Prednisolone

EMLc | ATC codes: H02AB06

Indication	Infantile spasms ICD11 code: 8A62.0
INN	Prednisolone
Medicine type	Chemical agent
List type	Core
Formulations	**Oral > Liquid:** 1 mg per mL (EMLc) **Oral > Solid > tablet:** 1 mg (EMLc) ; 5 mg (EMLc) ; 10 mg (EMLc)
EML status history	First added in 2025 (TRS 1064)
Sex	All
Age	Children (1 month - 12 years)
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Prednisolone
DrugBank	Prednisolone

Expert Committee recommendation

The Expert Committee recognized the importance of effective treatment options for infantile epileptic spasms syndrome. The Committee noted that early diagnosis and prompt treatment are critical to improving long-term developmental and seizure outcomes. The Committee also noted the antiseizure medicines currently included on the EMLc are not recommended as first-line treatments for infantile epileptic spasms syndrome. The Committee considered that the evidence presented in the application from systematic reviews and meta-analyses and randomized controlled trials supported the effectiveness and safety of high-dose prednisolone in the treatment of non-tuberous sclerosis complex associated infantile epileptic spasms syndrome. For infantile epileptic spasms syndrome secondary to tuberous sclerosis complex, the Committee noted that vigabatrin may be an alternative first-line treatment. The Committee noted the advantages of prednisolone over alternative first-line treatments (adrenocorticotrophic hormone and vigabatrin) in terms of ease of oral administration (in comparison with adrenocorticotrophic hormone which is administered subcutaneously or intramuscularly), cost–effectiveness, cost and affordability, and availability. Thus, the Committee considered prednisolone to be a more feasible treatment option, particularly in resource-constrained settings. The Expert Committee therefore recommended the inclusion of prednisolone on the core list of the EMLc for the new indication of treatment of infantile epileptic spasms syndrome.

Background

Prednisolone for use in the treatment of infantile epileptic spasms syndrome has not previously been evaluated for inclusion on the EMLc. Prednisolone for other indications (e.g. allergy, hypersensitivity, oncology) has been

included on the EMLc since the first list was published in 2007. First-line treatment options for infantile epileptic spasms syndrome include hormonal treatment with oral prednisolone or adrenocorticotrophic hormone and non-hormonal treatment with vigabatrin (1–3). Neither adrenocorticotrophic hormone nor vigabatrin are currently included on the EMLc.

Public health relevance

Infantile epileptic spasms syndrome, previously known as West syndrome, affects about 30 per 100 000 live births annually, accounting for about 10% of epilepsies in children younger than 3 years (4, 5). It is characterized by brief tonic contractions of axial muscles which typically occur in clusters, developmental regression and a hallmark electroencephalogram pattern known as hypsarrhythmia showing chaotic, high-amplitude, excessive slowing and multifocal epileptiform discharges (4). It typically presents between 1 and 24 months of age, with a peak incidence between 3 and 12 months. Both sexes are affected, with a slightly higher incidence in males. The condition is associated with an underlying epileptic encephalopathy that results in developmental slowing, arrest or regression, which usually begins or worsens at the onset of spasms (6). Without treatment, the long-term developmental and cognitive outcomes can be severe (4). Most children with infantile epileptic spasms syndrome have poor outcomes, with about 75% experiencing long-term cognitive deficits and 66% experiencing ongoing seizures (6). Delays in treatment initiation are associated with lower likelihood of clinical response, worse developmental outcomes and worse epilepsy outcomes (6, 7). If left untreated, mortality can exceed 30% (8).

Benefits

A 2022 systematic review and network meta-analysis of 17 randomized controlled trials (987 participants aged 2 months to 3 years) compared effectiveness estimates and rankings of non-surgical interventions for infantile epileptic spasms syndrome (9). The most commonly reported treatments were high-dose adrenocorticotrophic hormone (nine randomized controlled trials, 237 participants), high-dose prednisolone (seven randomized controlled trials, 316 participants), high-dose vigabatrin (six randomized controlled trials, 219 participants), low-dose adrenocorticotrophic hormone (four randomized controlled trials, 75 participants), and prednisone (two randomized controlled trials, 26 participants). The primary outcomes analysed were electroclinical and clinical remissions within 1 month of starting treatment. Electroclinical remission was reported by 16 randomized controlled trials (17 treatment pairs). Results of a fixed-effect frequentist meta-analysis showed that all treatments were superior to placebo except for prednisone and vigabatrin (low-dose and high-dose). Network risk difference (RD) estimates for prednisolone were −0.42 (95% confidence interval (CI) −0.78 to 0.18) (low-dose) and −0.59 (95% CI −0.78 to −0.31) (high-dose). No significant differences were seen between prednisolone and high-dose adrenocorticotrophic hormone (RD 0.25, 95% CI −0.08 to 0.59 (low-dose); RD 0.09, 95% CI −0.17 to 0.34 (high-dose). High-dose prednisolone was superior to both low- and high-dose vigabatrin. Network ranking indicated that high-dose adrenocorticotrophic hormone had the highest probability of being the best intervention, followed by methylprednisolone and low-dose adrenocorticotrophic hormone in combination with magnesium sulfate. High-dose prednisolone (with and without vitamin B6) ranked fourth and sixth, respectively; low-dose prednisolone ranked tenth (9). Clinical remission was reported by 13 randomized controlled trials (14 treatment pairs). Results of a fixed-effect frequentist meta-analysis showed that low-dose adrenocorticotrophic hormone (with and without magnesium sulfate), high-dose adrenocorticotrophic hormone (with and without vitamin B6) and high-dose prednisolone (with and without vitamin B6) were superior to placebo. Network RD estimates for high-dose prednisolone were −0.53 (95% CI −0.82 to −0.23; without vitamin B6) and −0.52 (95% CI −0.90 to −0.14; with vitamin B6). High-dose prednisolone was superior to low-dose prednisolone (RD 0.27, 95% CI 0.03 to 0.50), prednisone (RD 0.48, 95% CI 0.05 to 0.91) and high-dose vigabatrin (RD 0.28, 95% CI 0.11 to 0.44). High-dose adrenocorticotrophic hormone was superior to low-dose prednisolone, but no significant difference was seen between high-dose adrenocorticotrophic hormone and high-dose prednisolone (with and without vitamin B6). Network ranking indicated that low-dose adrenocorticotrophic hormone in combination with magnesium sulfate had the highest probability of being the best intervention, followed by high-dose adrenocorticotrophic hormone and high-dose adrenocorticotrophic hormone in combination with vitamin B6. High-dose prednisolone (with and without vitamin B6) ranked sixth and fourth, respectively; low-dose prednisolone ranked ninth (9). The application

identified other systematic reviews and meta-analyses that provide evidence of no significant differences between adrenocorticotrophic hormone and oral corticosteroids (prednisone, prednisolone) for electroclinical and/or clinical response (10–14). Of note, while vigabatrin was shown to be inferior to hormonal therapies, some studies indicate that it is superior to hormonal therapies in infantile spasms due to tuberous sclerosis complex (15–17). Studies assessing long-term outcomes in children with infantile epileptic spasms syndrome treated with prednisolone/prednisone or adrenocorticotrophic hormone generally found developmental and neurological outcomes to be similar between treatment groups (18–20).

Harms

Adverse effects associated with the use of prednisolone are well known and can be significant. Long-term use can be associated with hypothalamic–pituitary–adrenal axis suppression, increased risk of infection, effects on cardiovascular and renal function, gastrointestinal adverse effects, reduced bone density, cataracts and glaucoma. Treatment of infantile epileptic spasms syndrome with prednisolone is usually short-term (4–5 weeks). A 2022 systematic review and meta-analysis of three randomized controlled trials (343 participants) compared the safety of prednisolone/prednisone and adrenocorticotrophic hormone for treatment of infantile epileptic spasms syndrome (12). Pooled data showed no significant differences between treatments for irritability (relative risk (RR) 0.79, 95% CI 0.57 to 1.10), increased appetite (RR 0.78, 95% CI 0.57 to 1.08), weight gain (RR 0.86, 95% CI 0.56 to 1.32) and gastrointestinal upset (RR 0.60, 95% CI 0.35 to 1.02). Corticosteroid therapy, even short-term as proposed for infantile epileptic spasms syndrome, can complicate vaccination protocols. Live or live-attenuated vaccines are contraindicated during the regimen and for 2–3 months afterward due to the risk of infection. Response to killed vaccines may be diminished, particularly for individuals receiving high doses.

Cost / cost effectiveness

A 2020 study evaluated the cost–effectiveness of adrenocorticotrophic hormone versus oral corticosteroids in the first-line treatment of infantile epileptic spasms syndrome from a patient perspective (14). The study used cost data from the United States for a 14-day course of treatment: 100 464 United States dollars (US$) for adrenocorticotrophic hormone and US$ 210 for prednisolone. The base-case analysis reported incremental cost–effectiveness ratios of US$ 333 and about US$ 1.43 million per case of spasms resolved for prednisolone and adrenocorticotrophic hormone, respectively. Results were robust to multiple sensitivity analyses and different assumptions. The authors concluded prednisolone at 4−8 mg/kg a day to be more cost-effective than adrenocorticotrophic hormone under a wide range of assumptions. A 2024 study in India assessed the societal financial burden linked to infantile epileptic spasms syndrome (21). For 92 children with infantile epileptic spasms syndrome enrolled between August 2022 and March 2023, median medication charges were 20 502 Indian rupees (₹) (US$ 251.80) and consultation charges were ₹2975 (US$ 36.50). The highest costs were due to medications. Median medication costs were ₹15 400 (US$ 172.50) for adrenocorticotrophic hormone, ₹3021 (US$ 55.40) for vigabatrin and ₹540 (US$ 6.60) for prednisolone. Median direct non-medical costs were ₹31 650 (US$ 388.40), and median indirect costs were ₹10 100 (US$ 124.07). The median loss of days due to hospital visits was 12. The application reported the price of prednisolone 5 mg as US$ 0.06, US$ 0.01, US$ 0.02 and US$ 0.05 per tablet in Brazil, Ghana, Kenya and the Philippines, respectively. Costs per recommended treatment course were all below US$ 15.

WHO guidelines

WHO guidelines for the treatment of infantile epileptic spasms syndrome are not currently available. Hormonal therapy with prednisolone or adrenocorticotrophic hormone, with or without vigabatrin, is recommended as first-line treatment for non-tuberous sclerosis complex associated infantile epileptic spasms syndrome in various national and institutional guidelines.

Availability

Prednisolone has wide global market availability and is already included on many national medicines lists for other

indications.

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