UK national guidance of clinical monitoring of bone and endocrine outcomes in individuals with DMD on vamorolone and switching from classic glucocorticoid to vamorolone: Recommendations of the Endocrine & Bone Working Group of DMD Care UK, 2025

Background:

Monitoring of bone and endocrine outcomes in individuals with Duchenne Muscular Dystrophy (DMD) on vamorolone should follow existing clinical recommendations for all individuals with DMD on classic glucocorticoids (prednisolone or deflazacort) as part of the recommendations of the Bone and Endocrine Working Group of DMD Care UK. **Adrenal suppression (1,2),** vertebral fractures (3 [presented but not peer-reviewed]) and weight gain (1) are still reported in individuals treated with vamorolone. There is currently no information on the impact of vamorolone on the risk of long bone fracture and pubertal delay.

Adrenal suppression occurs with vamorolone and therefore vamorolone should NOT be stopped abruptly. Testing of the adrenal axis is mandatory if the decision is made to discontinue vamorolone.

Vamorolone is also a mineralocorticoid antagonist. Vamorolone should NOT be used for sick day dosing.
During acute illness, there should be a low threshold to check electrolytes for low sodium and/or high potassium for those treated with vamorolone. This is especially relevant in individuals on renin angiotensin aldosterone system inhibitors (e.g. ACE inhibitors, angiotensin receptor blockers, mineralocorticoid receptor antagonists) where similar electrolyte abnormalities may occur.

At the initiation of vamorolone or swapping from classic glucocorticoid (prednisolone or deflazacort) to vamorolone:

1. Counsel families about the risk of adrenal suppression and symptoms of adrenal insufficiency (Table 1).

Table 1: Possible symptoms of steroid-induced adrenal insufficiency (especially if symptoms are unexplained and/or new in onset)

Loss of appetiteJ	Myalgia (muscle aches)
Nausea /vomiting	Arthralgia (joint aches)
Fatigue	Mood changes
Headache	Loss of motor skills (out of keeping with natural progression)
Abdominal pain	

2. Ensure a sick day plan is in place using oral hydrocortisone (Table 2) for acute illness with a fever e.g. flu, infection, childhood illnesses (usually not well enough to go to school), prior to first intravenous bisphosphonate infusion and a plan for emergency injection with hydrocortisone with severe illness and/or vomiting illness (Table 3).

Table 2: Simplified oral sick day dosing with moderate illness developed for use in DMD as part of the DMD Care UK clinical guidance.

Body Weight	Hydrocortisone
10 to 25 kg	5 mg four times a day
26 to 50 kg	10 mg four times a day
>50 kg	15 mg four times a day

Note to Table 2: *Oral sick day dosing with moderate illness laid out in the BSPED Emergency Management of Adrenal Insufficiency can also be used. Vamorolone should be continued while following sick day dosing with hydrocortisone.*

Table 3: IM dose of hydrocortisone for severe illness

Age	IM hydrocortisone
Less than 1 year	25 mg
1 - 5 years	50 mg
6 years and over	100 mg

3. Undertake a clinical assessment at the time of vamorolone initiation (whether first treatment or switching from prednisone/deflazacort) and annually for individuals on vamorolone:

- Discuss the risk of adrenal insufficiency and ensure the sick day steroid plan if in place.
- Height (if ambulant) or segmental body part measurement e.g. ulnar length (if non-ambulant)
- Weight.
- DXA for bone density if age 4 years or over [Note that there is limited normative data for interpretation of DXA bone density in those under 4 years and the procedure may not be well tolerated]. (Repeat DXA if previous DXA was > 9 months if switching from prednisolone/deflazacort to vamorolone),
- Vertebral fracture assessment with DXA vertebral fracture assessment (VFA) or lateral thoracolumbar spine radiographs include imaging up to T4 [Note that lateral spine imaging with spine radiographs can be performed at any age]. (Repeat lateral spine imaging if previous imaging was > 9 months if switching from prednisolone/deflazacort to vamorolone).
- Pubertal assessment if aged 12 years or older.
- Monitoring of 25 hydroxy-vitamin D level (If previous blood test was > 9 months).

Management of adrenal suppression when switching from classic glucocorticoid (prednisolone/deflazacort) to vamorolone

All individuals with DMD on treatment doses of daily classic glucocorticoid (prednisolone or deflazacort) are assumed to have adrenal insufficiency due to adrenal suppression.

- Current published information shows that 94.7% of individuals with DMD on vamorolone 6 mg/kg daily have biochemical evidence of adrenal suppression after 48 weeks of treatment. However, only 52.4% of individuals with DMD on vamorolone 2 mg/kg daily have biochemical evidence of adrenal suppression after 48 weeks of treatment (2).
- This suggests that individuals transitioning to 6 mg/kg/day of vamorolone are less likely to develop symptoms of adrenal insufficiency when transitioning from classic glucocorticoids (prednisolone or deflazacort).
- However, vamorolone <6 mg/kg/day may be insufficient to prevent symptoms of adrenal insufficiency when transitioning from classic glucocorticoids (prednisolone or deflazacort).

There is currently limited information on the equivalent dosing of classic glucocorticoid (prednisolone or deflazacort) with vamorolone. Adrenal withdrawal symptoms can mimic symptoms of adrenal insufficiency (Table 1) and may occur despite the individual being on high glucocorticoid doses during a taper or may happen when switching from classic glucocorticoid to vamorolone. Adrenal withdrawal occurs due to the reliance on a high dose of glucocorticoid.

Given that vamorolone at 6 mg/kg causes adrenal suppression in nearly all individuals, starting at this dose should be strong enough to cover adrenal suppression when switching from classic glucocorticoids. However, the maximum prescribable dose of vamorolone is 240 mg, which means that for individuals weighing more than 40 kg, the dose would be less than 6 mg/kg, potentially not strong enough to cover adrenal suppression. Therefore, we recommend the following for safe management when switching from classic glucocorticoids to vamorolone.

Switching from a classic glucocorticoid (prednisolone/deflazacort) to vamorolone 6 mg/kg (Error! Reference source not found.**)**

Switch directly from the classic glucocorticoid (daily or intermittent) to daily vamorolone at 6 mg/kg.

- Re-educate on sick day plans (Table 2 and Table 3). Educate on recognising symptoms of adrenal insufficiency (Table 1).
- Phone review for symptoms of adrenal insufficiency within 7 days of switching from classic glucocorticoid to vamorolone (ask and document symptoms listed in Table 1).
- If symptoms are present (unexplained and/or new in onset), consider starting physiological replacement of oral hydrocortisone (Table 4) for a period of 4 weeks. Suggest discussing with endocrinology.
- Discontinue physiological replacement of oral hydrocortisone after 4 weeks. Phone review for symptoms of adrenal insufficiency within 7 days of discontinuation of physiological replacement of oral hydrocortisone.

Table 4: Possible physiological hydrocortisone replacement dosing for use when switching from classic glucocorticoid to vamorolone but less than 6 mg/kg

Weight (kg)	**Dose of hydrocortisone (physiological replacement)**
18 – 25	2.5 mg, 2.5 mg, 2.5 mg
26 - 38	5.0 mg, 2.5 mg, 2.5 mg
39 - 53	5.0 mg, 5.0 mg, 2.5 mg
54 - 69	5.0 mg, 5.0 mg, 5.0 mg
70 - 90	7.5 mg, 5.0 mg, 5.0 mg

Note to table 4: *Estimated surface area is based on weight as laid out in the British National Formulary for Children. The above physiological hydrocortisone replacement dose provides approximately 8-10 mg/m^2 of hydrocortisone for each weight band. Precise body surface area dosing based on height and weight is also appropriate if this is the clinical decision of the clinician/site. For individuals < 18 kg or >90 kg, please discuss with endocrinology.*

Switching from classic glucocorticoid to vamorolone but less than 6 mg/kg (Error! R eference source not found.**)**

Switch directly from classic (daily or intermittent) glucocorticoid to daily vamorolone at the planned prescribed dose (i.e. < 6 mg/kg)

- On the first day of receiving daily vamorolone, start physiological replacement of oral hydrocortisone for a period of 4 weeks (Table 4)
- Re-educate on sick day plans (Table 2 and Table 3). Educate on recognising symptoms of adrenal insufficiency (Table 1).
- Phone review for symptoms of adrenal insufficiency within 7 days of switching from classic glucocorticoid to vamorolone (ask and document symptoms listed in Table 1).
- After the period of 4 weeks of treatment with physiological replacement of oral hydrocortisone, continue with daily vamorolone only (i.e. stop physiological replacement of oral hydrocortisone).
- Phone review for symptoms of adrenal insufficiency within 7 days of discontinuing physiological replacement of oral hydrocortisone.
- If symptoms of adrenal insufficiency are present upon discontinuation of physiological replacement of oral hydrocortisone, restart physiologic replacement of oral hydrocortisone (Table 4) for another 4 weeks. Suggest discussing with endocrine.

If symptoms are present (unexplained and/or new in onset) whilst receiving physiological replacement of oral hydrocortisone and vamorolone, consider increasing oral hydrocortisone dose for example to sick day dose for a few weeks until resolution of symptoms (Table 2).

- Following resolution of symptoms, wean sick day dose of hydrocortisone (Table 2) to physiological replacement of oral hydrocortisone (Table 4) over a period of approximately 8 weeks.
- Discontinue physiological replacement of oral hydrocortisone after 8 weeks.
- Phone review for symptoms of adrenal insufficiency within 7 days of discontinuation of physiological replacement of oral hydrocortisone.

<u>Swapping from vamorolone to classic glucocorticoid</u>

- Guidance on switching from vamorolone to classic glucocorticoid is not yet available and will be developed.

Discontinuing vamorolone

- Due to adrenal suppression leading to adrenal insufficiency, discontinuation of vamorolone should not happen abruptly.
- Gradual weaning similar to the approach undertaken when discontinuing classic glucocorticoid should be followed.
- Testing of the adrenal axis is mandatory.
- Detailed guidance is not yet available but will be developed.

References

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2. Ahmet A et al. Adrenal Suppression From Vamorolone and Prednisone in Duchenne Muscular Dystrophy: Results From the Phase 2b Clinical Trial. J Clin Endocrinol Metab 2025 21;110(2):334-344.
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Endorsed by the Clinical Committee of the British Society for Paediatric Endocrinology and Diabetes

Based on principles laid out in the revised PJ Nicholoff Steroid Protocol developed by the Adrenal Working Group of International Consortium OPTIMIZE DMD.
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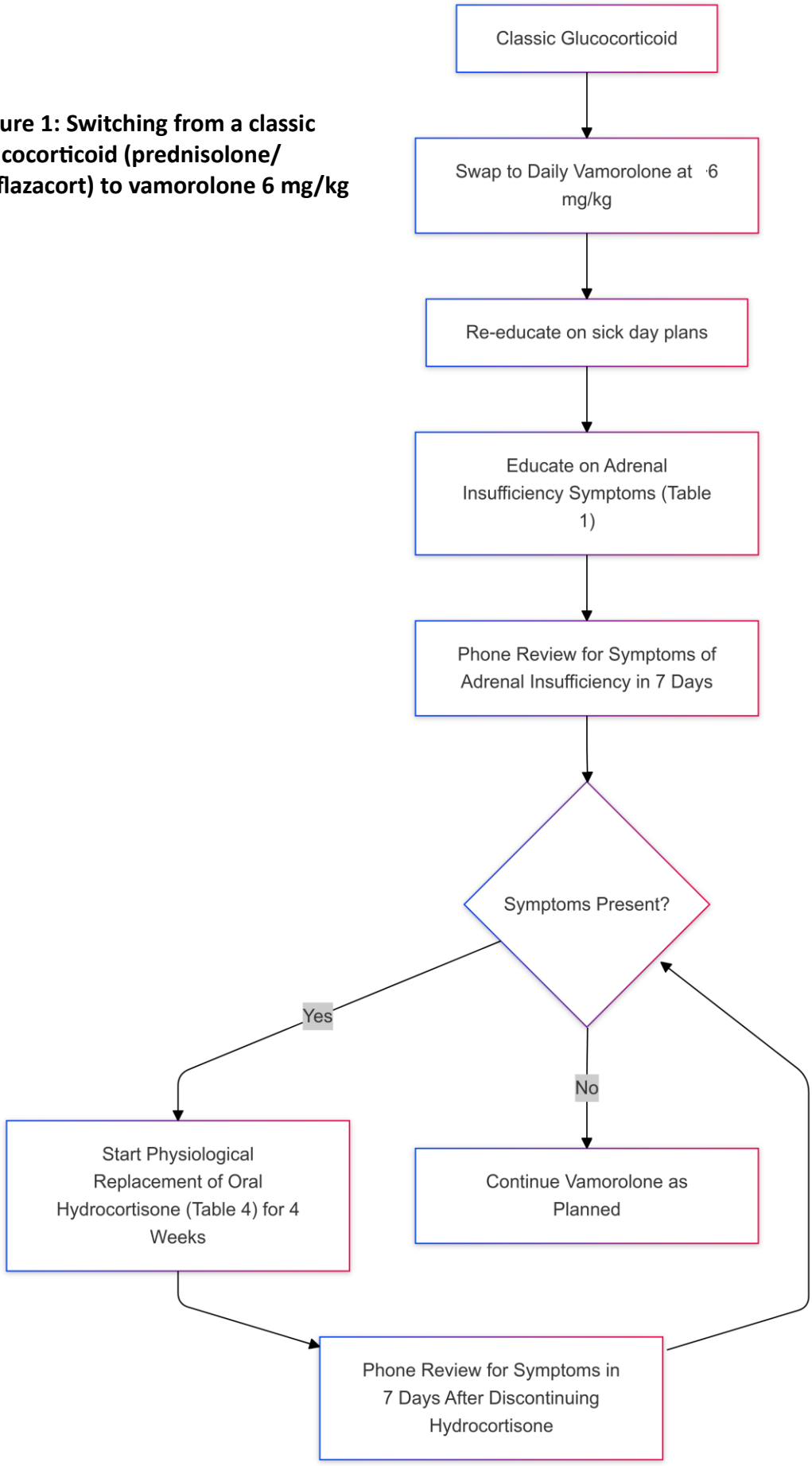
Figure 1: Switching from a classic glucocorticoid (prednisolone/ deflazacort) to vamorolone 6 mg/kg



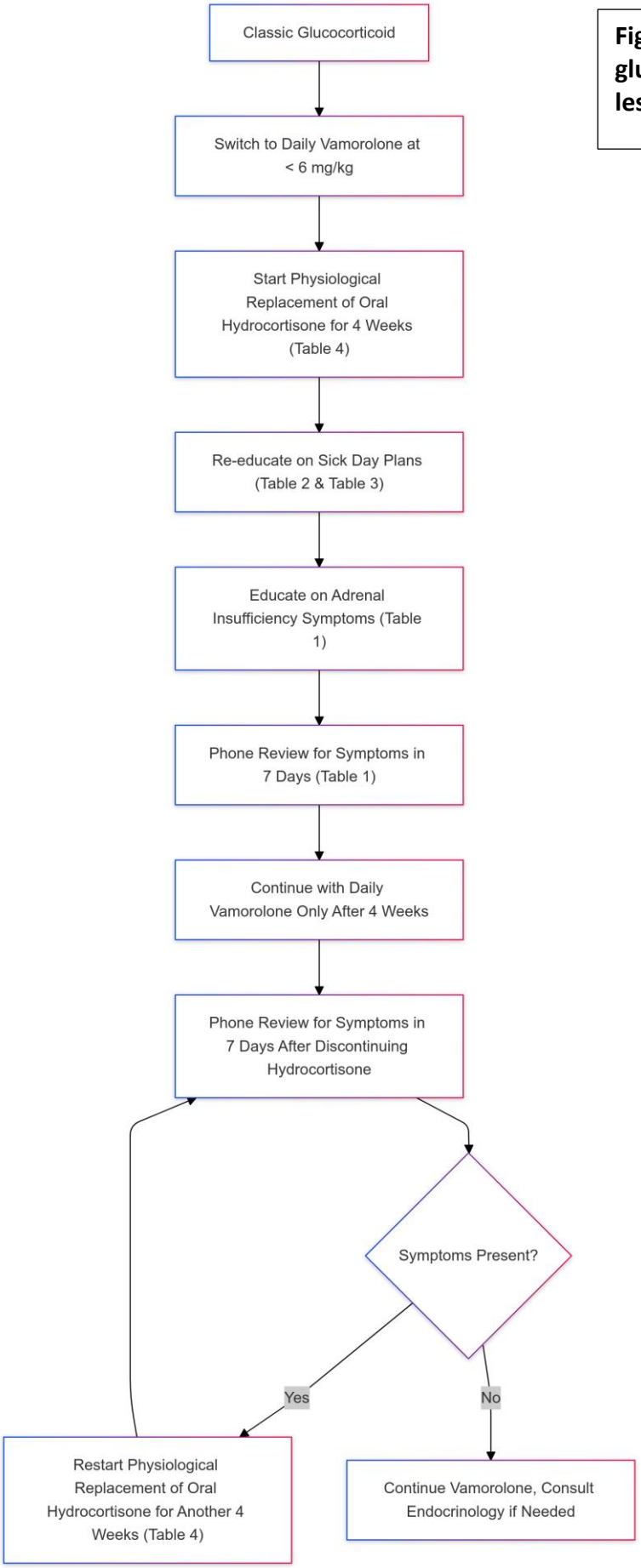


Figure 2: Switching from classic glucocorticoid to vamorolone but less than 6 mg/kg