

## Adjusting doses of Zycortal - 1. Joni

### History and clinical signs

Joni, a 10-year-old neutered female West Highland white terrier (weighing 8.4 kg) was diagnosed with hypoadrenocorticism when she was 6 years old and has been on fludrocortisone ever since.

She was given her first injection of Zycortal at 2.2 mg/kg s.c. and started on 2 mg p.o. of prednisolone once daily (0.23 mg/kg).

Her electrolyte concentrations were measured at 10 and 28 day recheck appointments. On presentation for her second injection at day 28, she was doing really well.



Joni

### Diagnostic investigations

#### 10 days post-injection

Blood test parameters	Result	Reference Range
Sodium (mmol/l)	158	136-159
Potassium (mmol/l)	3.6	3.4-5.8
Sodium: potassium ratio	44	> 27

#### 28 days post-injection

Blood test parameters	Result	Reference Range
Sodium (mmol/l)	150	136-159
Potassium (mmol/l)	3.8	3.4-5.8
Sodium: potassium ratio	39	> 27

#### Comments

- The sodium and potassium concentrations were within the reference range at day 10 and 28 therefore the dose of Zycortal should be maintained
- The electrolytes were within the reference range at day 28 so Zycortal should be given

### Subsequent history and clinical signs

The second dose of Zycortal was given at the same dose of 2.2 mg/kg s.c. and the dose of prednisolone was maintained at 2 mg q24h p.o..

Joni was presented again 10 and 28 days later. Her owner reported that she was well in herself with a good appetite.

A blood sample was taken for electrolyte concentrations on each occasion:

#### 10 days post-injection number 2 (38 days after starting Zycortal)

Blood test parameters	Result	Reference Range
Sodium (mmol/l)	155	136-159
Potassium (mmol/l)	3.8	3.4-5.8
Sodium: potassium ratio	41	> 27

#### 28 days post-injection number 2 (56 days after starting Zycortal)

Blood test parameters	Result	Reference Range
Sodium (mmol/l)	150	136-159
Potassium (mmol/l)	4.7	3.4-5.8
Sodium: potassium ratio	32	> 27

#### Comments

- Because the sodium and potassium concentrations 10 and 28 days after injection were within the reference ranges the dose of Zycortal should continue to be repeated every 28 days (range 25 days to 1 month to suit the owners)

### Subsequent history and clinical signs

The third dose of Zycortal was given at a dose of 2.2 mg/kg s.c. and the dose of prednisolone was maintained at 2 mg q24h.

Joni's owners were taught to give the injections.

Her electrolytes were re-measured on the day of injection once every 4 months for the first year and at 6 monthly intervals thereafter.

Using Zycortal **5** golden guidelines:



The case studies within this document have been devised for illustrative purposes

ZYCORTAL: Zycortal contains desoxycortone pivalate

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# Using Zycortal 5 golden rules:

## 1 Manage client expectations at the beginning

- It may take several visits and multiple monitoring blood tests to find the right dose of Zycortal and a glucocorticoid for each dog. This is also true for dogs previously receiving fludrocortisone therapy
- Dogs being treated properly should be happy dogs with a normal appetite. However it is important to remember that they are not normal dogs. They have a chronic disease and will need lifelong medication and monitoring
- Owners should understand that the dose of Zycortal is adjusted by assessing electrolytes and clinical signs, whereas the glucocorticoid (mainly in the form of prednisolone) dose is adjusted according to the clinical history (so their observations matter)

## All dogs must receive daily glucocorticoid treatment titrated to effect based on clinical signs

- Glucocorticoid deficiency causes lethargy (which can be severe), inappetance, weakness and gastrointestinal signs
- Equally too much glucocorticoid causes polyuria/polydipsia, poor hair regrowth and increased bodyweight. Remember too much Zycortal can also cause polyuria/polydipsia
- The starting prednisolone dose rate is 0.2-0.4 mg/kg q24h for newly diagnosed cases. The final dose varies between individual animals and a good proportion of dogs will ultimately be stable at 0.05-0.1 mg/kg q24h. For dogs requiring particularly small doses of glucocorticoid, cortisone acetate could be considered as an alternative
- Glucocorticoid dose adjustments should be 25 to 50% of the previous dose. Try to wait two weeks to assess the effect
- At times of metabolic stress or illness, the glucocorticoid dose may need to be increased (2 to 4 times)

## 3 Use a Zycortal dosing interval of either every 4 weeks, or every month: give a dose appropriate to that interval

- The preferred approach of EU & US endocrinologists is to adjust the dose and keep the interval constant, rather than adjusting the interval and keeping the dose constant
- The initial Zycortal dose is 2.2 mg/kg subcutaneously. Should a dose change be required, it is more likely that dogs will require a dose reduction than a dose increase
- A benefit of a four weekly or a monthly interval is the ease, both for the vet and the client, in booking repeat appointments

## Evaluate Zycortal treatment success at days 10 and 28 after every dose, until stable

- Decide if you are giving too much or too little Zycortal to each dog by assessing electrolytes and clinical signs
- Aim to keep potassium and sodium within their reference ranges (RRs) throughout the dosing interval
- Adjust the Zycortal dose at day 28 in 10-20% steps with the aim of achieving electrolytes within their RRs at day 10 and day 28
  - Monitoring electrolytes at day 10 enables assessment of the peak effect of the dose
  - Monitoring electrolytes at day 28 enables assessment of the duration of the dose
- Electrolytes should be within their RRs before administering a repeat Zycortal dose
  - If potassium is below and/or sodium is above their RRs at day 28:
    - Do not inject Zycortal, even at a lower dose
    - Repeat electrolyte testing every 7 days until they are within their RRs
    - Then re-inject Zycortal at a lower dose and recheck at day 10 and day 28 post-injection
  - If potassium is above and/or sodium is below their RRs at day 28 Zycortal must be injected. The dose should be increased, and/or the dose interval shortened
- Once the dose has been determined, a stable dog will have electrolytes within their respective RRs at days 10 and 28 during at least two consecutive treatment cycles using that same dose. Thereafter dogs should be reassessed every 4-6 months at the time of injection.
- In cases of lack of expected efficacy; before increasing the Zycortal dose, consider whether the dog was adequately hydrated at injection, the product was adequately re-suspended, and whether the injection was successfully administered

## 5 If you have problems then get help

- Check laboratory results that do not look right. e.g. contamination of the sample with potassium EDTA from a haematology tube can cause an artefactual increase in serum potassium
- If a dog receiving Zycortal therapy is ill:
  - Giving more glucocorticoid is rarely wrong
  - Consider potassium supplementation if the dog is symptomatic and potassium <3 mmol/l.
- Contact Dechra Technical Services for support regarding individual cases

## Adjusting doses of Zycortal - 2. Belle

### History and clinical signs

Belle, a 1-year-old female entire Labradoodle (weighing 28.4 kg) was diagnosed with hypoadrenocorticism when she was 7 months old and has been on fludrocortisone ever since.

She was given her first injection of Zycortal at 2.2 mg/kg s.c. and started on 5 mg p.o. of prednisolone once daily (0.18 mg/kg).

Her electrolyte concentrations were measured at 10 and 28 day recheck appointments. On presentation for her second injection at day 28, she was doing really well.

### Diagnostic investigations

#### 10 days post-injection

Blood test parameters	Result	Reference Range
Sodium (mmol/l)	<b>165</b>	136-159
Potassium (mmol/l)	<b>3.3</b>	3.4-5.8
Sodium: potassium ratio	50	> 27

\*Abnormal results in red and bold

#### Comments

- The sodium concentration was not within the reference range at day 10 therefore the dose of Zycortal should be reduced
- The electrolytes were within the reference range at day 28 so Zycortal should be given

### Subsequent history and clinical signs

The second dose of Zycortal was given at a reduced dose of 1.8 mg/kg s.c. and the dose of prednisolone was maintained at 5 mg q24h p.o.. A recheck was booked for 10 days later as the dose of Zycortal was changed.

Belle was presented again 10 and 28 days later. Her owner reported that she was drinking and urinating too much. She was well in herself with a good appetite. A blood sample was taken for electrolyte concentrations on each occasion:

#### 10 days post-injection number 2 (38 days after starting Zycortal)

Blood test parameters	Result	Reference Range
Sodium (mmol/l)	159	136-159
Potassium (mmol/l)	<b>3.3</b>	3.4-5.8
Sodium: potassium ratio	48	> 27

\*Abnormal results in red and bold

#### Comments

- Because the potassium concentration 10 days after injection was not within the reference ranges, the next dose of Zycortal should be reduced

### Subsequent history and clinical signs

The third dose of Zycortal was given at a reduced dose of 1.4 mg/kg s.c. and the dose of prednisolone was maintained at 5 mg q24h p.o..

Belle was presented 10 and 28 days later (66 and 84 days after starting Zycortal). She was well in herself with a good appetite. The electrolytes were all within their reference ranges on both occasions and so the fourth dose of Zycortal was given at the same dose of 1.4 mg/kg s.c.. Further rechecks 10 days and 28 days after this injection confirmed that this was the correct dose for Belle.

Blood test parameters	Results				Reference Range
	3rd injection + 10 days	3rd injection + 28 days	4th injection + 10 days	4th injection + 28 days	
Sodium (mmol/l)	152	140	156	138	136-159
Potassium (mmol/l)	3.8	4.1	3.9	4.9	3.4-5.8
Sodium: potassium ratio	40	34	40	28	> 27

#### Comments

- Prednisolone should be maintained at 5 mg once daily and Zycortal at 1.4 mg/kg s.c. every 28 days
- Belle's owners were happy to come into the practice for the nurse to give the injections
- Her electrolytes will be re-measured on the day of injection once every 4 months for the first year and at 6 monthly intervals thereafter



Belle

#### 28 days post-injection

Blood test parameters	Result	Reference Range
Sodium (mmol/l)	150	136-159
Potassium (mmol/l)	3.8	3.4-5.8
Sodium: potassium ratio	39	> 27

## Adjusting doses of Zycortal - 3. Willow

### History and clinical signs

Willow, an 8-year-old female neutered Utonagan (weighing 34.4 kg) was diagnosed with hypoadrenocorticism last year and has been on fludrocortisone ever since.

She was given her first injection of Zycortal at 2.2 mg/kg s.c. and started on 10 mg p.o. of prednisolone once daily (0.3 mg/kg).

Her electrolyte concentrations were measured at a 10 day recheck appointment and 28 days after the initial injection when she came in for her second injection. On presentation, she was doing well. Her heart rate was 98 bpm with a sinus tachycardia documented on ECG evaluation. Her owner reported that Willow was drinking and urinating a lot more over the previous 2 weeks.

### Diagnostic investigations

#### 10 days post-injection

Blood test parameters	Result	Reference Range
Sodium (mmol/l)	153	136-159
Potassium (mmol/l)	3.8	3.4-5.8
Sodium: potassium ratio	40	> 27
Chloride	111	102-120

#### Comments

- The polyuria and polydipsia (PU/PD) were likely to be due to too much prednisolone and because the electrolyte concentrations were within the reference ranges the PU/PD was unlikely to be due to too much Zycortal

### Subsequent history and clinical signs

The dose of prednisolone was reduced to 7.5 mg q24h p.o. and the second dose of Zycortal was given at the same dose of 2.2 mg/kg s.c.. Blood samples were taken for electrolyte concentrations 10 and 28 days after the second Zycortal injection. At day 28 her owner reported that Willow was still drinking and urinating too much. She was well in herself with a good appetite.

#### 10 days post-injection (38 days after starting Zycortal)

Blood test parameters	Result	Reference Range
Sodium (mmol/l)	158	136-159
Potassium (mmol/l)	3.5	3.4-5.8
Sodium: potassium ratio	45	> 27
Chloride	117	102-120

#### Comments

- Because the electrolyte concentrations were no longer within the reference ranges, the next dose of Zycortal should be postponed for 7 days
- Low potassium does not cause polyuria or polydipsia and so the dose of prednisolone was still too high and should be reduced

### Subsequent history and clinical signs

The dose of prednisolone was reduced to 5 mg q24h p.o..

Willow was presented 7 days later. Her owner reported that she was no longer drinking and urinating too much. She was well in herself with a good appetite. A blood sample was taken for electrolyte concentrations before the third Zycortal injection:

#### 35 days post-injection number 2 (63 days after starting Zycortal)

Blood test parameters	Result	Reference Range
Sodium (mmol/l)	150	136-159
Potassium (mmol/l)	3.8	3.4-5.8
Sodium: potassium ratio	39	> 27
Chloride	115	102-120

#### Comments

- Because the electrolyte concentrations were within the reference ranges at day 35, the next dose of Zycortal should be given, however as potassium was below reference range at day 28 a lower dose is indicated
- Prednisolone dose should be maintained

### Subsequent history and clinical signs

The third dose of Zycortal was given at a reduced dose of 1.8 mg/kg s.c.. Willow was presented 10 and 28 days after each injection. Her owner reported that she was doing better than she has ever done in the past. The electrolytes were all within their reference ranges on both occasions and so the fourth dose of Zycortal was given at the same dose of 1.8 mg/kg s.c.. Further rechecks 10 days and 28 days after this injection confirmed that this was the correct dose for Willow.

Blood test parameters	Results				Reference Range
	3rd injection + 10 days	3rd injection + 28 days	4th injection + 10 days	4th injection + 28 days	
Sodium (mmol/l)	152	140	156	150	136-159
Potassium (mmol/l)	4.0	4.3	4.1	5.0	3.4-5.8
Sodium: potassium ratio	38	33	38	30	> 27

#### Comments

- Prednisolone should be maintained at 5 mg once daily and Zycortal at 1.8 mg/kg s.c. every 28 days
- Willow's owners were happy to learn how to give the injections and to give Willow a treat afterwards
- Her electrolytes will be re-measured on the day of injection once every 4 months for the first year and at 6 monthly intervals thereafter



Willow

#### 28 days post-injection

Blood test parameters	Result	Reference Range
Sodium (mmol/l)	148	136-159
Potassium (mmol/l)	3.9	3.4-5.8
Sodium: potassium ratio	38	> 27
Chloride	110	102-120

