

I.9 Prednisolone – infantile spasm – EML

Reviewer summary

☒ Supportive of the proposal

☐ Not supportive of the proposal

Justification (based on considerations of the dimensions described below):

About 30 out of every 100,000 babies are affected by IESS, a severe epileptic condition that accounts for about 10% of epilepsies in children under three years old. It is marked by developmental regression and infantile spasms. Prompt therapy with appropriate, globally recognized first-line medicines has been shown to improve outcomes.

IESS is distinct from other epilepsy syndromes in that it has well-established and recognized first-line treatment options. These include non-hormonal treatment with vigabatrin or hormonal treatment with oral prednisolone or ACTH (also referred to as adrenocorticotrophic hormone or tetracosactide depot injections).

In the non-Tuberous Sclerosis Complex (TSC) IESS population, hormonal treatments appear to be more effective than vigabatrin, according to results from systematic reviews and meta-analyses. In comparison to alternative hormonal medications (such as ACTH injections), prednisolone has been found to be equivocal (or superior) in efficacy, similar in adverse effect profile, and much more cost-effective, according to numerous network meta-analyses and head-to-head trials.

I support the inclusion of oral prednisolone under section 5 Medicines for diseases of the nervous system, specifically in the sub-section for antiseizure medications with a special indication for infantile epileptic spasms syndrome (IESS).

Does the EML and/or EMLc currently recommend alternative medicines for the proposed indication that can be considered therapeutic alternatives?

☐ Yes ☒ No ☐ Not applicable

(<https://list.essentialmeds.org/>)

Does adequate evidence exist for the efficacy/effectiveness of the medicine for the proposed indication?

☒ Yes ☐ No ☐ Not applicable

In the non-Tuberous Sclerosis Complex (TSC) IESS population, hormonal treatments appear to be more effective than vigabatrin, according to results from systematic reviews and meta-analyses.

A total of six meta-analyses and systematic reviews evaluating IESS therapy options were found. In order to assess the three first-line treatments (prednisolone, ACTH, and +/- vigabatrin) against one another or against second-line medicines, the included reviews used the best available data. When compared to the other first-line therapies of ACTH and vigabatrin, as well as other non-standard treatments with alternative anti-seizure medications, these reviews found that high-dose oral prednisolone was a more effective or non-inferior, equally safe, and more economical treatment for IESS.

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

☒ Yes ☐ No ☐ Not applicable

Despite its effectiveness, corticosteroids have hazards that need to be carefully managed. Their effect on endocrine function is a major worry; prolonged usage may inhibit the hypothalamic-pituitary-adrenal (HPA) axis, which could result in adrenal insufficiency when stopping the drug.

Infection risk can be elevated with corticosteroid use. Corticosteroids are often only used for severe instances of active tuberculosis that necessitate concurrent anti-tuberculous treatment. Certain preventive measures may be necessary for patients exposed to measles or chickenpox, particularly those who lack immunity, to reduce the likelihood of developing a serious infection.

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<p>Other possible side effects include impacts on the central nervous system, such as heightened irritability and decreased sleep in children; these side effects go away after treatment and can be controlled with clinical supervision.</p> <p>They raise the risk of osteoporosis and growth inhibition in children by decreasing bone production and increasing resorption, which puts bone density at risk.</p>	
<p>Overall, does the proposed medicine have a favourable and meaningful balance of benefits to harms?</p>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable
<p>Are there any special requirements for the safe, effective and appropriate use of the medicines?</p> <p>Baseline testing with full blood count, electrolytes, glucose, creatinine and urea, urinalysis, weight, and blood pressure should be performed. Screening for risk of tuberculosis should be performed; if high risk area, chest x-ray should be considered. Guidelines recommend weekly blood pressure and urine monitoring during course at minimum, if feasible, weekly laboratory studies with electrolytes and blood counts is also often recommended.</p>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Not applicable
<p>Are there any issues regarding price, cost-effectiveness and budget implications in different settings?</p> <p>When comparing prednisolone with ACTH, the two medications show comparable efficacy, safety, and tolerability characteristics. Therefore, this application believes that prednisolone should be chosen for the treatment of IESS if there is no discernible difference between the two medications due to its significantly lower cost, ease of storage and administration without the need for injections or frequent trips to the doctor, and widespread availability.</p> <p>Associated hospitalization and nursing care costs are lower for the oral treatment (prednisolone) in comparison to ACTH, which is a required intramuscular injection. Access to ACTH is limited by required nursing needs and training of caregivers for injections.</p>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not applicable
<p>Is the medicine available and accessible across countries?</p> <p>Prednisolone is available in multiple generic forms and is widely available in countries. A recent study has investigated availability of several medicines, including prednisolone in over 60 LMICs, representing 84% of the global LMIC population. The study concluded that oral prednisolone was affordable and available in between 70-80% of facilities, and that other essential medicines were found to be less available in comparison to it.</p> <p>Prednisolone is included in 131 out of 137 national essential medicines lists according to the WHO Global Essential Medicines dashboard, which has been key to improve its availability and affordability.</p>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable
<p>Does the medicine have wide regulatory approval?</p>	<input checked="" type="checkbox"/> Yes, for the proposed indication <input type="checkbox"/> Yes, but only for other indications (off-label for proposed indication) <input type="checkbox"/> No <input type="checkbox"/> Not applicable