Diabetes mellitus: What's New Pussycat? (& Puppy dog)

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Resident in Internal Medicine

This talk is sponsored by

NovaVet
DIAGNOSTICS

OUTLINE

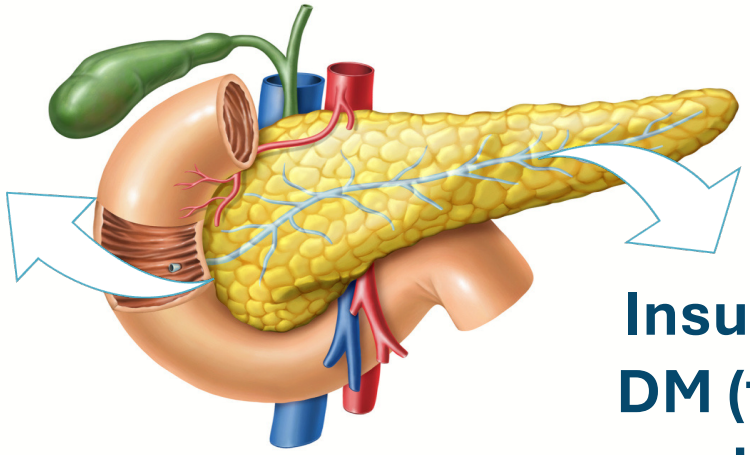
1. Definitions
2. Goals of treatment
3. Monitoring
4. Toujeo
5. Senvelgo

DEFINITION

Diabetes mellitus (DM) is characterized by hyperglycaemia resulting from inadequate insulin secretion, inadequate insulin action or both.

Clinical signs include polyuria, polydipsia, polyphagia and weight loss.

Insulin deficient DM (beta-cell-related disorders)



Insulin resistant DM (target-organ disorders)

GOALS OF DIABETIC TREATMENT

- Avoid hypoglycaemia
- Prevent diabetic ketoacidosis
- Prevent excessive weight loss
- Reduce PU/PD to an acceptable level
- Euglycaemia –diabetic remission if realistic
- Avoid Euthanasia

DIABETIC REMISSION (CATS)

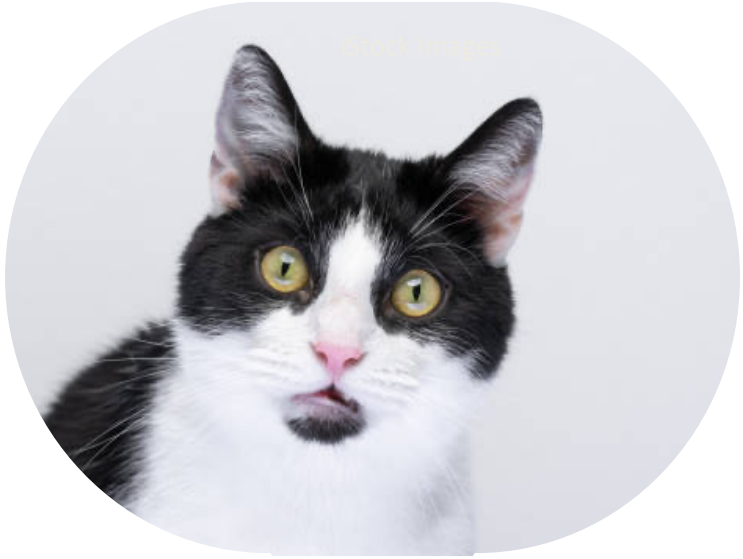
- Remission rates vary depending on study (~30-50%)
- Specific insulin formulation is more likely to lead to remission? → insufficient evidence.
- Diet is important: low carbohydrate
- Tight glycaemic control
- Achieving diabetic remission is the ideal goal to limit financial and emotional burden on owners and reduce euthanasia rate
- These cats remain metabolically abnormal

Remission ≠ equal cure

Ongoing care is required

CHALLENGES OF INSULIN THERAPY

Needs to be safe, effective and sustainable



Limitations of available insulin formulations – there is no perfect insulin

Stress on caregiver – pet owner bond, costs, impact on pet and owners' quality of life

veterinary sciences

MDPI

Article

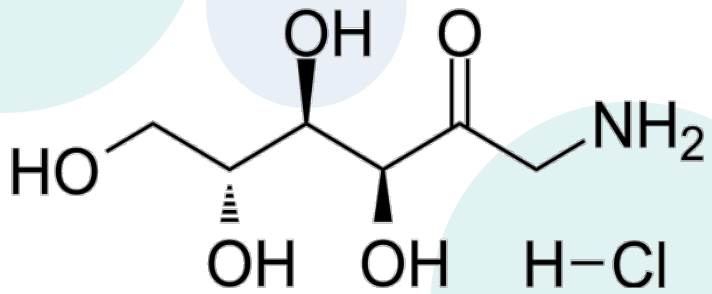
The Big Pet Diabetes Survey: Perceived Frequency and Triggers for Euthanasia

Stijn J.M. Niessen [1,2,*], Katarina Hazuchova [1], Sonya L. Powney [3], Javier Guitian [4], Antonius P.M. Niessen [5], Paul D. Pion [6], James A. Shaw [2] and David B. Church [1]

Academic Editor: Patrick Butaye
Received: 17 January 2017; Accepted: 10 May 2017; Published: 14 May 2017

Up to 30% of cats are euthanased within 1 year of being diagnosed with diabetes.

MONITORING



https://www.zoetisus.com/products/diagnostics/instruments/alphatrak/
https://www.sciencephoto.com/media/1397969/view/glucose-urine-test-results
https://www.usmed.com/products/continuous-glucose-monitoring/freestyle-libre-3-plus-sensor/
https://www.medchemexpress.com/fructosamine-hydrochloride.html

MONITORING

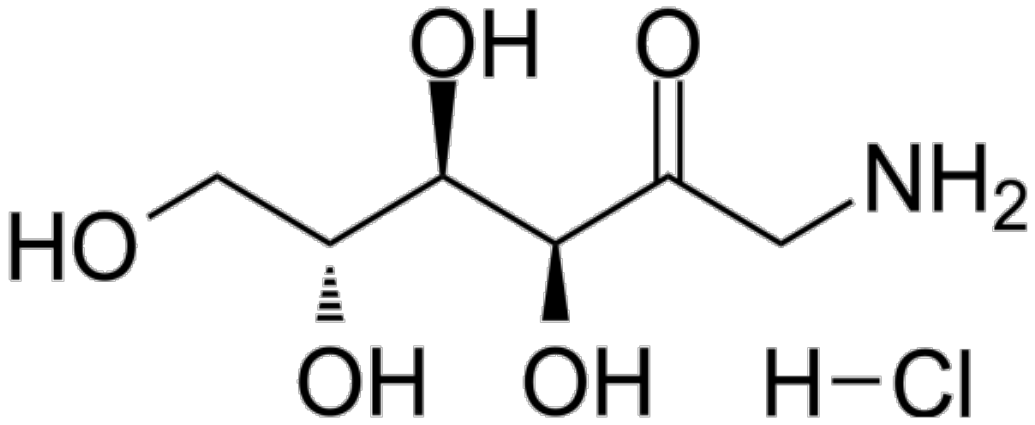
- Clinical signs
- Fructosamine?
- Blood glucose curves
- Continuous interstitial glucose monitoring

FACTOR	SCORE
Unintended Weight Loss 0 = None, or gained since last examined 1 = Mild (<5% loss) 2 = Moderate (5-10% loss) 3 = Severe (>10% loss)	...
Polyuria and polydipsia 0 = Normal 1 = Mild (some increase noted by owner) 2 = Moderate (increased filling of water bowl) 3 = Severe (constantly at bowl)	...
Appetite 0 = Normal or decreased appetite (if decreased appetite exclude DKA or concurrent disease) 1 = Mild polyphagia (finishes eagerly) 2 = Moderate polyphagia (finishes eagerly and begs for more) 3 = Severe polyphagia (obsessed with food)	...
Attitude/activity 0 = Normal 1 = Mild decrease (a bit less running and jumping) 2 = Moderate decrease (a lot less running and jumping) 3 = Severe decrease (lying about all the time) (*consider DKA in the ill patient with diabetes mellitus)	...
TOTAL SCORE	...

ESVE European Society of Veterinary Endocrinology

https://www.esve.org/alive/search.aspx

FRUCTOSAMINE?



FRUCTOSAMINE

Journal of Feline Medicine and Surgery (2008) **10**, 583–592
doi:10.1016/j.jfms.2008.08.005

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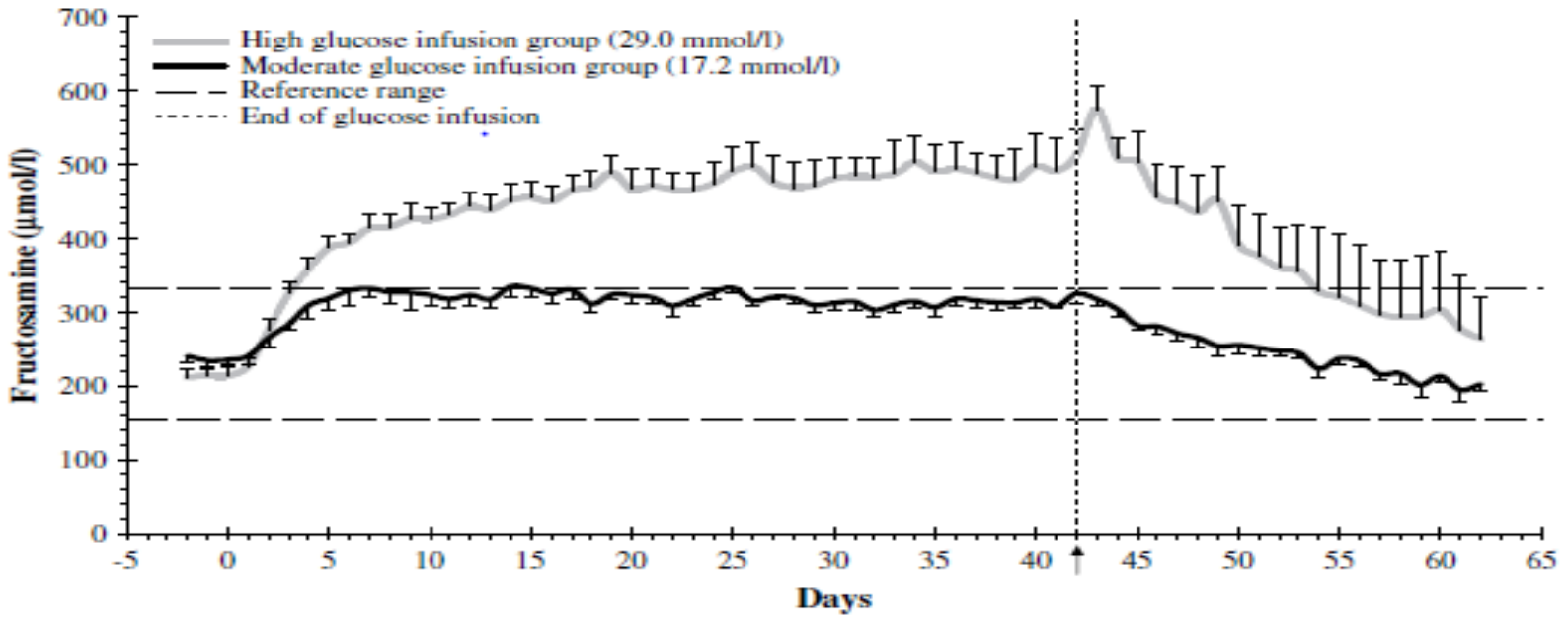


FRUCTOSAMINE

Received: 14 October 2020 | Revised: 12 January 2021 | Accepted: 12 February 2021

DOI: 10.1002/vetr.244

Vet Record

ORIGINAL RESEARCH

Evaluation of fructosamine concentration as an index marker for glycaemic control in diabetic dogs

Florian K. Zeugswetter[1] | Raphael Beer[1] | Ilse Schwendenwein[2]

Fructosamine did not correlate with mean interstitial glucose
Fructosamine did not differ between dogs with and without hypoglycaemic episodes

Fructosamine has moderate clinical utility but if there are discordant clinical signs or concerns of hypoglycaemia continuous glucose monitoring is recommended

Received: 17 March 2022 | Revised: 29 August 2022 | Accepted: 7 September 2022

DOI: 10.1002/vetr.2236

Vet Record

ORIGINAL RESEARCH

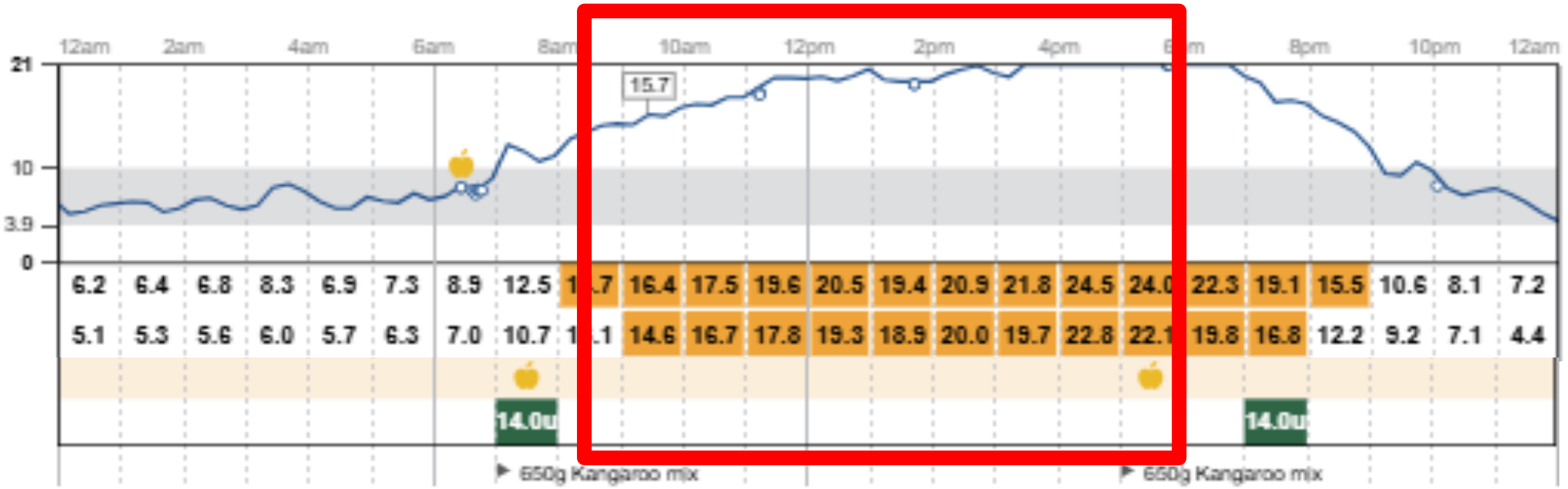
Clinical utility of serum fructosamine in long-term monitoring of diabetes mellitus in dogs

Sharon Kuzi | Michal Mazaki-Tovi | Wiessam Abu Ahmad | Yael Ovadia | Itamar Aroch

GLUCOSE CURVES

GLUCOSE CURVES

LibreView



https://petcontrolhq.com/products/blood-glucose-meter-monitor-dog-cat-diabetes

MONITORING

Received: 1 February 2020 | Accepted: 25 September 2020
DOI: 10.1111/jvim.15930

STANDARD ARTICLE

Journal of Veterinary Internal Medicine Open Access
ACVIM American College of Veterinary Internal Medicine

Comparison between a flash glucose monitoring system and a portable blood glucose meter for monitoring dogs with diabetes mellitus

Francesca Del Baldo[1] | Claudia Canton[1] | Silvia Testa[1] | Harry Swales[2] | Ignazio Drudi[3] | Stefania Golinelli[1] | Federico Fracassi[1]

Good concordance between insulin dose recommendations based on the freestyle monitors and peripheral blood glucose Freestyle monitors allow more accurate identification of nadir, hypoglycaemic episodes & assessment of day-to-day variations

MONITORING

Original Article

Journal of Feline Medicine and Surgery
2022, Vol. 24(8) e223–e231

DOI: 10.1177/1098612X221104051
journals.sagepub.com/home/jfm

This paper was handled and processed by the European Editorial Office (ISFM) for publication in *JFMS*

SAGE

Evaluation of the FreeStyle Libre, a flash glucose monitoring system, in client-owned cats with diabetes mellitus

Marieke Knies[1,2], Erik Teske[2] and Hans Kooistra[2]

MONITORING

70% cats did not have a reaction to sensor placement

Minimal skin reactions

Satisfied owners

Median lifespan of the sensor was 10 days

Good correlation between interstitial and blood glucose measurements

Original Article

Journal of Feline Medicine and Surgery
2022, Vol. 24(8) e223–e231

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SAGE

Evaluation of the FreeStyle Libre, a flash glucose monitoring system, in client-owned cats with diabetes mellitus

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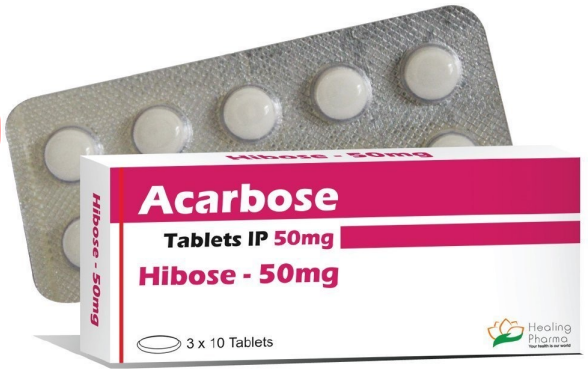
NON-INSULIN HYPOGLYCAEMIC AGENTS

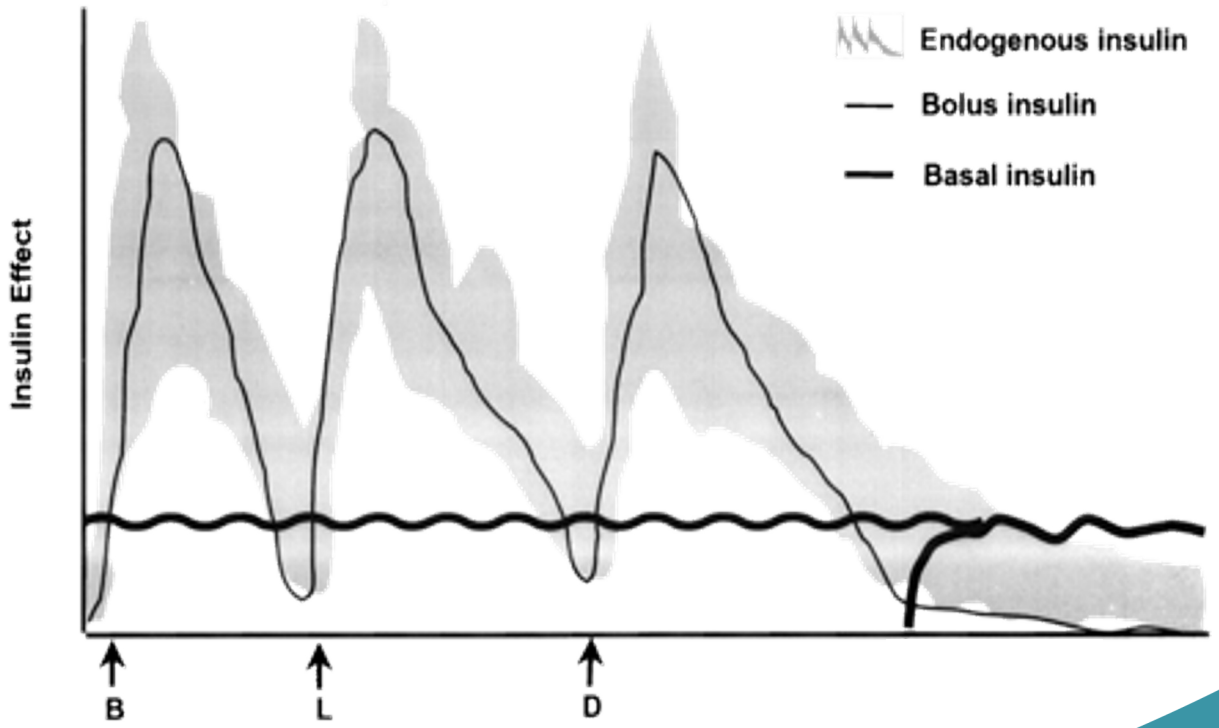


https://lemon.sa/

INSULIN SECRETION

Endogenous insulin is secreted in 2 phases:

- Basal phase: insulin is secreted at a relatively constant rate
- Bolus phase: insulin is secreted in response to absorption of nutrients during a meal



https://www.jabfm.org/content/18/3/199/tab-figures-data

TOUJEO

- More flexible feeding options
- Still recommend diabetic friendly diets → e.g. lower carbohydrate/wet food diets
- Good glycaemic control can be achieved with basal insulin alone
- Meals can be skipped without risking hypoglycaemia = decreased stress for owners

TOUJEO (DOGS)

IMPORTANT

Received: 15 November 2023 | Accepted: 1 May 2024

DOI: 10.1111/jvim.17106

STANDARD ARTICLE

Journal of Veterinary Internal Medicine Open Access

ACVIM American College of Veterinary Internal Medicine

A dose titration protocol for once-daily insulin glargine 300 U/mL for the treatment of diabetes mellitus in dogs

Antonio Maria Tardo[1] | Linda Mary Fleeman[2] | Federico Fracassi[1] | Alisa Saule Berg[3] | Aria L. Guarino[3,4] | Chen Gilor[3]

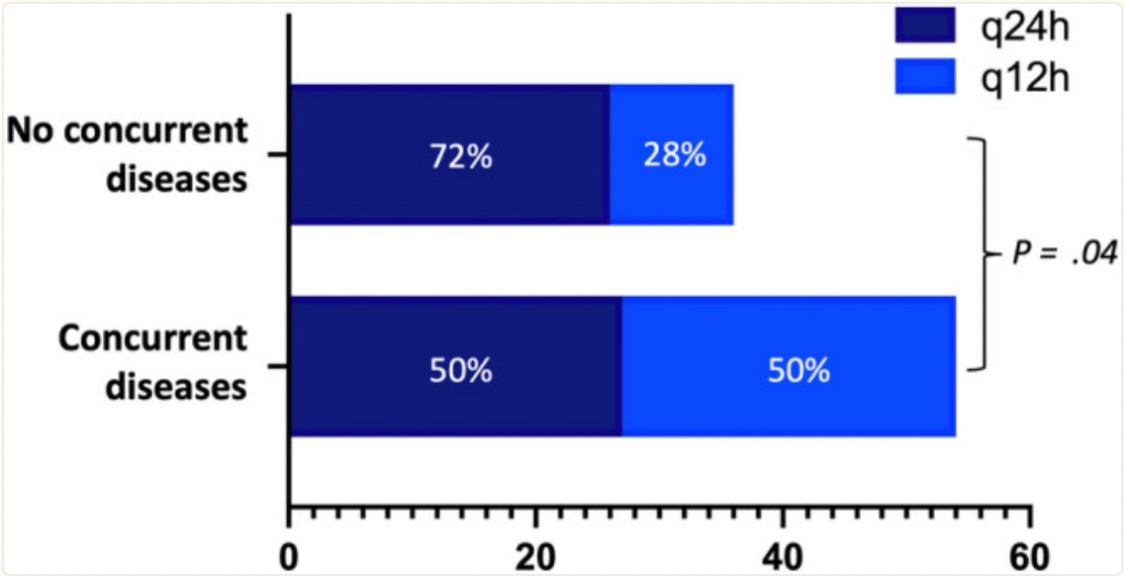
TOUJEO (DOGS)

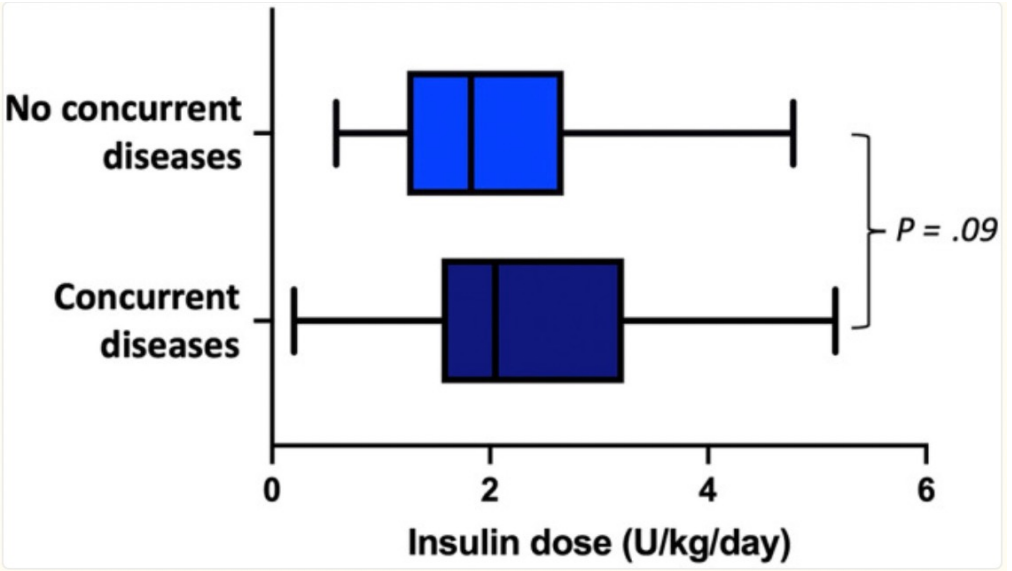
Starting dose: 0.5iu/kg SC SID if newly diagnosed

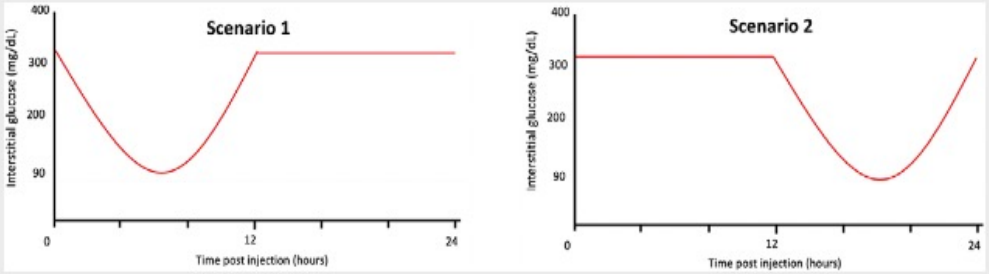
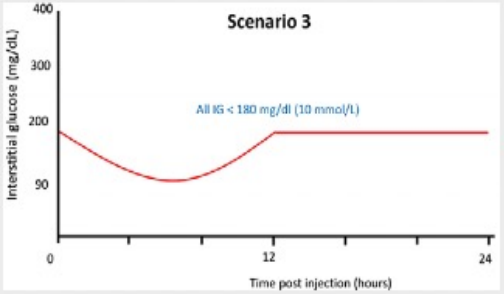
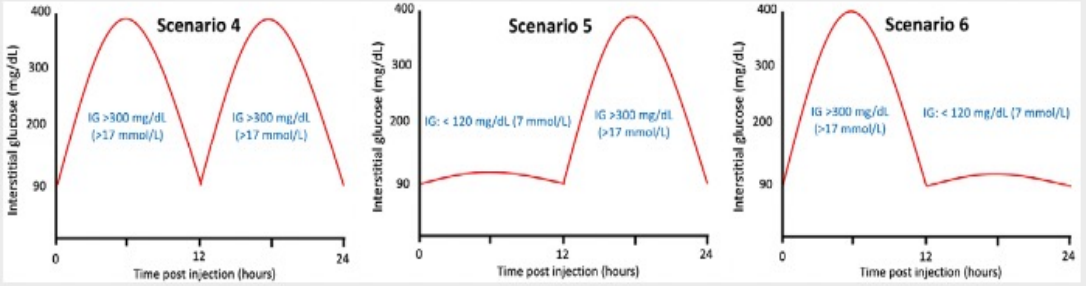
Add 33% to previous insulin dose, rounded down to nearest unit if previously treated with another insulin

- **Excellent glycaemic control in 65%, good in 26%, moderate in 7%, poor in 1 dog**
- **No differences in levels of glycaemic control between dogs with and without concurrent diseases**
- **Median time to achieve glycemic control was 16 days.**
- **Clinical hypoglycaemia in 6% dogs. Most episodes were mild but seizures possible**
- **No dogs developed DKA during the study period**

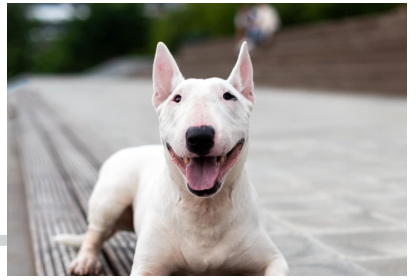
TOUJEO (DOGS)


q24h
q12h
No concurrent diseases
Concurrent diseases
72%
28%
50%
50%
P = .04
0
20
40
60

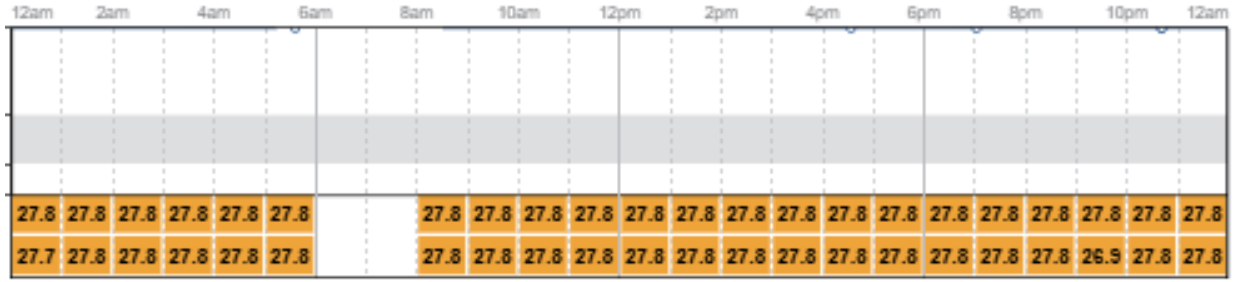

No concurrent diseases
Concurrent diseases
P = .09
0
2
4
6
Insulin dose (U/kg/day)

IG nadir and/or mean	Graphic illustration of interstitial glucose pattern	Recommended dose adjustments for	
		Dogs >8 kg	Dogs <8 kg
Nadir 150-350 mg/dL (8.3-19 mmol/L)		↑10%-30% q24h	↑1 U q24h
Nadir 80-150 mg/dL (4.4-8.3 mmol/L), or nadir <80 mg/dL (<4.4 mmol/L) and mean IG >120 mg/dL (>6.6 mmol/L)		Switch to q12h dosing (with a 30% dose reduction per injection) and re-evaluate the following 3-5 days. Adjust Toujeo dose to achieve nadir between 90 and 300 mg/dL (5-17 mmol/L)	
		No change	
		Maintain IGla300 q24h and add meal-time bolus injections • Scenario 4: at hours 0 and 12 • Scenario 5: at hour 12 • Scenario 6: at hour 0 OR changing the timing and/or quantities fed at meals	
Nadir <80 mg/dL (<4.4 mmol/L) and mean IG <120 mg/dL (<6.6 mmol/L)		↓10%-30% q24h	↓1 U q24h

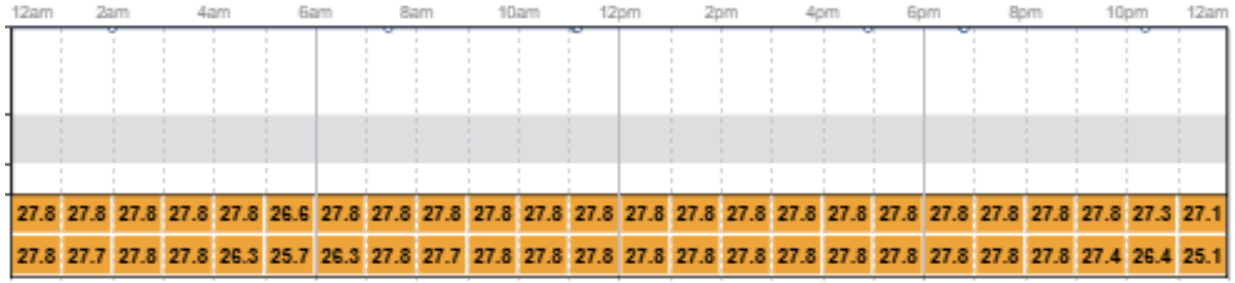
TOUJEO (DOGS)



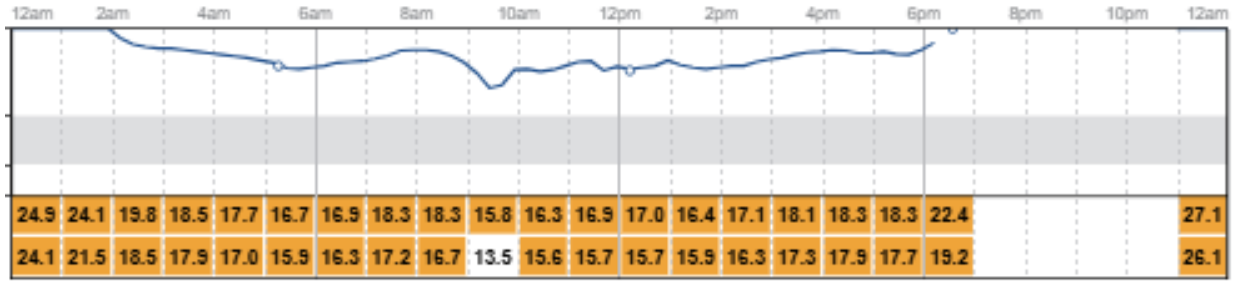
Toujeo day 1
15iu SID



Toujeo day 2
15iu SID



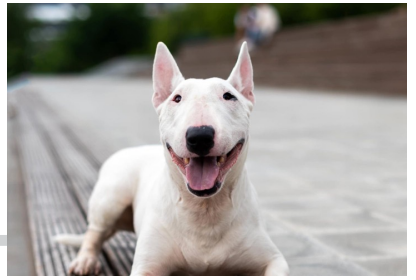
Toujeo day 3
18IU SID



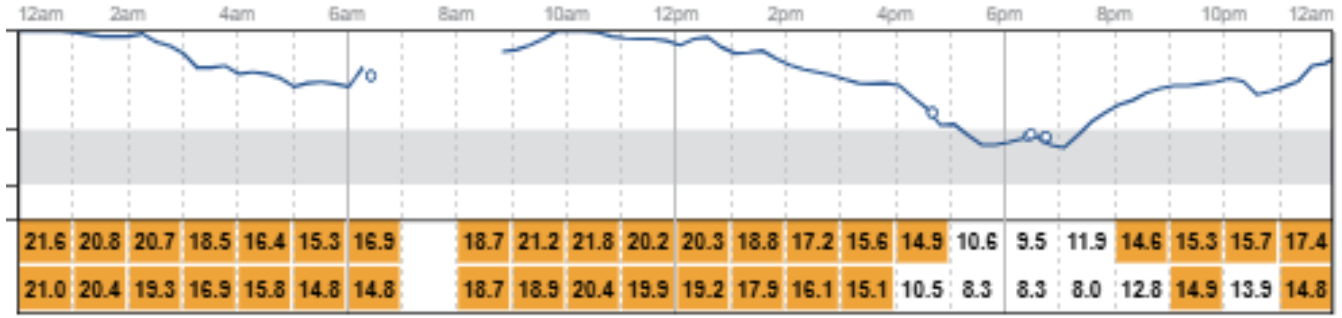
Step 1: Increase toujeo q24h if glucose >19mmol/L

Step 2: Nadir 8.3-19mmol/L Monitor for q3-5d

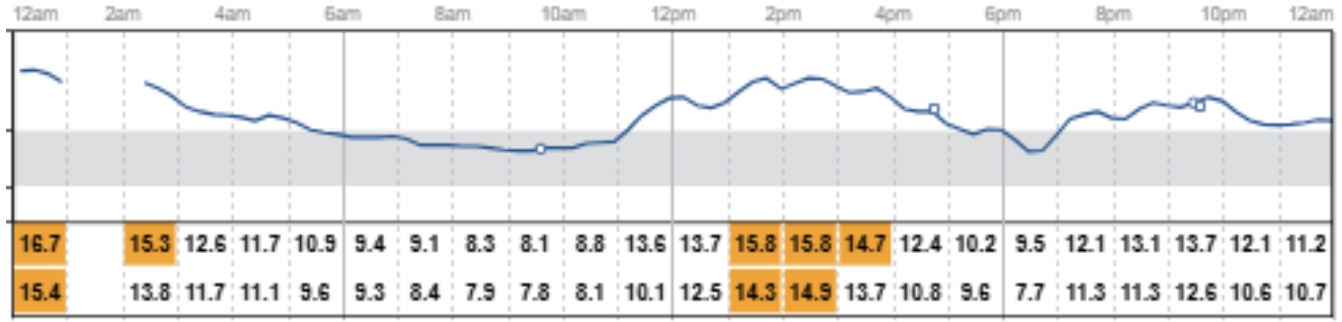
TOUJEO (DOGS)



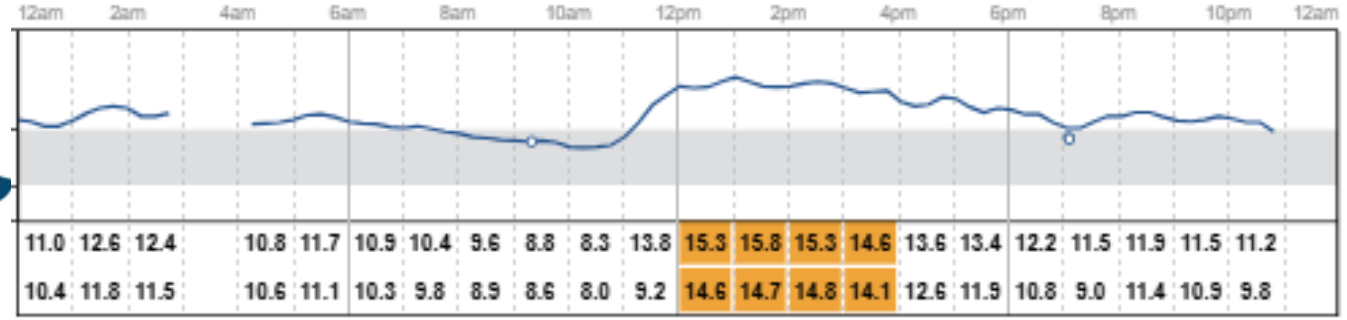
Toujeo day 4
18IU SID



Toujeo day 7
22IU SID

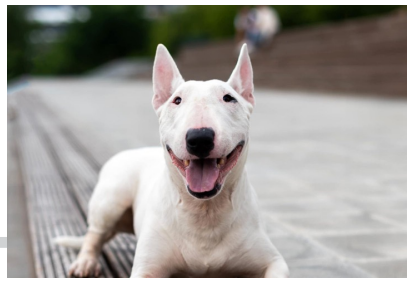


Toujeo day 10
22IU SID

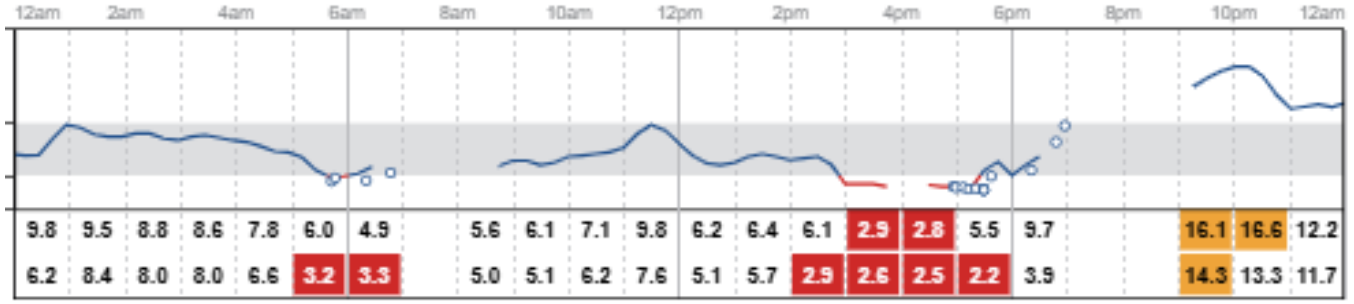


Repeat step 2: Nadir 8.3-19mmol/L
Monitor for q3-5d

TOUJEO (DOGS)

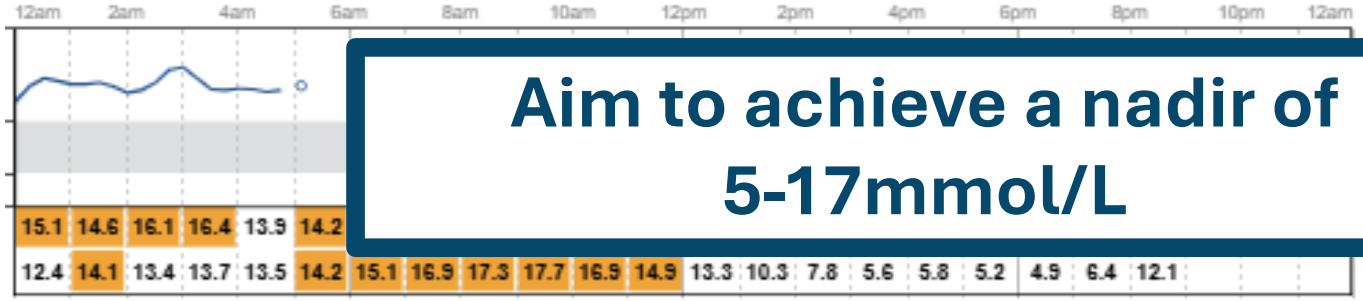


Toujeo day 11
23IU SID



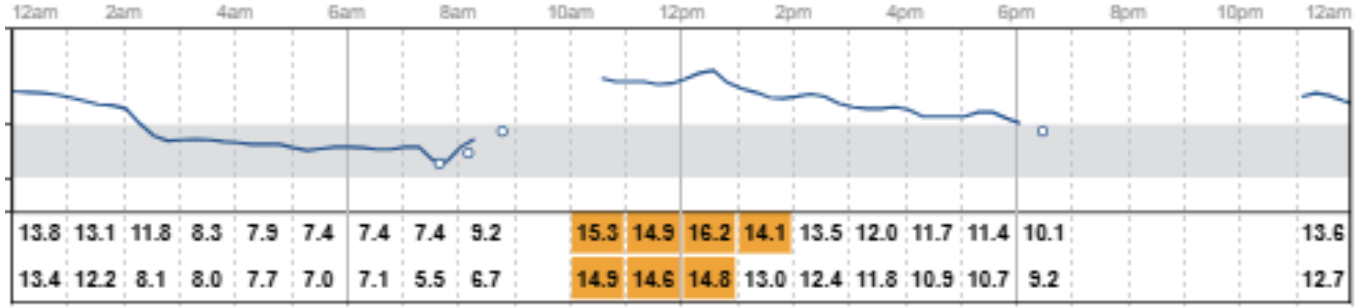
Nadir <4.4mmol/L, mean interstitial glucose <6.6mmol/L
DECREASE by 10-30%

Toujeo day 12
22IU SID



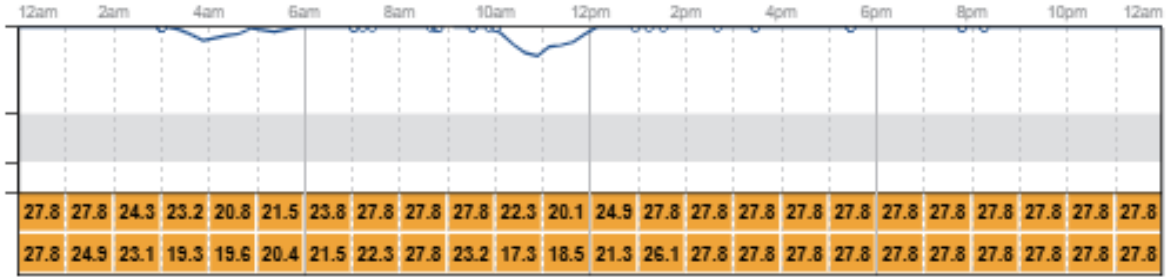
Aim to achieve a nadir of 5-17mmol/L

Toujeo day 14
22IU SID

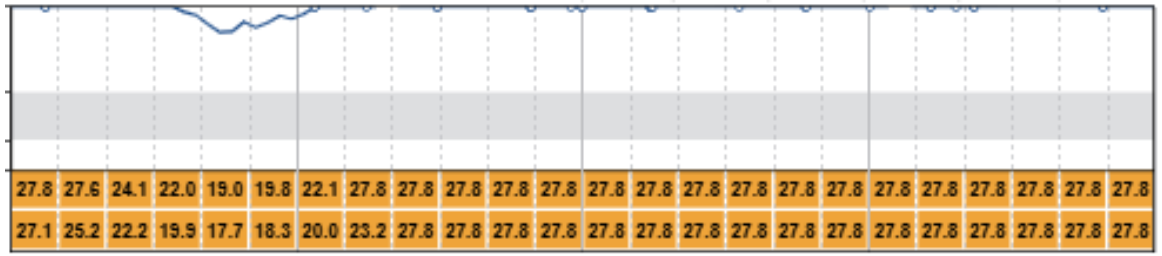


TOUJEO (DOGS)

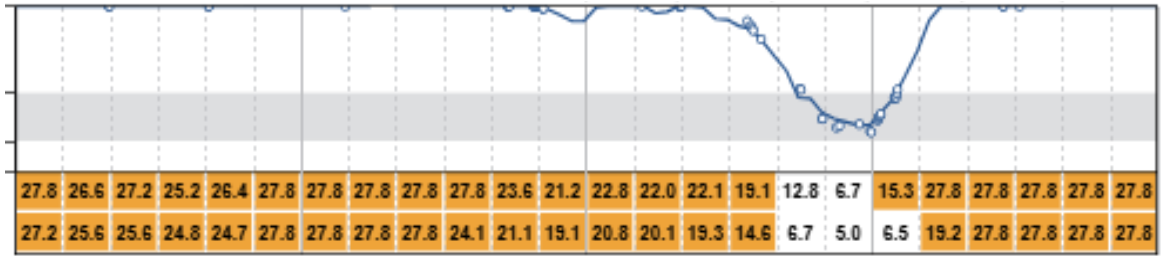
Caninsulin 15iu BID



Toujeo day 1 20IU SID AM



Toujeo day 5 28IU SID AM

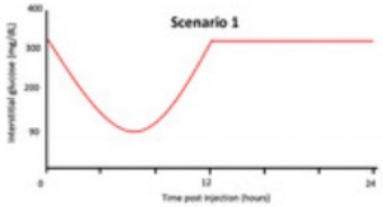


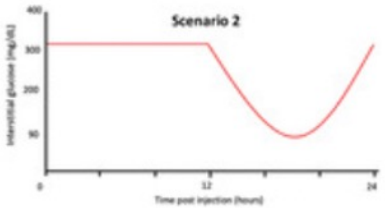
Step 1: Add 33% to previous dose of insulin

Step 2: Increase toujeo if >19mmol/L daily.
If nadir 8.3-19mmol/L
Monitor for 3-5 days

https://bowwowinsurance.com.au/dogs/dog-breeds/miniature-schnauzer/

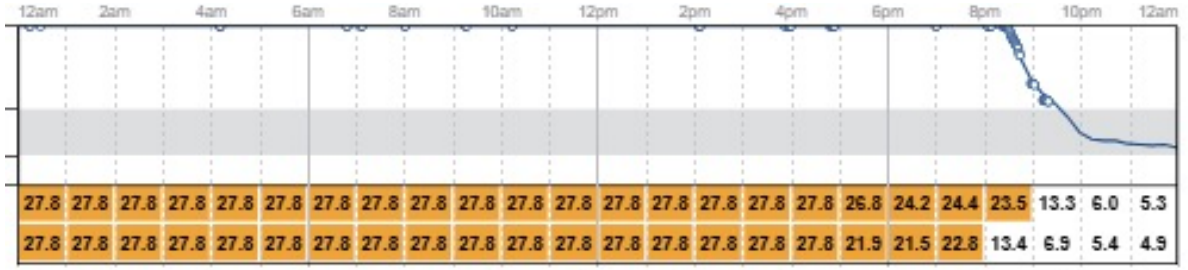
TOUJEO (DOGS)



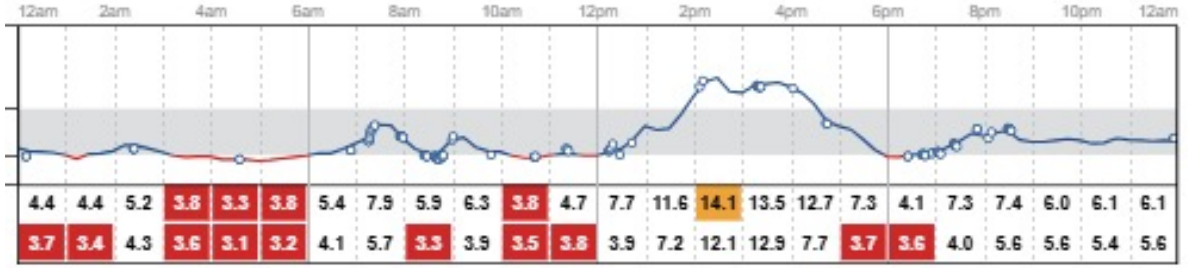


Nadir 4.4-8.3 mmol/L or nadir <4.4mmol/L and mean IG >6.6mmol/L
Reduce each dose by 30% and monitor for 3-5 days.

Toujeo day 6
20iu BID

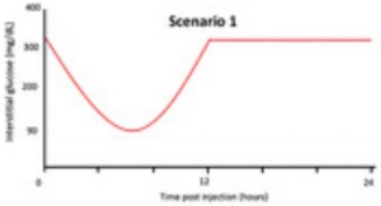


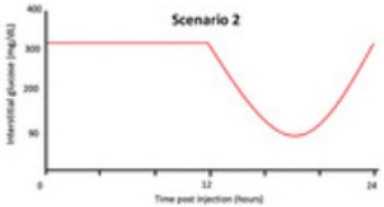
Toujeo day 7
20iu BID



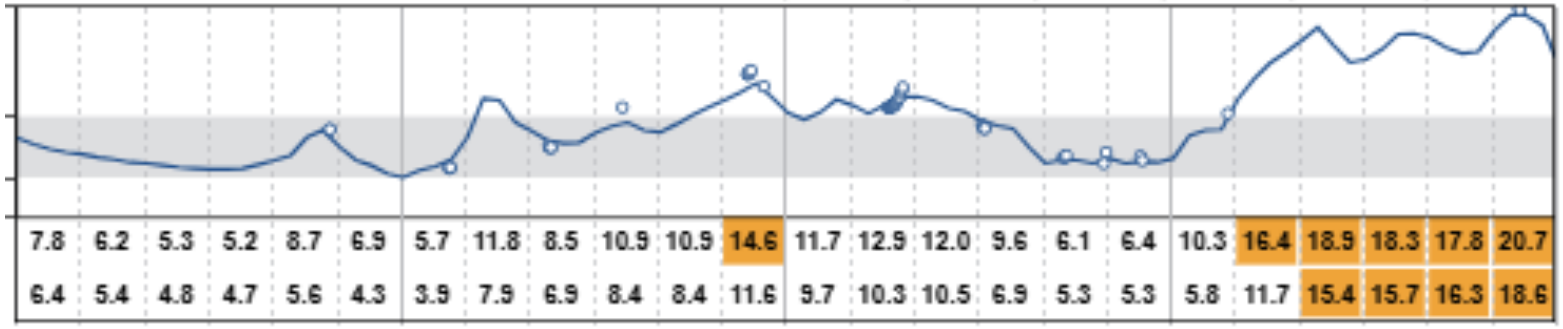
Toujeo day 8
20iu BID

TOUJEO (DOGS)





Toujeo day 13
21iu BID

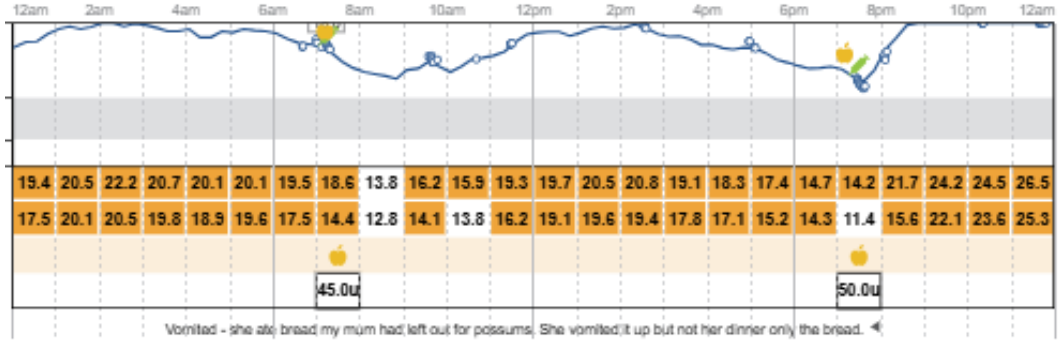


7.8	6.2	5.3	5.2	8.7	6.9	5.7	11.8	8.5	10.9	10.9	14.6	11.7	12.5	12.0	9.6	6.1	6.4	10.3	16.4	18.9	18.3	17.8	20.7
6.4	5.4	4.8	4.7	5.6	4.3	3.9	7.9	6.9	8.4	8.4	11.6	9.7	10.3	10.5	6.9	5.3	5.3	5.8	11.7	15.4	15.7	16.3	18.6

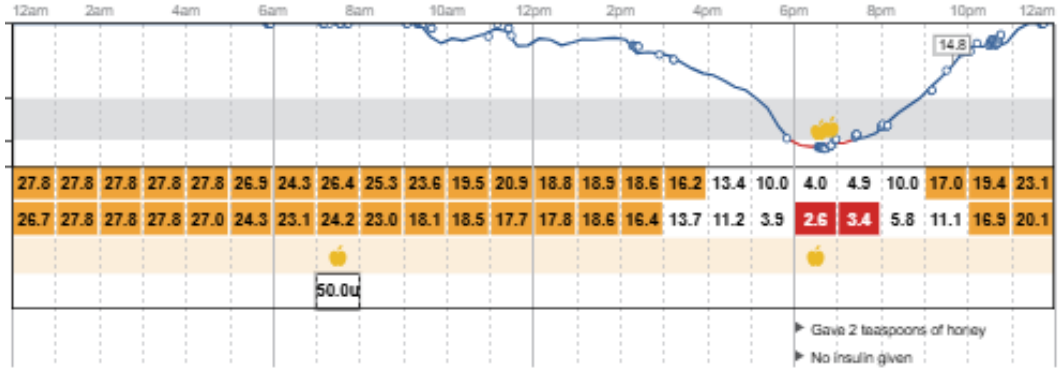
Aim to achieve a nadir of 5-17mmol/L

TOUJEO (DOGS)

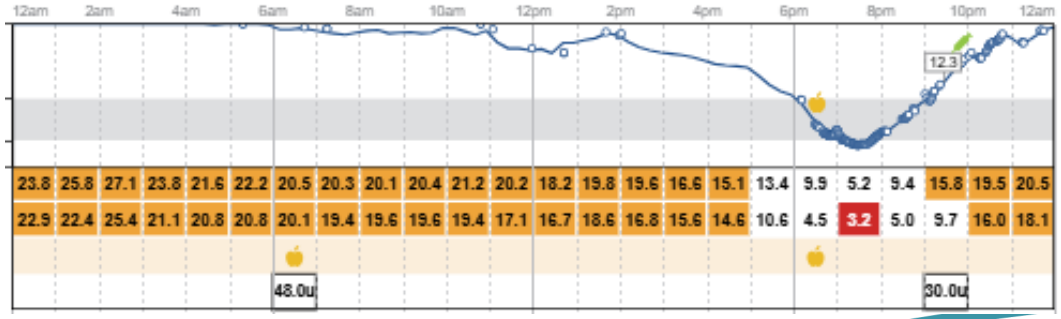
Caninsulin
18iu AM
20iu PM



Caninsulin
20iu AM

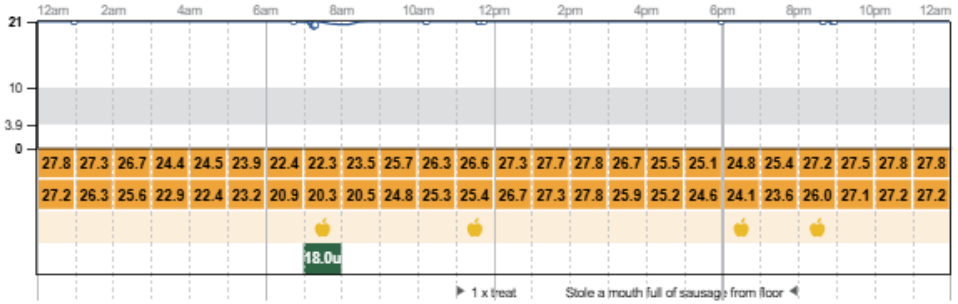


Caninsulin
19iu AM
12iu PM

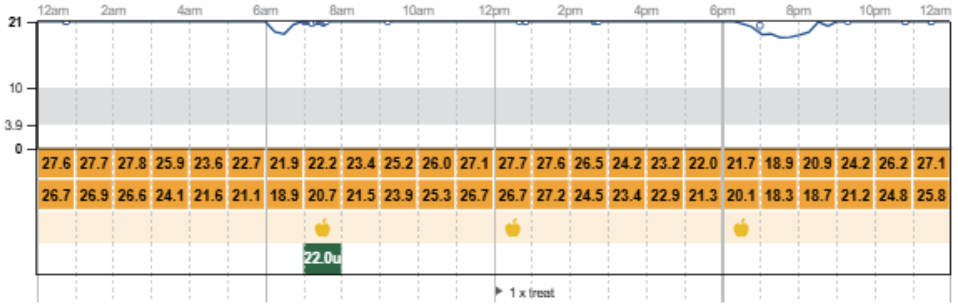


TOUJEO (DOGS)

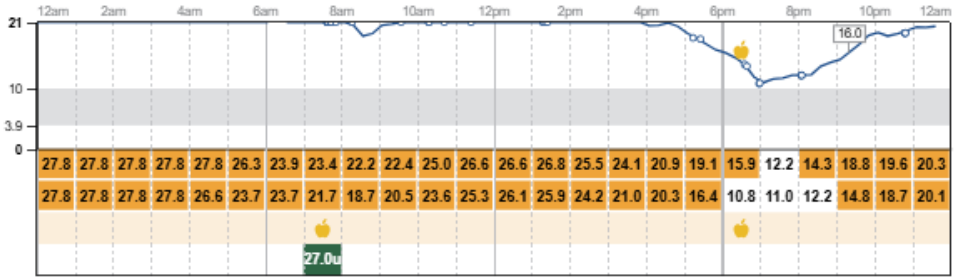
Toujeo day 1
18iu



Toujeo day 2
22iu



Toujeo day 3
27iu

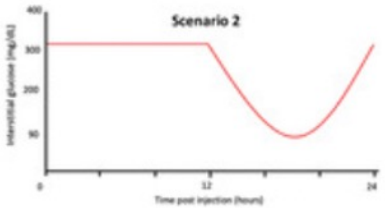


Step 1: Increase toujeo q24h if glucose >19mmol/L

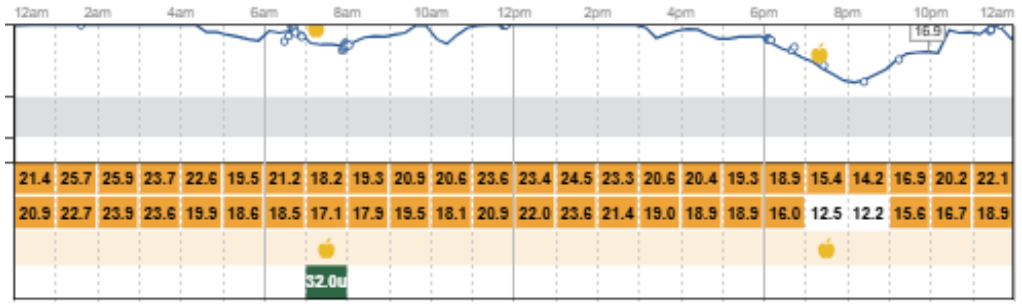
Step 2: If nadir is between 8.3-19mmol/L, monitor for 3-5 days

https://petsonline.com.au/dog-breeds/labrador/size

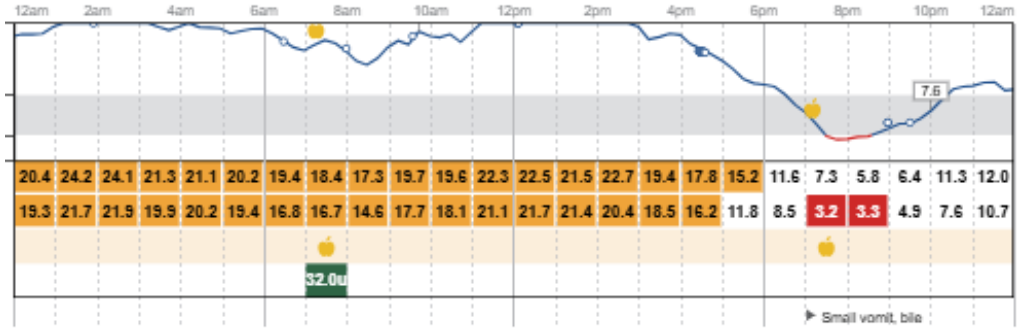
TOUJEO (DOGS)



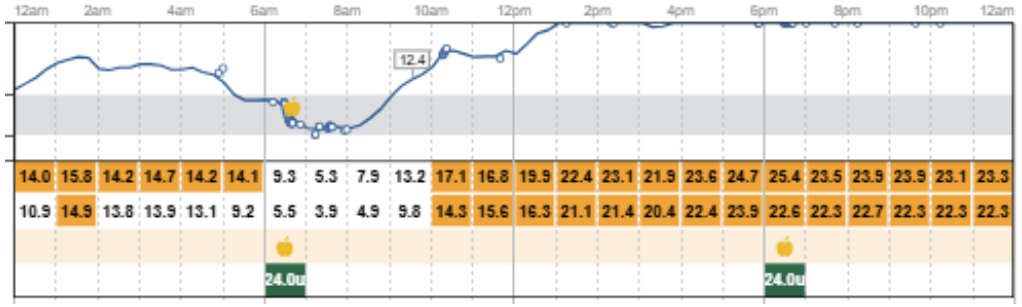
Toujeo day 6 32iu



Toujeo day 7 32iu



Toujeo day 8 24iu BID



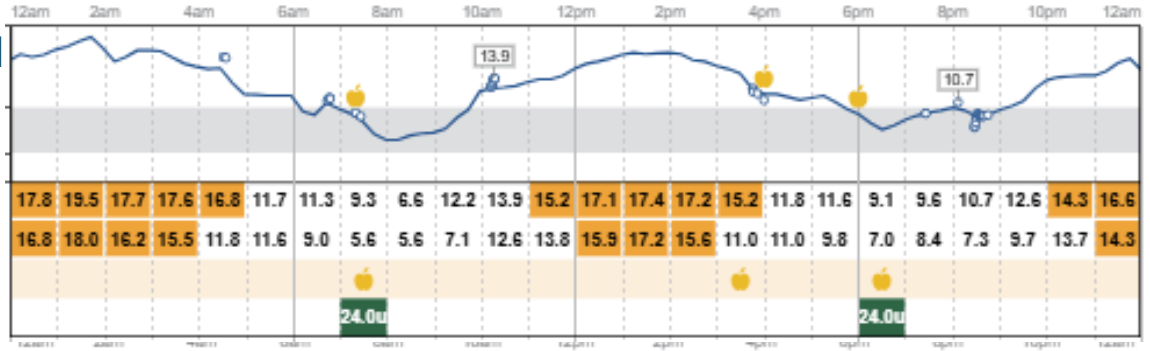
Nadir 4.4-8.3 mmol/L or nadir <4.4mmol/L and mean IG >6.6mmol/L

Reduce each dose by 30% and monitor for 3-5 days.

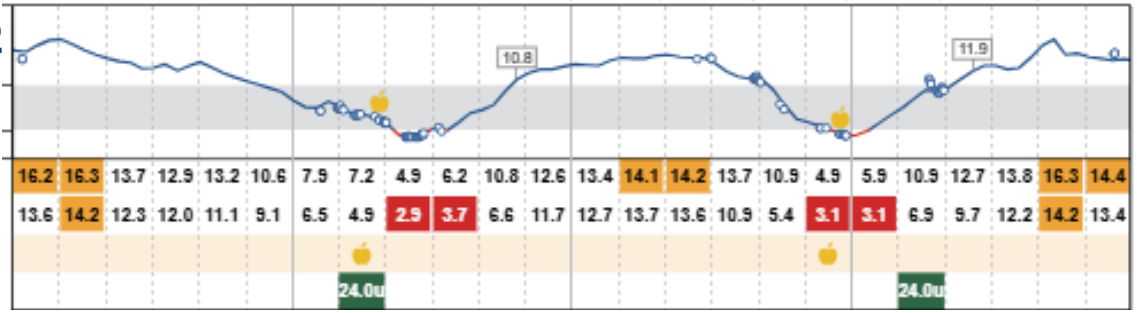
Aim to achieve a nadir of 5-17mmol/L

TOUJEO (DOGS)

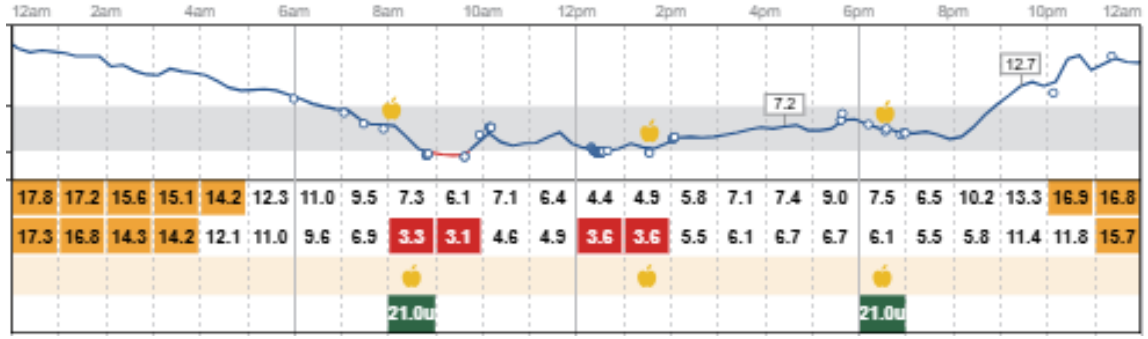
Toujeo day 11
24iu BID



Toujeo day 12
24iu BID



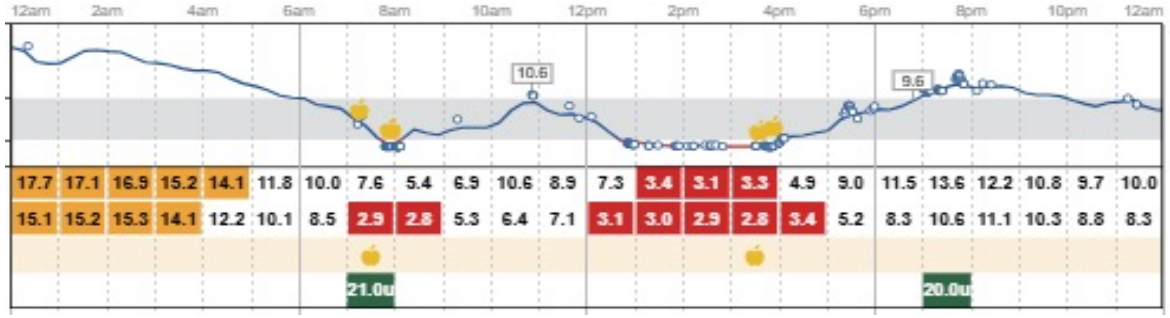
Toujeo day 13
21iu BID



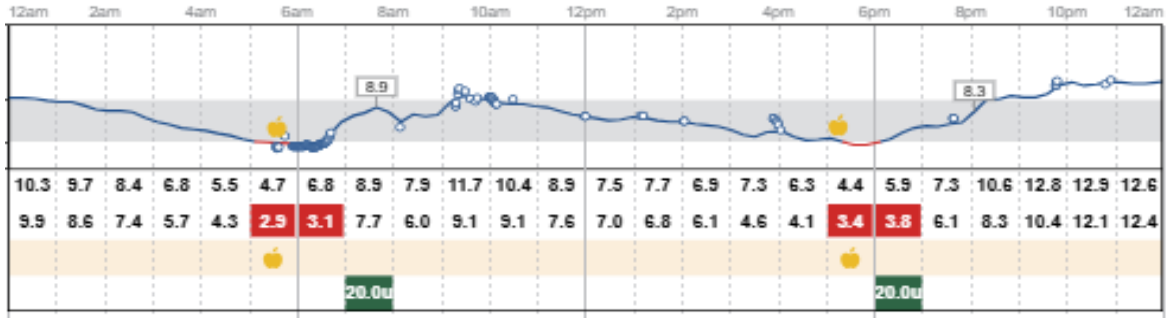
Aim to achieve a nadir of 5-17mmol/L

TOUJEO (DOGS)

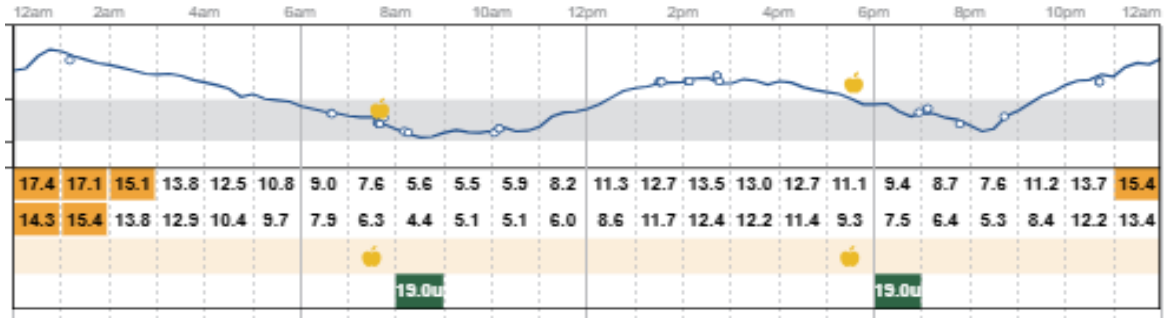
Toujeo day 14
21iu AM,
20iu PM



Toujeo day 15
20iu BID

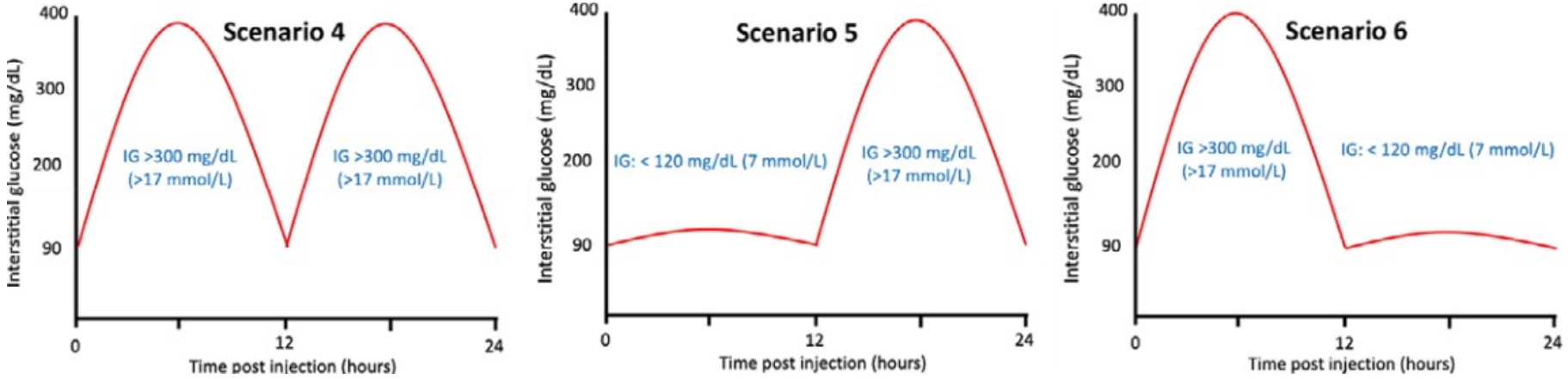


Toujeo day 20
19iu BID



Aim to achieve a nadir of 5-17mmol/L

TOUJEO (DOGS)



Maintain q12-24h and add meal-time bolus injections or change timing/quantity fed at meals

Nadir <4.4mmol/L and mean interstitial glucose <6.6mmol/L → reduce by 10-30% (>8kg)/1U (<8kg)

TOUJEO (CATS)

Original Article

Insulin glargine 300 U/ml for the treatment of feline diabetes mellitus

Guido Linari[1], Linda Fleeman[2], Chen Gilor[3], Lucia Giacomelli[1] and Federico Fracassi[1]

Journal of Feline Medicine and Surgery
2022, Vol. 24(2) 168–176

DOI: 10.1177/1098612X211013018
journals.sagepub.com/home/jfm

This paper was handled and processed by the American Editorial Office (AAFP) for publication in *JFMS*

SAGE

Most cats do not have postprandial bolus insulin requirements, have a slow transit time, grazers and fed a low carbohydrate diet

Basal insulin negates the need for timing insulin administration to a meal

TOUJEO (CATS)

Original Article

Insulin glargine 300 U/ml for the treatment of feline diabetes mellitus

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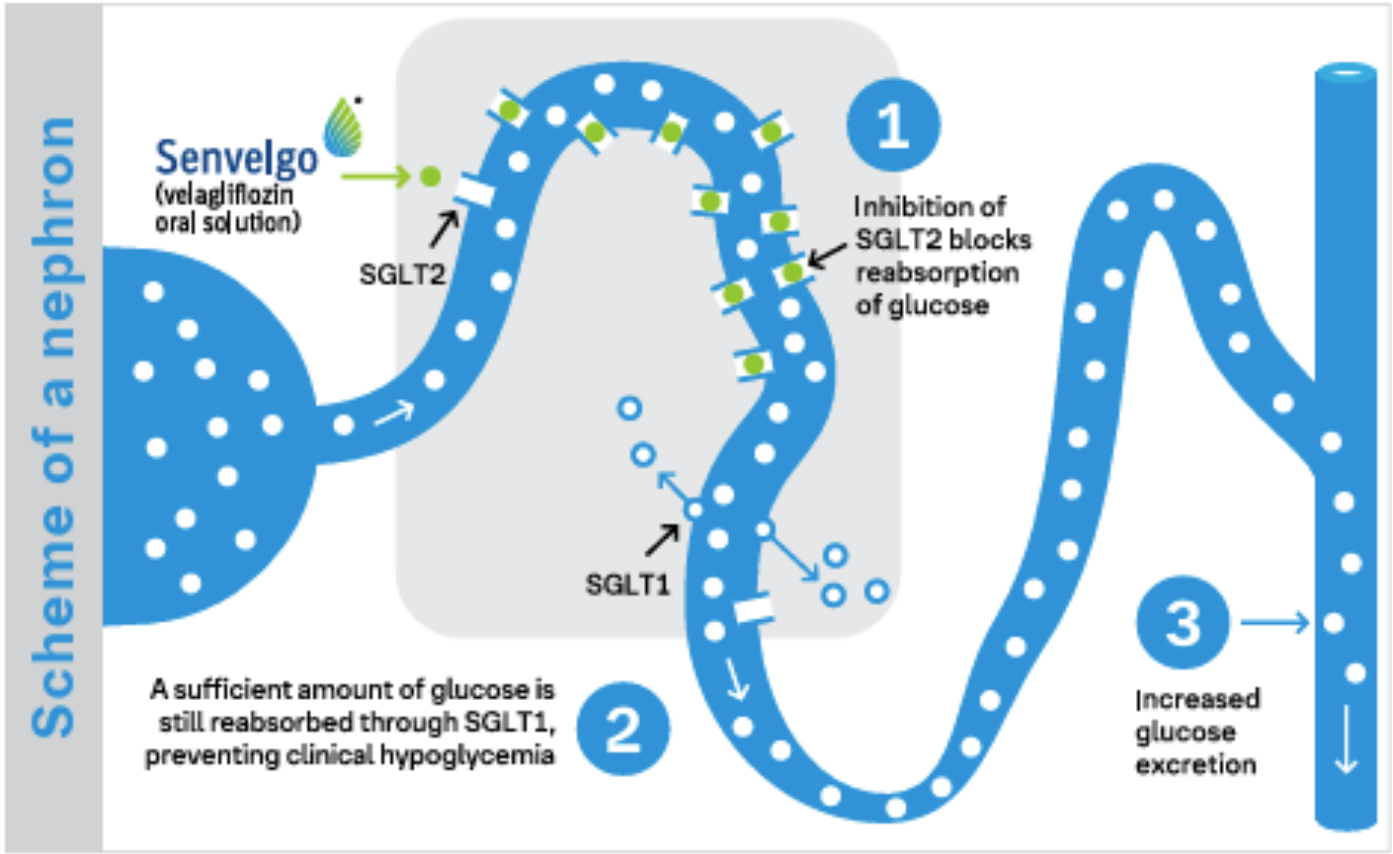
SAGE

- At 8th BGC, there was clinical improvement in PUPD, polyphagia, weight loss and lethargy
- 4 cats achieved remission in < 100 days (newly diagnosed DM)
- 12.5% cats had biochemical hypoglycaemia
- No incidences of clinical hypoglycaemia


DIN 02543427
Senvelgo
Solution orale de vélagliflozine à 15 mg/mL
Usage vétérinaire seulement
Pour les chats
Mise en garde : Garder hors de la portée des enfants. Voir la notice pour obtenir
SENVELGO
Boehringer Ingelheim
Shutterstock Video
https://orleansrx.ca/

SENVELGO



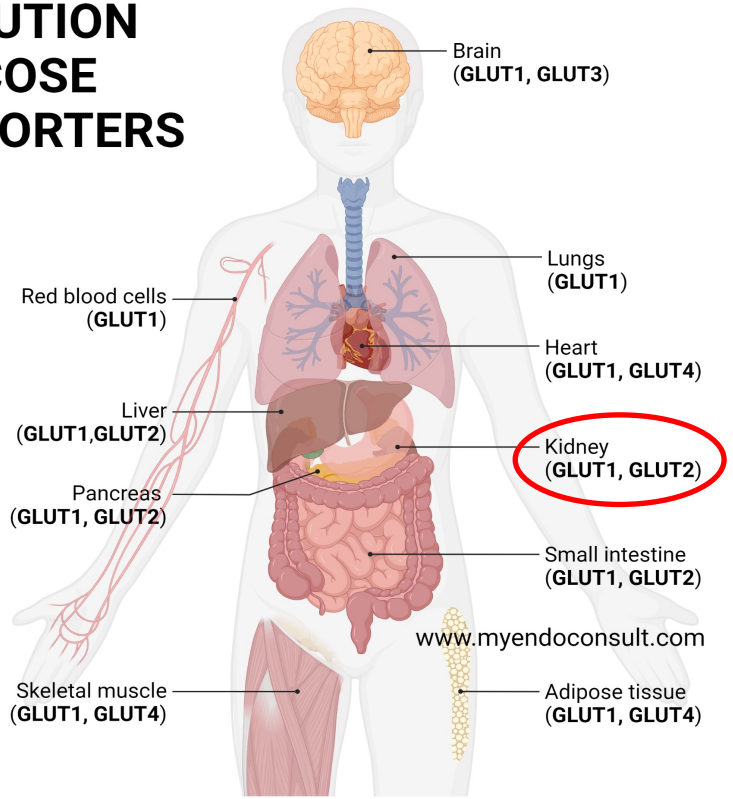
Velagliflozin is an orally administered sodium-glucose cotransporter-2 inhibitor (SGLT2 inhibitor).

https://BioRender.com/v21n984.

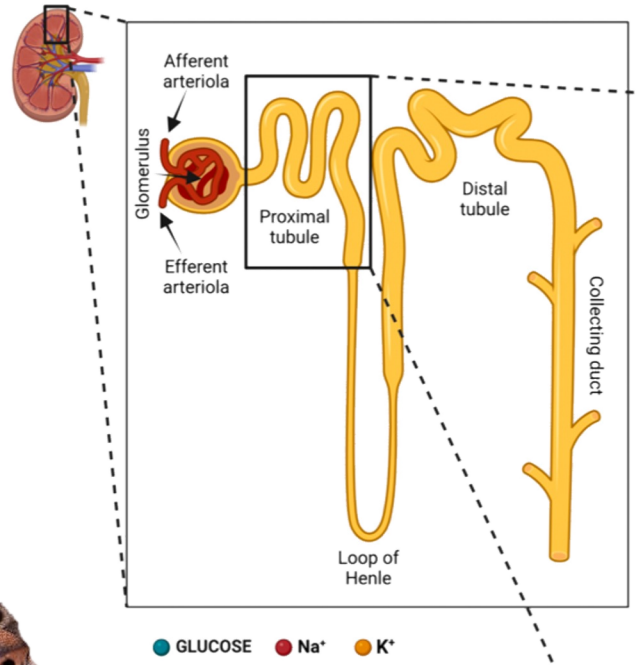
SENVELGO

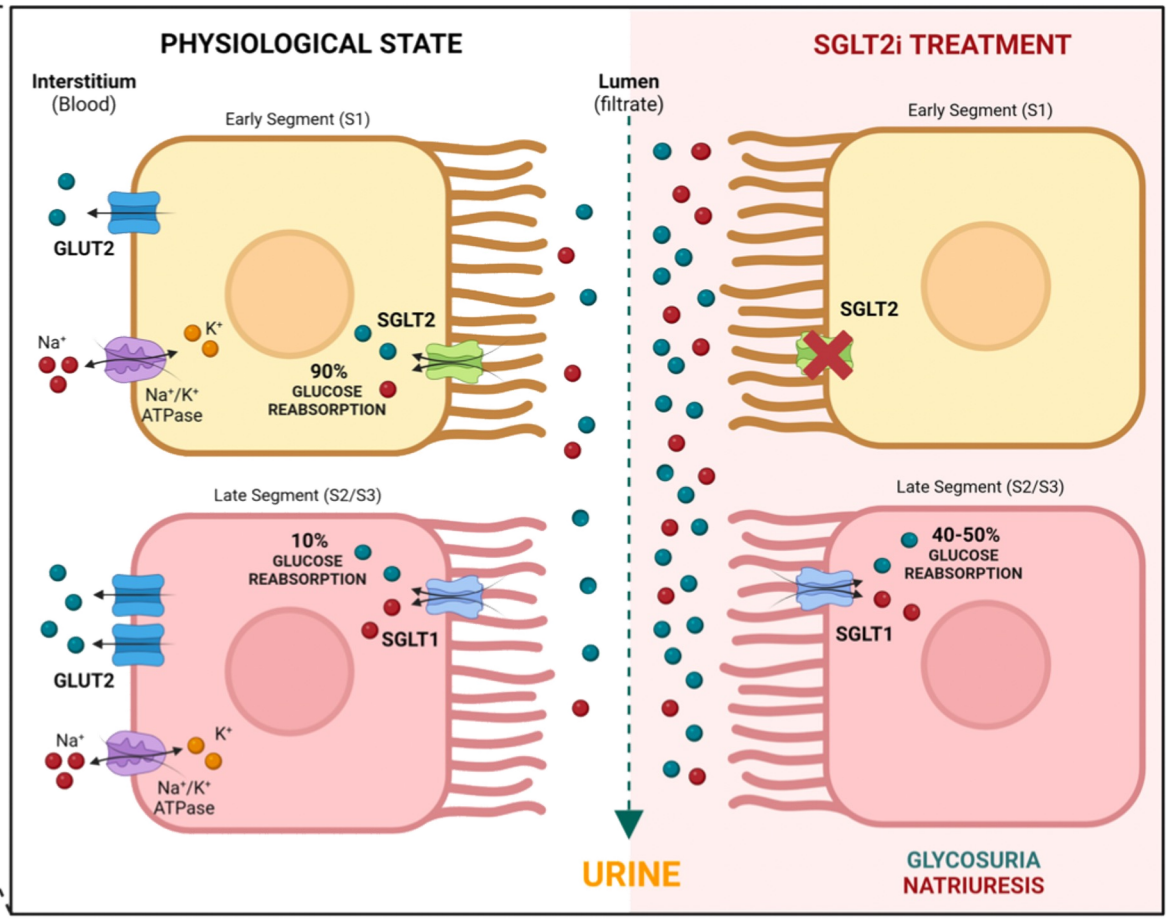
GLUT1 GLUT2 GLUT3 GLUT4 GLUT5 GLUT6

DISTRIBUTION OF GLUCOSE TRANSPORTERS



SENVELGO





SENVELGO

- Once-daily oral liquid solution that can be administered directly into the cat’s mouth or applied onto a small amount of food.
- Reduces hyperglycemia, leading to sustained glycemic control starting in as soon as 7 days
- Significantly reduces risk of clinical hypoglycemic events
- Precise dosing tailored to the weight of the cat
- Less intensive monitoring in stabilised cats
- Convenient oral liquid well-accepted by most cats.
- Easy storage – no refrigeration necessary before or after opening
- Backed by the Feline Diabetes Patient Support Program

https://senvelgo.ie/sites/default/files/2024-03/Senvelgo-IE-Vet-Management-Guide.pdf

Is the cat eating, drinking and interacting with no vomiting, diarrhoea, dehydration, lethargy or cachexia?

YES

HAPPY DIABETIC

Check for ketones

If ketones are present

Neg If ketones are not present

Start SENVELGO® 1 mg / kg PO once daily[a]
(according to bodyweight syringe markings)

INITIAL MONITORING FIRST 14 DAYS

MONITORING FOR KETOSIS / DKA / eDKA

~ Every 1-3 days	Ketones
~ Day 7 at the clinic	Ketones, history, PE
~ Day 14 at the clinic	Ketones, history, PE

Neg If ketones are not present & the cat has no signs of DKA

LONG-TERM MONITORING

ONGOING MONITORING FOR KETOSIS / DKA / eDKA & GLYCAEMIC CONTROL

- Recheck at week 4 and then routinely every 3 months
- Check for ketones in the urine or via a blood sample
- Glycaemic control (e.g. fructosamine)
- Clinical control (e.g. thirst, appetite, PE, hydration, BW)

NO

UNHAPPY DIABETIC

NOT CURRENTLY SUITABLE FOR SENVELGO®

- Manage concurrent conditions
- Treat ketosis / ketoacidosis[b] according to standard protocols
- Reassess suitability for Senvelgo® once stable*

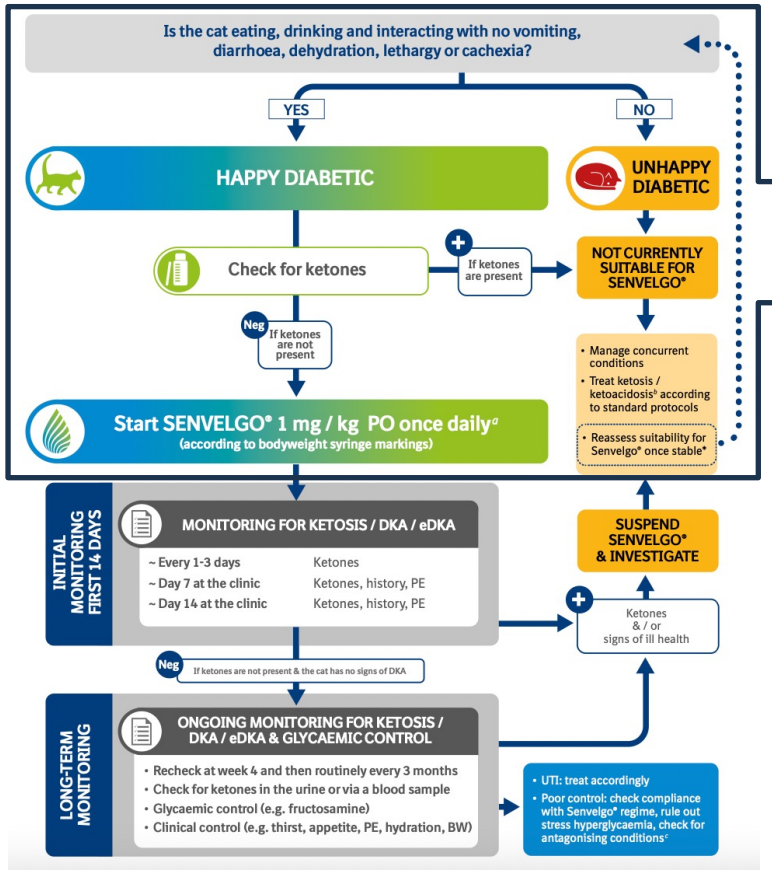
SUSPEND SENVELGO® & INVESTIGATE

Ketones & / or signs of ill health

- UTI: treat accordingly
- Poor control: check compliance with Senvelgo® regime, rule out stress hyperglycaemia, check for antagonising conditions[c]

https://senvelgo.ie/sites/default/files/2024-03/Senvelgo-IE-Vet-Management-Guide.pdf

SENVELGO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NO
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UNHAPPY DIABETIC
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If ketones are present
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SUSPEND SENVELGO® & INVESTIGATE
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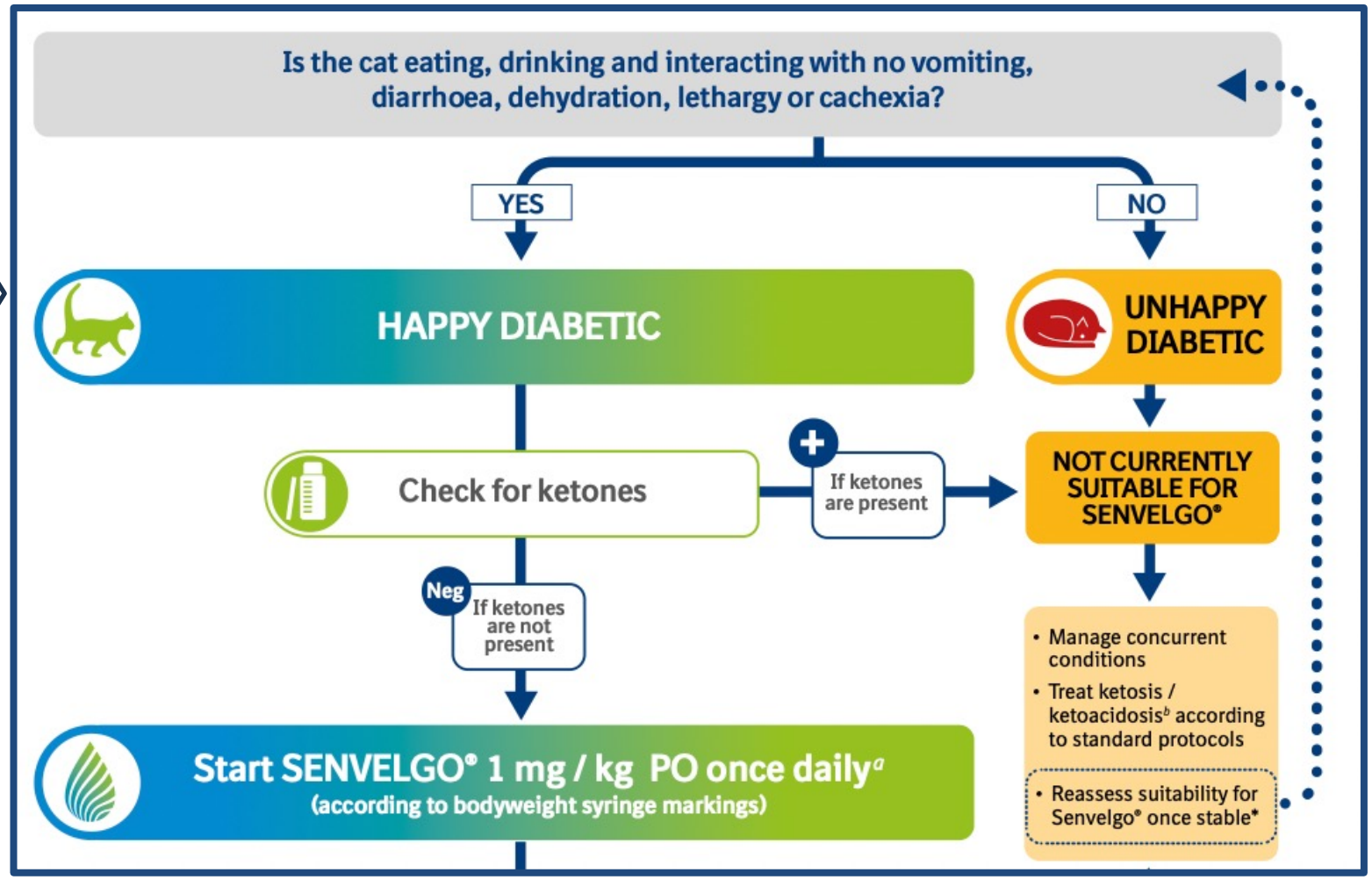
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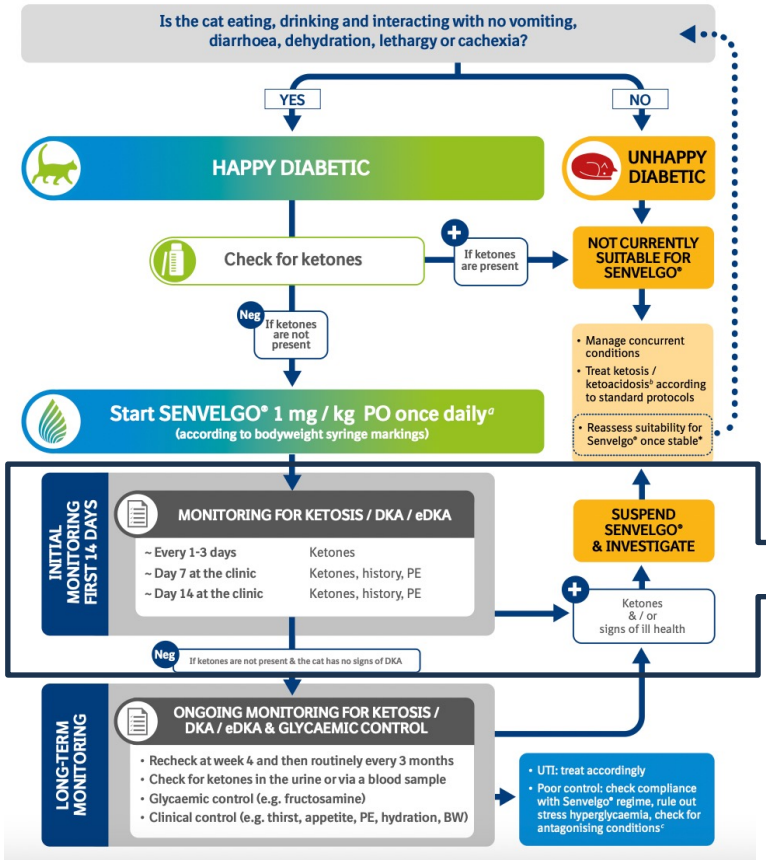
SENVELGO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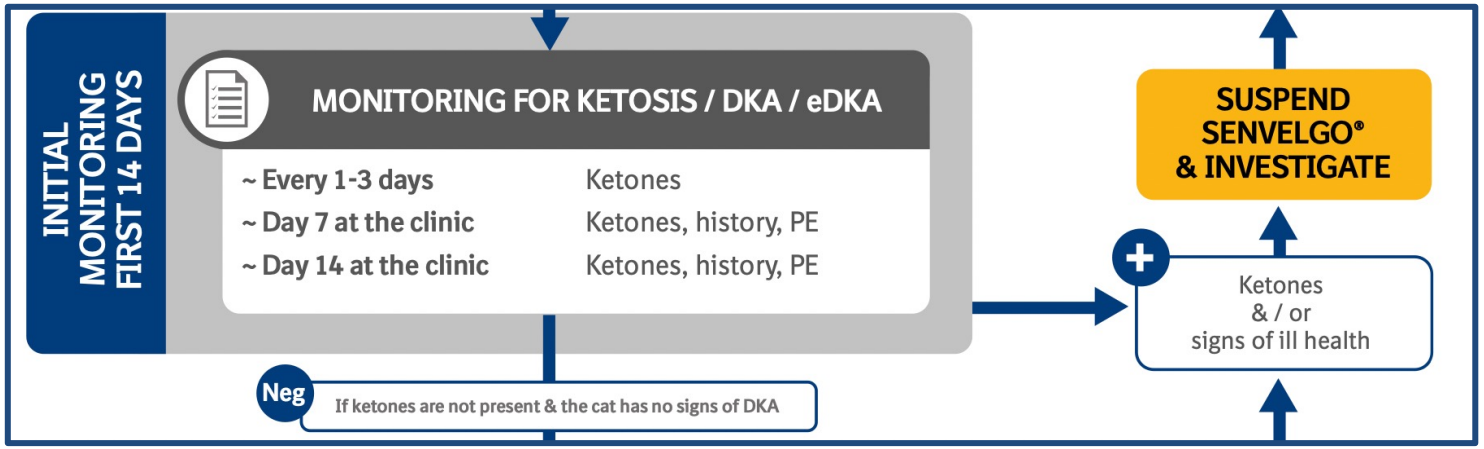
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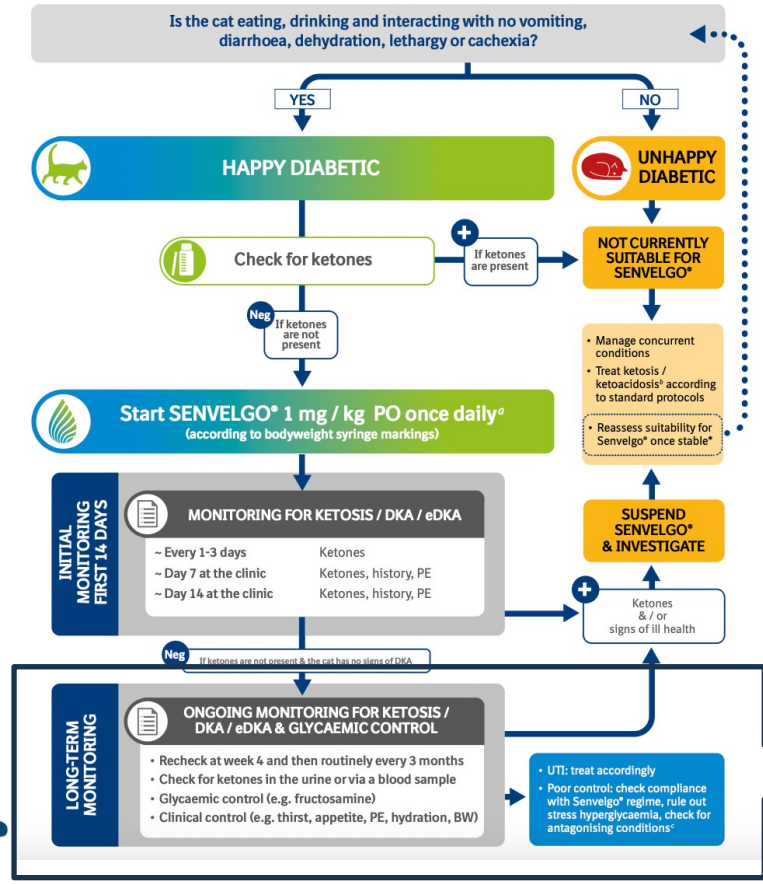
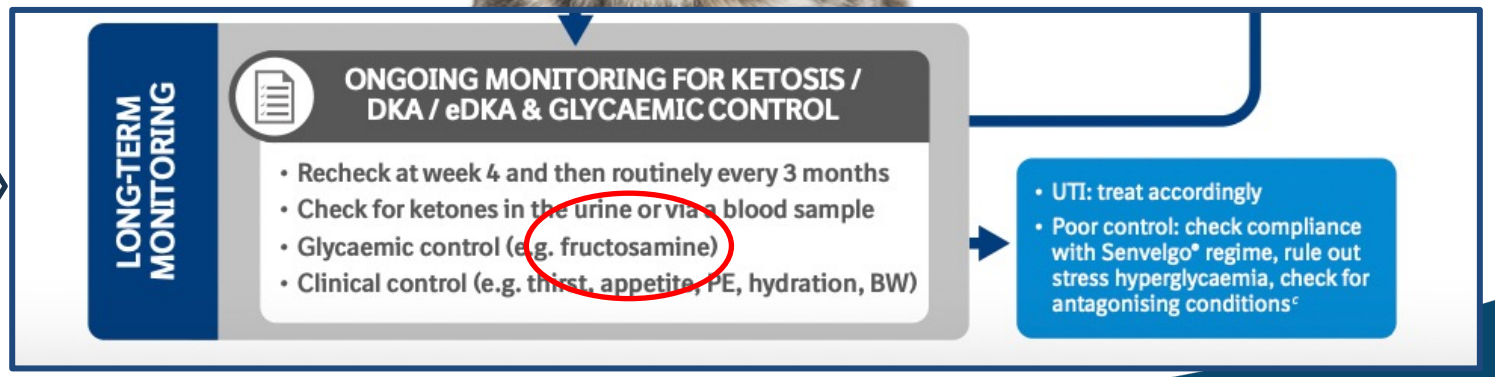
SENVELGO





https://senvelgo.ie/sites/default/files/2024-03/Senvelgo-IE-Vet-Management-Guide.pdf

SENVELGO

Received: 7 November 2023 | Accepted: 14 May 2024

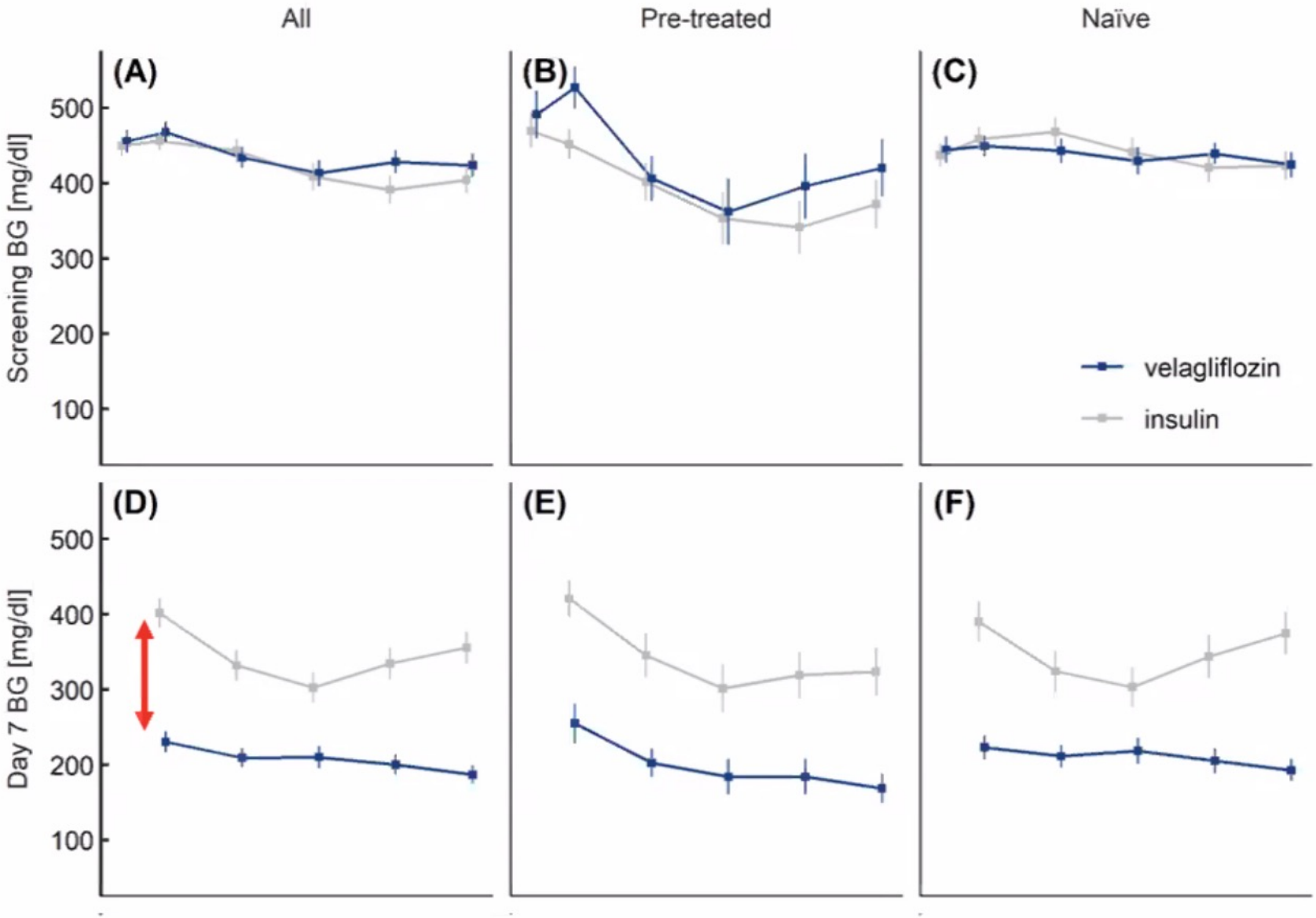
DOI: 10.1111/jvim.17124

Journal of Veterinary Internal Medicine Open Access ACVIM American College of

Efficacy and safety of once daily oral administration of sodium-glucose cotransporter-2 inhibitor velagliflozin compared with twice daily insulin injection in diabetic cats

Stijn J. M. Niessen[1,2] | Hans S. Kooistra[3] | Yaiza Forcada[1,2] | Charlotte R. Bjørnvad[4] | Balazs Albrecht[5] | Franziska Roessner[5] | Esther Herberich[5] | Carla Kroh[5]

- **Study: 127 diabetic cats (JVIM 2024), velagliflozin vs Caninsulin.**
- **Results: Non-inferior—54% velagliflozin vs 42% Caninsulin successfully managed.**
- **Blood glucose: Lower in velagliflozin group.**
- **Hypoglycaemia: 14% in velagliflozin (none clinical).**
- **DKA: 7% velagliflozin cats (mostly early), none in Caninsulin.**
- **Limitations: Compared to Caninsulin (not glargine), BG curves used—not CGM.**


All
Pre-treated
Naïve
(A)
(B)
(C)
(D)
(E)
(F)
Screening BG [mg/dl]
Day 7 BG [mg/dl]
500
400
300
200
100
velagliflozin
insulin

JAVMA

AVMA

Velagliflozin, a once-daily, liquid, oral SGLT2 inhibitor, is effective as a stand-alone therapy for feline diabetes mellitus: the SENSATION study

Ellen N. Behrend, VMD, PhD, DACVIM[1]* ; Cynthia R. Ward, VMD, PhD, DACVIM[2]; Victor Chukwu, DrPH[3]; Audrey K. Cook, BVM&S, DACVIM, DECVIM, DABVP[4]; Carla Kroh, Dr med vet[5]; Patty Lathan, VMD, MS, DACVIM[6]; Jacky May, DVM[7]; Thomas Schermerhorn, VMD, PhD, DACVIM[8] ; J. Catharine Scott-Moncrieff, VetMB, MS, DACVIM, DECVIM[9]; Rebecca Voth, DVM[10]

- Day 180: 81% had a BG and/or fructosamine within reference interval
- 88.6% improvement in PU, 87.7% improvement in PD
- 7.1% DKA, less common in newly diagnosed diabetics, occurring within 14 days of treatment
- No clinical hypoglycaemia (<3.3mmol/L)

JAVMA

AVMA

Velagliflozin, a once-daily, liquid, oral SGLT2 inhibitor, is effective as a stand-alone therapy for feline diabetes mellitus: the SENSATION study

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EUGLYCAEMIC DKA

A cat on an SGLT2 inhibitor may have a normal blood glucose despite substantial ketonemia

BG <13.9mmol/L + ketonaemia + metabolic acidosis

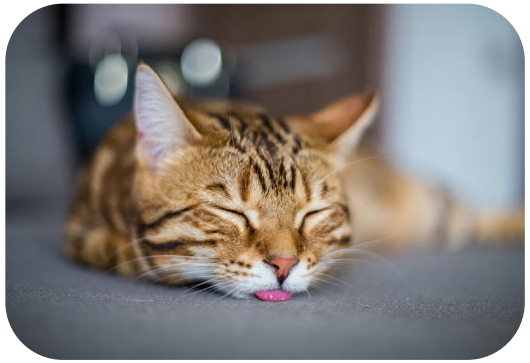
Treatment protocols are similar to hyperglycaemic DKA but dextrose should be administered with insulin concurrently

DISCONTINUE SENVELGO

SENVELGO ADVERSE EFFECTS

Diarrhoea (52.3%)

Urinary tract infections (7.1%)



Nonclinical hypoglycaemia (13%)

Weight loss (44%)

https://www.cixju.shop/
elanco.com
https://www.turmerry.com/
Shutterstock

Old vs New

Glargine, Toujeo and Senvelgo have not been directly compared to determine rates of diabetic remission (cats)

Toujeo and Senvelgo can potentially be administered once daily

Costs: 5kg cat, 0.5 IU/kg BID

Drug	Volume	$/unit	Duration	$/week
Lantus	300 units	$0.043	50 days	$4.50
Toujeo	450 units	$0.057	75 days	$5.20
Senvelgo	30ml	$12.20	90 days	$28.30
Caninsulin	400 units	$0.096	66 days	$16.63

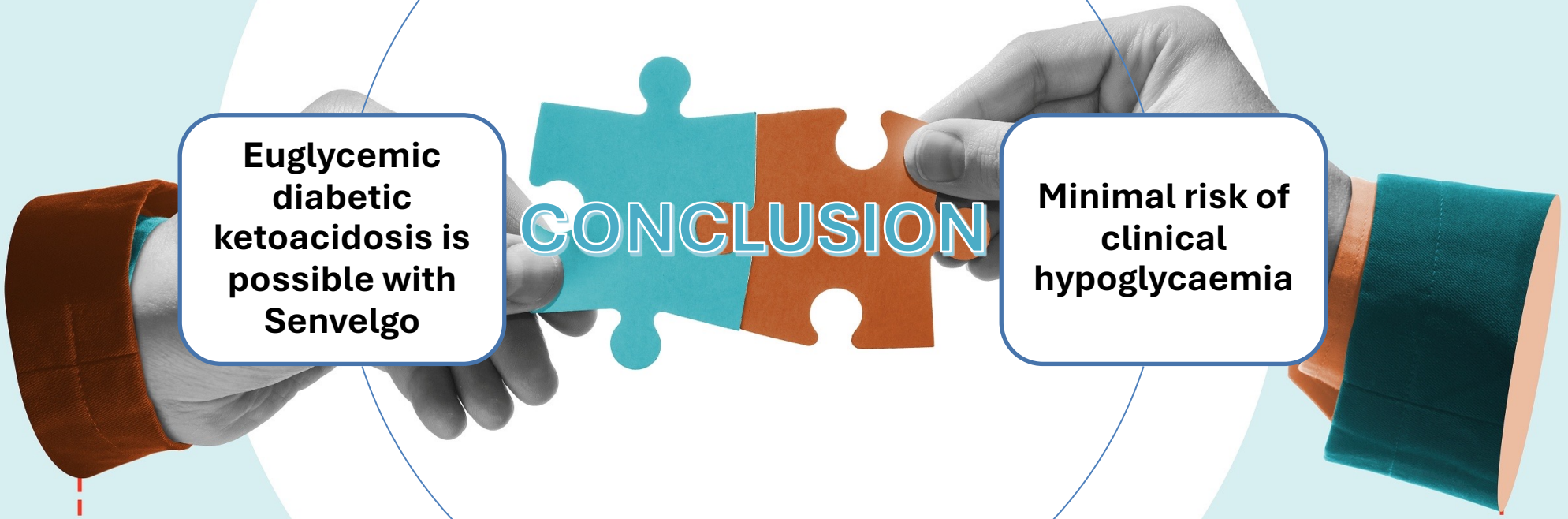
+ cost of glucose sensor

+ cost of urine dipsticks

*prices from Pet Pharmacy

Toujeo and Senvelgo are promising new therapies for management of diabetes mellitus

Euglycemic diabetic ketoacidosis is possible with Senvelgo



Minimal risk of clinical hypoglycaemia

Glucose monitoring has improved with the use of continuous glucose monitors

REFERENCES

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QUESTIONS?

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