of DKA are present. Clinical signs, such as unintended weight loss, dehydration, lethargy, anorexia (inappetence), vomiting, cachexia may indicate DKA. DKA is a potentially life-threatening complication of diabetes mellitus.

Based on post marketing pharmacovigilance reports (European database of suspected adverse drug reaction reports - Search (adrreports.eu)), daily monitoring of ketones is recommended for the first 7 days then every 1-3 days for the following week. In the event of confirmed or suspected DKA or diabetic ketonuria, immediate discontinuation of treatment and appropriate investigation are required.

In the summary of product characteristics (SPC), DKA is listed as a common adverse event, expected in 1-10% of Senvelgo® treated cats. DKA cases, including fatalities, have been reported from post-marketing pharmacovigilance data, including cases where unsuitable cats were switched from insulin therapy to Senvelgo®. Most of these DKA cases occurred between 0 and 4 days after starting treatment.

Furthermore, the use of SGLT-2 inhibitors may lead to the development of euglycemic DKA (absence of hyperglycaemia), a life-threatening emergency that is characterised by euglycemia, metabolic acidosis, and ketoacidosis. In case of (euglycaemic) DKA it is imperative to immediately initiate appropriate therapy. This includes the prompt initiation of insulin therapy despite normal blood glucose values, while monitoring/treating for hypokalaemia. The initiation of insulin is needed to stop the progression of ketoacidosis. Administration of dextrose or other carbohydrate source and appropriate nutritional support (to prevent or treat hepatic lipidosis), in addition to insulin, should be considered.

Information for cat owners

Owners should be provided with the product information and review it with veterinarians to seek to ensure that the owners understand the importance of closely monitoring the condition of their cat (including checking for urine ketones and/or any clinical signs of illness) and the importance of seeking prompt veterinary advice. Veterinarians will need to educate clients on how to recognise signs of DKA in a cat on Senvelgo®. Owners should use urine test strips daily for the first 7 days and every 1-3 days after that for the following week; and be encouraged to bring cats to the veterinary clinic/practice for monitoring of ketones, especially within the first 2 weeks of initiating therapy, since screening for the

presence of ketone bodies should ideally also be performed on plasma. Owners should be advised to discontinue Senvelgo® and consult a veterinarian immediately if their cat develops anorexia, lethargy, sudden weight loss, vomiting or if ketone bodies are detected in their cat's urine (e.g. using urine test strips).

Full information on patient selection and monitoring are provided in sections 3.3 and 3.5 of the SPC. The SPC is available following this link: Senvelgo 15 mg/ml - Oral solution | UPD (europa.eu).

The positive benefit-risk balance for Senvelgo® remains unchanged with no changes in the product information (e.g. SPC, PL) at present.

Call for reporting

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Veterinarians are recommended to report any suspected adverse events via the national reporting system: (<insert details on the national reporting system>) or the marketing authorisation holder or its local representative (<insert details or cross reference to company contact below if appropriate>) in accordance with national reporting requirements.

Company contact point

Should you have any questions or require additional information, please contact:

<Contact point details for access to further information, including relevant website address(es), telephone numbers and a postal address>

TOPIC-SPECIFIC COMMUNICATION PLAN FOR: Direct animal health care professional communication on *Risk of diabetic ketoacidosis (DKA) in cats with diabetes mellitus - Important information*	
Medicinal product(s)/active substance(s)	Senvelgo / velagliflozin
Marketing authorisation holder(s)	Boehringer Ingelheim Vetmedica GmbH
Issue and objectives of the communication	To communicate important information about the use of Senvelgo®, including those situations that may require immediate intervention.
Target audience	Senvelgo® prescribing veterinarians Details for each country to be discussed and agreed with the National Competent Authorities (NCAs) of the countries where Senvelgo® is marketed.
Member States where the communication will be distributed	EEA countries where Senvelgo is marketed.
Stakeholders to coordinate with	European Medicines Agency (EMA) NCAs of the EEA countries where Senvelgo® is marketed Distributors in Finland (Vetcare Oy) and Iceland (Vistor hf). Veterinary associations in the EEA countries where Senvelgo is marketed (if applicable).
Means of dissemination	This may vary in different Member States due to local distribution models/local laws. Examples: paper/digital dissemination (e.g. email) to prescribing veterinarians for whom the MAH has contact details available. Publication on the websites of the NCAs of the countries where Senvelgo® is marketed (where applicable).
Follow-up and measurement of effectiveness	Acknowledgement of receipt of DaHPC from veterinarians will be considered as admissible under local law Frequencies of reported adverse events (i.e. early DKA, death associated with DKA) will be monitored.

Timetable	Date
Preparation of draft DaHPC and communication plan	9 July 2024
DaHPC and communication plan agreed by CVMP	18 July 2024
Publication of agreed DaHPC and communication plan on EMA website	19 July 2024
Submission of translated DaHPC to the national competent authorities for review	25 July 2024
Agreement of translations by national competent authorities	01 August 2024
Dissemination of the DaHPC	09 August 2024
Evaluation of effectiveness	6 months from submission of the next conclusion on the benefit-risk balance, which will be submitted 31 August 2024 i.e. 28 February 2025