

ALGORITHM

Senvelgo[®] patient management guide



Senvelgo 
(velagliflozin)



GUIDE FOR MANAGING DIABETIC CATS WITH SENVELGO®



Diagnosis of diabetes mellitus according to ALIVE criteria



HAPPY DIABETIC

The cat is eating, drinking and interactive with no vomiting, diarrhoea, dehydration, lethargy or cachexia



UNHAPPY DIABETIC



Check for ketones

If ketonuria or excessive ketonaemia

If NO ketonuria or excessive ketonaemia

NOT CURRENTLY SUITABLE CANDIDATE FOR SENVELGO®

- See Unsuitable SENVELGO® candidate protocol for treatment recommendations
- Once clinical signs have resolved, check for ketones and consider SENVELGO®



Start SENVELGO® 1 mg/kg PO once daily

INITIAL MONITORING FIRST 14 DAYS



MONITORING FOR KETOSIS/DKA/eDKA

- ~ Day 2/3 Ketones (at home)
- ~ Day 7 Ketones, glycaemic parameters, PE, weight
- ~ Day 14 Ketones, glycaemic parameters, PE, weight

Ketones/DKA/eDKA detected; see Unhappy on SENVELGO® recommendations

LONG-TERM MONITORING



MONITORING FOR KETOSIS/DKA/eDKA AND GLYCAEMIC CONTROL

- Recheck at Week 4 and then every 3 months
- Check ketones, glycaemic parameters, PE, weight

Ketones/DKA/eDKA/unsatisfactory glycaemic control detected; see Unhappy on SENVELGO® recommendations



If the patient is unwell at any time, evaluate for DKA/eDKA

Flowchart abbreviations:
DKA: diabetic ketoacidosis
eDKA: euglycaemic diabetic ketoacidosis

PE: physical examination
PO: per os
~: approximately

For further information, please see the extended version of the SENVELGO® patient management guide.

INTRODUCING

SEVELGO[®], THE GDAB AND ALIVE

Introducing the Global Diabetes Advisory Board

Meet the authors of this management guide. Introducing the Global Diabetes Advisory Board (GDAB), a collaboration of respected feline diabetes experts from Europe and North America:

Ellen Behrend, PhD, DACVIM

Professor Emerita, Auburn University, Auburn, USA

Sylvie Daminet, PhD, DACVIM

Professor, Ghent University, Ghent, Belgium

Federico Fracassi, PhD, Dipl ECVIM-CA

Professor, University of Bologna, Bologna, Italy

Ruth Gostelow, PhD, DACVIM, Dipl. ECVIM-CA

Lecturer, Royal Veterinary College, London, UK

Katarina Hazuchova, PhD, Dipl. ECVIM-CA

Senior Clinician, Justus Liebig University, Gießen, Germany

Hans Kooistra, PhD, Dipl. ECVIM-CA

Professor, Utrecht University, Utrecht, The Netherlands

Susan Little, DABVP

Professor, Bytown Cat Hospital, Ottawa, Canada

Stijn Niessen, PhD, Dipl. ECVIM-CA, Chair (GDAB)

Honorary Professor, Royal Veterinary College, London, UK

Dan Rosenberg, PhD

Associate Professor, Micen Vet Centre, Créteil, France

Cynthia Ward, PhD, DACVIM

Professor Emerita, University of Georgia, Athens, USA

Introducing ALIVE

Project ALIVE was founded by the European Society of Veterinary Endocrinology (ESVE) in 2016 and endorsed by the Society for Comparative Endocrinology (SCE) in 2017. It aims to expand the function of both societies by creating a common voice within veterinary endocrinology and focuses on creating agreement over the definition of common terminology.²

Diagnosis of diabetes mellitus in cats

The ALIVE criteria for diagnosis of diabetes mellitus in cats consist of either³:

1. Blood glucose ≥ 15 mmol/L (≥ 270 mg/dL) with classic clinical signs of hyperglycaemia* with at least ONE of the following:

- Increased serum fructosamine
- Glucosuria on more than one occasion[†]

2. Blood glucose > 7 mmol/L and ≤ 15 mmol/L (> 125 mg/dL and ≤ 270 mg/dL) with at least TWO of the following:

- Classic clinical signs of hyperglycaemia*
- Increased serum fructosamine
- Glucosuria on more than one occasion[†]

Diagnosis of concurrent disease

Prior to initiating treatment, screening for ketosis should be performed. Clinical signs such as dehydration, lethargy, anorexia (inappetence), acute vomiting and cachexia alongside hyperglycaemia and presence of blood or urine ketone bodies may indicate that the cat has diabetic ketoacidosis (DKA) or may be at higher risk of developing DKA. Insulin-pretreated diabetic cats may be at higher risk for DKA.¹

In line with diabetes mellitus treatment guidelines,⁴ cats should also be evaluated for concurrent diseases including pancreatitis, urinary tract infection, neoplasia and acromegaly as these conditions may increase the risk of developing ketoacidosis. The following conditions should be resolved prior to treatment start: dehydration, suspected or confirmed DKA, clinical pancreatitis, acute vomiting, chronic diarrhoea and cachexia.¹ SENVELGO® is safe for use in cats with chronic kidney disease (CKD) stages 1 and 2 but has not been tested in cats with CKD stages 3 and 4.

Diagnostic tests to be performed in any diabetic cat include^{4,5}:

- **Haematology, biochemistry, blood/urine ketones, urine analysis**
- **Additional tests could be considered based on the presentation of the individual patient**

* Classic clinical signs of hyperglycaemia include polyuria, polydipsia, polyphagia and weight loss. Other differentials for these signs should be ruled out.

[†] Urine sample should be a naturally voided sample acquired in a home environment at least 2 days after any stressful events.

UNSUITABLE

SEVELGO® CANDIDATE PROTOCOL

Ketonuria/excessive ketonaemia:

- Excessive ketonaemia: blood ketone concentration exceeding the upper end of the reference interval of the employed ketometer/assay
- May indicate development or presence of DKA and should be resolved prior to starting treatment with SEVELGO®
- Unhappy cat with ketones/ketosis – see DKA/eDKA recommendations (page 6)

Clinical signs:

- Lethargy, inappetence or acute vomiting
 - May indicate presence of DKA, pancreatitis or other concurrent diseases
 - The cause should be evaluated and treated (resolution of clinical signs) prior to starting treatment with SEVELGO®
- Dehydration
 - SGLT-2 inhibitors may cause osmotic diuresis (glucosuria); dehydration should be resolved prior to treatment start with SEVELGO®
- Cachexia
 - Due to the glucosuric effect (energy loss) and reduced fat reserves, cachexia should be resolved prior to treatment start with SEVELGO®
- Diarrhoea
 - SGLT-2 inhibitors may decrease stool consistency; therefore, diarrhoea should be resolved prior to treatment start with SEVELGO®

Insulin treatment may be required during resolution phase of the conditions listed above, especially if resolution is not anticipated to occur within 2 days.

UNHAPPY ON SENVELGO®

RECOMMENDATIONS

- Stop SENVELGO® treatment until condition has resolved
- Ketosis/ketonuria detected
 - May indicate development or presence of DKA/eDKA
 - Unhappy cat with ketones/ketosis – **see DKA/eDKA recommendations** (below)
- Persistent hyperglycaemia
 - Check compliance with SENVELGO® administration
 - If hyperglycaemia persists, this may indicate stress hyperglycaemia (consider fructosamine or continuous glucose monitoring) or SENVELGO® being ineffective and long-term treatment with insulin may be necessary
- Once ketosis and/or concurrent disease resolved/controlled consider SENVELGO®, closely monitoring for ketones

DKA/eDKA recommendations

Defining DKA and eDKA

- **DKA** – a potentially fatal metabolic complication of diabetes mellitus that consists of the biochemical triad of hyperglycaemia, ketonaemia or ketonuria and metabolic acidosis
 - **eDKA** – due to the mode of action of SENVELGO®, cats that develop DKA while being treated with SENVELGO® may have a normal or near-normal blood glucose (<14 mmol/L [<250 mg/dL]), a condition known as **euglycaemic DKA (eDKA)**
-
- Stop SENVELGO® treatment until DKA/eDKA and underlying concurrent disease are resolved
 - Initiate standard DKA protocol for DKA and eDKA patients with a short-acting insulin and intravenous fluid therapy. Supplement with glucose/dextrose if blood glucose <15 mmol/L (<270 mg/dL)
 - Cats with eDKA require the same standard DKA protocol as cats with hyperglycaemic DKA, including short-acting insulin therapy and glucose/dextrose, despite normal/near-normal glucose
 - Once the patient is clinically well, treat with either a longer-acting insulin or consider SENVELGO®, closely monitoring for ketones. Given the current lack of knowledge, it is not known if SENVELGO® can be reinstated (decision needs to be taken on a case-by-case basis)

MONITORING

CATS ON SENVELGO®

Monitoring in the clinic

Recheck appointments in the clinic are recommended at 1, 2 and 4 weeks and then every 3 months. Cats with diabetes mellitus and treated with SENVELGO® should be monitored according to standard diabetes mellitus treatment guidelines including:

Initial monitoring: First 14 days

1. History and clinical examination including body weight and hydration status
 - Prior to initiating treatment and on Days 7 and 14 of treatment
2. Evaluate glycaemic parameters
 - Blood glucose on Days 7 and 14
 - If spot blood glucose remains >15 mmol/L (>270 mg/dL) at 2 weeks, consider stress hyperglycaemia and/or owner compliance issues
 - Fructosamine at Day 14 and/or continuous blood glucose monitoring can be useful to rule out stress hyperglycaemia and to get a more complete understanding of the cat's glycaemic state
3. Ketones
 - Evaluate blood or urine ketones on Days 7 and 14 (and Day 2/3 if client is unable to check urine ketones at home)
 - In case of ketonuria or excessive ketonaemia, SENVELGO® treatment should be discontinued and insulin treatment started while the cause of the ketosis is investigated

Long-term monitoring

1. History and clinical examination including body weight and hydration status
 - At Week 4 and then every 3 months
 - Ideal body condition score should be aimed for
2. Evaluate glycaemic control
 - Blood glucose or fructosamine starting from Week 4 and then every 3 months
 - If hyperglycaemia is persistent and non-responsive to SENVELGO®, SENVELGO® should be stopped and insulin therapy initiated
3. Ketones
 - Evaluate blood or urine ketones at Week 4 and then every 3 months
 - In case of ketonuria or excessive ketonaemia, SENVELGO® treatment should be discontinued and insulin treatment started while the cause of the ketosis is investigated



If the patient is unwell at any time, evaluate for DKA/eDKA

Monitoring at home

Cat owners should be asked to monitor¹:

Initial monitoring: First 14 days

1. Clinical signs of diabetes

- Polyuria, polydipsia and polyphagia

2. Urine or blood ketones

- Check at Day 2 or 3 with either urine ketone test strips or a handheld blood ketone meter
- In case of ketonuria or excessive ketonaemia, an urgent clinic recheck appointment is required

Long-term monitoring

1. Clinical signs of diabetes

- Polyuria, polydipsia and polyphagia

2. Urine or blood ketones

- Check for ketones with either urine ketone test strips or a handheld blood ketone meter whenever the cat is showing clinical signs of illness, such as reduced food intake, acute vomiting or decreased activity
- In case of ketonuria or excessive ketonaemia, an urgent clinic recheck appointment is required



If the patient is unwell at any time, veterinary attention should be sought

Dose considerations

- All efficacy and safety data are for a dose of SENVELGO® of 1 mg/kg and therefore most cats should remain on this dose long term
- A dose reduction to 0.5 mg/kg may be considered if persistent diarrhoea (>1 week duration) occurs
- Cats may require temporary discontinuation of therapy in clinical situations known to predispose to ketoacidosis



DIAGNOSTIC

METHODS

The following tables give the strengths and weaknesses of different methods for detection of ketosis and evaluation of glycaemic control.

Ketosis detection methods		
Testing method	Strengths	Weaknesses
Blood beta-hydroxybutyrate (BHA)	<ul style="list-style-type: none"> • Can be performed in vet clinic or at home with some cat owners using handheld meter • Rapid results • Provides a numerical ketone value that can be tracked to evaluate progression or resolution of ketosis • Can detect ketosis before DKA/eDKA develops • More sensitive than urine ketone evaluation 	<ul style="list-style-type: none"> • Not all vets have handheld meter in clinic • Many cat owners not able to collect blood at home or won't purchase handheld meter and test strips
Urine ketone test strips	<ul style="list-style-type: none"> • Can be performed at home by most cat owners • Rapid results • No equipment to purchase, only the test strips required 	<ul style="list-style-type: none"> • Not as sensitive as blood BHA • No numerical value for tracking progression/resolution of ketosis • May not be able to collect urine in dehydrated cats with DKA/eDKA
Blood ketone evaluation at reference lab	<ul style="list-style-type: none"> • Provides a numerical result that can be tracked to evaluate progression or resolution of ketosis 	<ul style="list-style-type: none"> • Time delay to obtain results • Potentially higher cost • Requires collection of a larger amount of blood than BHA handheld meter

Options for glycaemic control evaluation		
Testing method	Strengths	Weaknesses
Spot glucose check	<ul style="list-style-type: none"> • Easy to conduct with small blood sample • Result available quickly 	<ul style="list-style-type: none"> • Only provides glucose level at one point in time • Unable to exclude stress hyperglycaemia
Blood glucose curve	<ul style="list-style-type: none"> • Can be useful to rule out stress-related hyperglycaemia and in cases where glycaemic control has not been achieved 	<ul style="list-style-type: none"> • Time consuming and multiple blood samples required, collected over an 8–12-hour period • Usually requires hospitalisation unless owner is capable of collecting blood at home
Continuous blood glucose monitoring	<ul style="list-style-type: none"> • Allows continuous monitoring – can be useful to rule out stress hyperglycaemia and in cases where glycaemic control has not been achieved • Does not require multiple blood samples 	<ul style="list-style-type: none"> • Even with correct placement, a percentage of sensors do not function properly
Serum fructosamine	<ul style="list-style-type: none"> • Allows evaluation of blood glucose concentrations over a 1–3-week period • Not affected by stress hyperglycaemia 	<ul style="list-style-type: none"> • Can't evaluate blood glucose levels over periods of less than 1–2 weeks so cannot help elucidate cause for recent lack of glycaemic control • Requires submission to a reference lab and immediate results not available

INTRODUCING

SENVELGO®

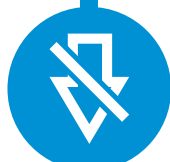
SENVELGO® is the convenient, once-daily oral solution that makes treating feline diabetes simple for vets, cats and their owners.¹⁻⁷



Once-daily oral solution that can be administered directly into the cat's mouth or applied onto a small amount of food



Senvelgo reduces hyperglycaemia, leading to sustained glycaemic control within one week



Eliminates risk of clinical hypoglycaemic events



Precise dosing tailored to the weight of the cat



No more glucose curves



Convenient oral liquid well-accepted by cats



Easy storage – no refrigeration necessary



3 months' supply for a 5 kg cat

SEVELGO

VELAGLIFLOZIN



15 mg/ml oral opløsning til kat

Indikation: Til reduktion af hyperglykæmi hos katte med ikke-insulinkrævende diabetes mellitus. **Dosering:** Den anbefalede dosis er 1 mg/kg legemsvægt administreret én gang dagligt. Lægemidlet kan administreres enten direkte i munden eller sammen med en lille mængde foder. **Bivirkninger:** Diarré eller tynd afføring, polydipsi eller polyuri, vægttab, dehydrering, opkastning, diabetisk ketoacidose (DKA), diabetisk ketonuri, urinvejsinfektion, hypersalivation, hypercalcæmi. **Kontraindikationer:** Må ikke anvendes til katte med kliniske tegn eller laboratorieværdier med tegn på diabetisk ketoacidose (DKA). Må ikke anvendes til katte med svær dehydrering. **Særlige advarsler:** Asymptomatisk hypoglykæmi baseret på enkeltmåling af blodglukose kan observeres sporadisk. Sikkerhed og virkning ved kombinationsbehandling med insulin eller anden blodglukosesænkende behandling og velagliflozin er ikke undersøgt hos katte. Kombinationsbehandling med insulin anbefales ikke. Ved mistanke om remission, bør det overvejes at seponere behandlingen, men fortsætte med andre behandlingstiltag. **Forsigtighedsregler:** Baseret på SGLT-2-hæmmers virkningsmekanisme er tilstrækkelig endogen insulinproduktion en forudsætning for vellykket behandling. Katte med tidligere insulinbehandlet diabetes er i højere risiko for at udvikle DKA og ketonuri når de påbegynder velagliflozinbehandling sammenlignet med nydiagnosticerede patienter. Veterinærlægemidlet må kun anvendes til katte med komorbiditet i overensstemmelse med den ansvarlige dyrlæges vurdering af benefit/risk-forholdet. Afbryd straks behandlingen i tilfælde af bekræftet eller mistanke om DKA eller diabetisk ketonuri. I tilfælde af DKA er det absolut nødvendigt omgående at indlede passende behandling. Ved indledning af behandlingen er kontrol af ketoner påkrævet hver 1 til 3 dage i de første to uger, samt når katten viser kliniske tegn på sygdom. Sikkerhed eller virkning af veterinærlægemidlet er ikke fastlagt hos katte under 1 år. Katte kan også have behov for midlertidig seponering af behandling i kliniske situationer som prædisponerer for ketoacidose. Opbevar den fyldte sprøjte utilgængelig for børn. **Indehaver af markedsføringstilladelse:** Boehringer Ingelheim Vetmedica GmbH **Kontaktoplysninger:** Boehringer Ingelheim Animal Health Nordics A/S, Weidekampsgade 14, 2300 København S. Tlf 39 15 88 88 www.vetportal.dk Ovenstående tekst er baseret på produktresumé dateret 20/11 2023. Der findes detaljerede oplysninger om dette veterinærlægemiddel i EU-lægemiddeldatabasen (<https://medicines.health.europa.eu/veterinary>).



15 mg/ml oral lösning för katt. Receptbelagd

Indikation: För minskning av hyperglykemi hos katter med icke-insulinberoende diabetes mellitus. **Kontraindikationer:** Använd inte till katter med kliniska tecken eller laboratorievärden som tyder på diabetisk ketoacidosis (DKA). Använd inte till katter med svår uttorkning. **Särskilda varningar:** Vid behandling med velagliflozin kan asymtomatisk hypoglykemi observeras sporadiskt baserat på enstaka blodglukosmätningar. Säkerheten och effekten av kombinationsbehandling med insulin eller andra blodsockersänkande behandlingar och velagliflozin har inte undersökts hos katter. Kombinationsbehandling med insulin rekommenderas inte. Vid misstanke om remission kan man överväga att avbryta behandlingen, men fortsätta med andra åtgärder. Om katten får ett återfall kan velagliflozinbehandlingen återupptas. Screening för diabetisk ketoacidosis (DKA) måste utföras före behandlingsstart. Säkerhet och effekt av läkemedlet hos katter med diabetes och komorbiditeter har inte undersökts fullständigt. Användning av läkemedlet till katter med komorbiditeter bör endast ske efter risk-/nytta-bedomning av den ansvariga veterinären. **Bivirkningar:** Diarré eller lös avföring, polydipsi eller polyuri, vikt förlust, uttorkning, kräkningar, diabetisk ketoacidosis (DKA), diabetisk ketonuri, urinvägsinfektion, hypersalivering, hyperkalcæmi. **Administreringsvägar och dosering:** Oral användning. Den rekommenderade dosen är 1 mg/kg kroppsvikt en gång dagligen. Läkemedlet kan administreras antingen direkt i munnen eller med en liten mängd mat. **Innehavare av godkännande för försäljning:** Boehringer Ingelheim Vetmedica GmbH. Information baserad på produktresumé daterad 20/11 2023 Ytterligare information finns tillgänglig på begäran: Boehringer Ingelheim Animal Health Nordics A/S, Box 467, 201 24 Malmö. Tel 040233400 www.vetportal.se



15 mg/ml mikstur, oppløsning til katt

Indikasjon: Til reduksjon av hyperglykemi hos katter med ikke-insulinavhengig diabetes mellitus. **Kontraindikasjoner:** Skal ikke brukes hos katter med kliniske symptomer på diabetisk ketoacidose (DKA) eller laboratorieværdier samsvarende med DKA. Skal ikke brukes hos katter med alvorlig dehydrering som krever intravenøst væsketilskudd. **Særlige advarsler:** Asymptomatisk hypoglykemi kan observeres sporadisk på enkeltmålinger av blodglukose under behandling med velagliflozin. Sikkerhet og effekt av kombinasjonsbehandling med insulin eller annen blodglukosesenkende behandling og velagliflozin hos katter har ikke blitt undersøkt. På grunn av virkningsmekanismen til insulin er det økt risiko for hypoglykemi, og kombinasjonsbehandling er derfor ikke anbefalt. På grunn av velagliflozins virkningsmekanisme kan det være vanskelig å identifisere katter som er i remisjon. Ved mistanke om remisjon bør det vurderes å seponere behandlingen, men videreføre andre tiltak (f.eks. karbohydratfattig kosthold, egnet vektkontroll) og overvåke nøye for glykemisk kontroll og tilbakevendende kliniske symptomer. Dersom katten får tilbakefall, kan behandlingen gjenopptas. Før behandlingstart skal det foretas screening for DKA. Behandling bør ikke startes eller gjenopptas dersom det foreligger ketonlegemer i en konsentrasjon som indikerer DKA. Sikkerhet og effekt av preparatet hos katter med diabetes og samtidige sykdomme har ikke blitt fullt utredet. Hos katter med samtidig sykdom skal preparatet bare brukes i samsvar med nytte/risikovurdering gjort av behandlende veterinær. Følgende tilstander bør korrigeres før behandlingsstart: dehydrering, mistenkt eller bekræftet DKA, anoreksi, klinisk pankreatitt, kronisk diaré, oppkast, kakeksi. På grunn av virkningsmekanismen til SGLT-2-hemmere kan DKA forekomme uten hyperglykemi (euglykemisk ketoacidose). Diagnostisering av euglykemisk DKA må baseres på kliniske symptomer, laboratoriefunn forenlig med metabolsk acidose og andre laboratoriefunn samsvarende med DKA. Ved DKA er det helt nødvendig å innlede egnet behandling med en gang. Dette omfatter umiddelbar oppstart av insulinbehandling til tross for normale blodglukoseverdier (euglykemisk ketoacidose), samtidig med overvåking/behandling for hypokalemi. Oppstart av insulinbehandling er nødvendig for å stoppe videre utvikling av ketoacidose. Tilførsel av glukose eller andre karbohydratkilder og egnet ernæringsstøtte bør overveies i tillegg til insulin. **Bivirkninger:** Diaré eller løs avføring, polydipsi eller polyuri, vekt tap, dehydrering, oppkast, diabetisk ketoacidose (DKA), diabetisk ketonuri, urinvejsinfeksjon, hypersalivering, hyperkalcæmi. **Administrasjonsvei og dosering:** Oral bruk. Den anbefalte dosen er 1 mg/kg kroppsvikt gitt én gang daglig. Doseringsregimet er det samme for katter tidligere behandlet med insulin/annet middel til diabetesbehandling. Ved bytte fra insulin skal kveldsdosen av insulin utelates fra dagen før oppstart av velagliflozinbehandling. Oppløsningen skal trekkes opp med doseringsprøyten som er vedlagt i pakkningen. Sprøyten er tilpasset flasken og har en kg-skala for kroppsvikt. Preparatet kan gis direkte i munnen eller på en liten mengde mat. **Innehaver av markedsføringstillatelsen:** Boehringer Ingelheim Vetmedica GmbH. **Dato for preparatomtale:** 20/11 2023. Preparat er underlagt reseptplikt. **Mer informasjon:** Boehringer Ingelheim Animal Health Nordics A/S, Weidekampsgade 14, 2300 København S, Danmark. Tel +45 39158888 www.vetportal.no

NOTES

AND REFERENCES



References: 1. SENVELGO® SPC 2. ALIVE Project. European Society of Veterinary Endocrinology. Accessed 28 July 2023. www.esve.org/alive/search.aspx 3. Niessen SJM, Bjornvad C, Church DB, et al. Agreeing Language in Veterinary Endocrinology (ALIVE): Diabetes mellitus – a modified Delphi-method-based system to create consensus disease definitions. *Vet J.* 2022;289:105910. doi: 10.1016/j.tvjl.2022.105910. 4. Behrend E, Holford A, Lathan P, Rucinsky R, Schulman R. AAHA diabetes management guidelines for dogs and cats. *J Am Anim Hosp Assoc.* 2018;54:1–21. 5. Nelson RW. Disorders of the endocrine pancreas. In: Nelson RW, Couto CG, eds. *Small Animal Internal Medicine*. 5th edition. Missouri: Elsevier; 2014:777–824.

Senvelgo

(velagliflozin)

