## A.2 Alfalcaldiol and calcitriol – disorders of bone and calcium metabolism – EML and EMLc

<table>
<thead>
<tr>
<th>Draft recommendation</th>
<th>☑ Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>☐ Not recommended</td>
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<tr>
<td>Justification:</td>
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<td></td>
<td>Although the conditions that need the proposed medications are rare, yet it is currently still the recommended treatment for the condition. Also, for X-linked hypophosphatemic rickets which should be treated with phosphorus (A33), the proposed medicine is necessary. Therefore, the availability of these medications is essential for treatment of the conditions.</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Does the proposed medicine address a relevant public health need?</th>
<th>☑ Yes</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>☐ No</td>
</tr>
<tr>
<td></td>
<td>☐ Not applicable</td>
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<tr>
<td>Comments:</td>
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<td>The conditions that need the proposed medications are rare (X-linked hypophosphatemic rickets, Vitamin D dependent rickets and hypoparathyroidism). Although chronic kidney diseases are increasing due to the increase in diabetes and hypertension prevalence, the latest guidelines on Chronic Kidney Disease–Mineral And Bone Disorder only recommends vitamin D analogues (alfalcaldiol) if vitamin D deficiency has been corrected (by colecalciferol or ergocalciferol) and symptoms of CKD–mineral and bone disorders persist, for people end-stage renal diseases (GFR category G4 or G5)¹²</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Does adequate evidence exist for the efficacy/effectiveness of the medicine for the proposed indication?</th>
<th>☑ Yes</th>
</tr>
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<tbody>
<tr>
<td>(this may be evidence included in the application, and/or additional evidence identified during the review process)</td>
<td>☐ No</td>
</tr>
<tr>
<td></td>
<td>☐ Not applicable</td>
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<tr>
<td>Comments:</td>
<td></td>
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<tr>
<td></td>
<td>For children with chronic kidney disease Stages 2–5 and on dialysis: moderate to low quality of evidence and level 2 in strength of recommendation³</td>
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<td></td>
<td>For X-linked hypophosphataemia: grade C (moderate) recommendation⁴</td>
</tr>
</tbody>
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² KDIGO 2017 Clinical Practice Guideline Update For The Diagnosis, Evaluation, Prevention, And Treatment Of Chronic Kidney Disease–Mineral And Bone Disorder (CKD-MBD)


### Does adequate evidence exist for the safety/harms associated with the proposed medicine?

- ☑ Yes
- ☐ No
- ☐ Not applicable

Comments:

- significant risk of hypercalcaemia and hyperphosphataemia

### Are there any adverse effects of concern, or that may require special monitoring?

- ☑ Yes
- ☐ No
- ☐ Not applicable

Comments:

- Monitor serum calcium and phosphate concentrations in people receiving alfacalcidol or calcitriol supplements due to significant risk of hypercalcaemia and hyperphosphataemia

### Are there any special requirements for the safe, effective and appropriate use of the medicines?

- ☑ Yes
- ☐ No
- ☐ Not applicable

Comments:

- Treatment would need to be supervised by a paediatric endocrinologist or an adult endocrinologist. Frequent dosage adjustments are required, including access to accurate growth assessment and access to appropriate biochemical monitoring. The latter includes the ability to measure serum calcium, serum phosphate, serum alkaline phosphatases (ALP) and ideally serum parathyroid hormone, together with assessment of urinary calcium excretion. Access to renal ultrasound for monitoring renal calcium accumulation is also important.

- Management should be balanced with phosphate therapy (phosphorus, application A33)

### Are there any issues regarding cost, cost-effectiveness, affordability and/or access for the medicine in different settings?

- ☐ Yes
- ☑ No
- ☐ Not applicable

Comments:

- Generic versions of these medicines are now available in many countries.

### Are there any issues regarding the registration of the medicine by national regulatory authorities?

- ☐ Yes
- ☑ No
- ☐ Not applicable

Comments:

- Approved by FDA, EMA, Australian Government, Health Canada, Japanese PMDA. However, currently no country included it in their EML. ⁵

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⁵ [https://global.essentialmeds.org/dashboard/medicines](https://global.essentialmeds.org/dashboard/medicines)
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<tr>
<th>Is the proposed medicine recommended for use in a current WHO guideline?</th>
<th>☒ Not applicable</th>
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(refer to: [https://www.who.int/publications/who-guidelines](https://www.who.int/publications/who-guidelines))

Comments: No WHO guidelines currently available for conditions which need the proposed medications.