Prednisolone

Essential medicine status

Section: 18. Medicines for endocrine disorders > 18.1. Adrenal hormones and synthetic substitutes

EMLc | ATC codes: H02AB06

Indication	Adrenocortical insufficiency ICD11 code: 5A74
INN	Prednisolone
Medicine type	Chemical agent
List type	Core (EML) (EMLc)
Formulations	Oral > Solid > tablet: 1 mg
EML status history	First added in 2025 (TRS 1064)
Sex	All
Age	Also recommended for children
Therapeutic alternatives	prednisone (ATC codes: H02AB07) Oral > Solid > tablet: 1 mg
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Prednisolone
DrugBank	Prednisolone

Expert Committee recommendation

The Expert Committee recognized the public health relevance of effective treatments for adrenal insufficiency and noted that fludrocortisone and hydrocortisone are currently included on the Model Lists for this indication. The Committee considered that the available evidence, while low-quality, supported the effectiveness of prednisolone in the treatment of adrenal insufficiency. Further, the evidence suggests that prednisolone may offer some advantages over hydrocortisone in terms of impact of treatment on weight, bone metabolism and cardiovascular outcomes. The Committee considered that low-dose prednisolone (i.e. 3 mg to 4 mg daily) was generally safe for the treatment of adrenal insufficiency. Documented harms of prednisolone are usually associated with higher doses. Overall, the Committee considered that the balance of benefits to harms was acceptable. The Committee noted that no evidence on cost–effectiveness was presented in the application, but that the price of prednisolone tends to be lower than the price of hydrocortisone in most settings. The Committee considered that the reduced impact on budgets of using prednisolone instead of hydrocortisone would be particularly relevant in resource-constrained settings. The Committee noted that the current availability of the 1 mg tablet formulation of prednisolone is limited. The Committee considered that its inclusion on the Model Lists could catalyse actions to improve availability and access. The Expert Committee therefore recommended the inclusion of prednisolone 1 mg tablets on the core list of the EML and EMLc for the treatment of adults and children with adrenal insufficiency. Listing is recommended for prednisolone with a square box, specifying prednisone 1 mg as a therapeutic alternative.

Background

Prednisolone has not previously been considered for inclusion on the Model Lists for the proposed indication. However, prednisolone 5 mg and 25 mg tablets and 5 mg/mL oral liquid are included on the Model Lists for other indications. Fludrocortisone 100 microgram tablets and hydrocortisone 5 mg, 10 mg and 20 mg tablets for use in adrenal insufficiency have been included on the EML and EMLc since 2009. At that time, the Expert Committee considered the findings of one small study of nine patients that compared hydrocortisone and prednisolone in the management of congenital adrenal hyperplasia. This study showed that

prednisone was associated with significantly greater adverse effects on growth than hydrocortisone. It was acknowledged that the use of other glucocorticoids such as dexamethasone and prednisolone was generally avoided in children due to adverse effects on growth (1).

Public health relevance

Primary adrenal insufficiency (Addison disease) has an estimated worldwide prevalence of 1 in 10 000 people. Causes include autoimmune-mediated adrenal failure, tuberculosis and infectious diseases. Secondary adrenal insufficiency has an estimated worldwide prevalence of 1 in 4000 people and is caused by adrenocorticotropic hormone deficiency due to hypothalamic-pituitary disease. It is often associated with other pituitary hormone deficiencies. Tertiary adrenal insufficiency (glucocorticoid-induced adrenal suppression) is the most common form, affecting up to 1 in 100 people worldwide who are on long-term glucocorticoid therapy at doses that cause adrenal suppression (2–4). Patients with adrenal insufficiency require lifelong glucocorticoid replacement therapy to manage their condition. The traditional treatment involves hydrocortisone, which is administered multiple times a day. Adrenal insufficiency is associated with increased mortality despite glucocorticoid replacement therapy, with a standardized mortality ratio > 2 (5).

Benefits

The application described having reviewed the evidence considered in the development of the United Kingdom's National Institute for Health and Care Excellence (NICE) guideline Adrenal insufficiency: identification and management (6) . The evidence review included six randomized controlled trials in adults with primary adrenal insufficiency which included comparisons of different formulations and dosing of hydrocortisone and standard care. None of the included studies included prednisolone. The evidence review included five randomized controlled trials that investigated the effect of oral glucocorticoids (hydrocortisone, prednisolone and dexamethasone) at different doses and dosing schedules in the management of congenital adrenal hyperplasia. One trial compared once daily prednisolone to three times daily hydrocortisone in 44 prepubertal and pubertal participants with 21-hydroxylase deficiency (7). After 1 year, participants taking daily prednisolone (2.4 to 3.5 mg/m2) showed stable bone maturation ratio, growth velocity and height gains compared with those taking three times daily hydrocortisone (10–15 mg/m2). The evidence review included four randomized controlled trials that compared different doses of oral hydrocortisone in adults with secondary adrenal insufficiency. No studies in children or people with tertiary adrenal insufficiency were identified. A retrospective observational study evaluated the cardiovascular risk profiles of prednisolone and hydrocortisone in the United Kingdom (8). Data from participants receiving prednisolone once daily (n = 64) or hydrocortisone three times daily (n = 82) as glucocorticoid replacement therapy for primary or secondary adrenal insufficiency were analysed. The mean daily dose was 3.7 mg and 20.5 mg for prednisolone and hydrocortisone, respectively. Results showed no significant differences between prednisolone and hydrocortisone for most cardiovascular risk factors including in total cholesterol (4.77 mmol/L versus 5.15 mmol/L; P = 0.07), low-density lipoprotein levels (2.75 mmol/L versus 2.90 mmol/L; P = 0.45), systolic (127 mmHg versus 129 mmHg) or diastolic (77 mmHg versus 79 mmHg; P = 0.19) blood pressure. Patients receiving prednisolone had a significantly lower waist-to-hip ratio (0.92 versus 0.95; P < 0.05). Patient satisfaction ratings were significantly higher in the prednisolone group. A 2016 study examined the pharmacokinetic profile of prednisolone in six patients with secondary adrenal insufficiency and three healthy volunteers (9). The mean prednisolone dose required for adequate replacement in patients with adrenal insufficiency was 3.86 mg. The mean maximal serum concentration (Cmax) was 114.0 microgram/L, with peak concentration at 1.43 hours. The pharmacokinetic profile of prednisolone was found to be similar to the published profile of a dual-release hydrocortisone formulation, suggesting that once-daily prednisolone can be used as an effective and lower-cost alternative to hydrocortisone.

Harms

The ongoing retrospective observational HYPER-AID study is comparing anthropometric, biochemical and subjective health outcomes between hydrocortisone and prednisolone in adults with adrenal insufficiency switching from one treatment to the other (10). Interim results from different study centres in the United Kingdom have been published in abstract form. At one tertiary care centre, 13 of 15 recruited patients completed the switch from hydrocortisone to prednisolone (11); 14 (92.3%) had secondary adrenal insufficiency. Results showed minor but statistically significant decreases in mean body mass index (from 31.56 kg/m2 to 30.87 kg/m2; P = 0.02) and waist circumference (from 106.11 cm to 103.26 cm; P = 0.01). No significant differences were observed in other cardiovascular or metabolic markers. Results from another centre reported that among 23 patients, 11 switched from

prednisolone to hydrocortisone and experienced significant weight gain of 3.2 kg (P < 0.004) (12). Results from other centres have reported varying effects of switching from hydrocortisone to prednisolone in terms of weight, body mass index and waist circumference. In general, cardiovascular markers showed no significant differences (13, 14). A 2017 multicentre study evaluated risk factors for cardiovascular disease in patients with adrenal insufficiency receiving prednisolone (n = 50) or hydrocortisone (n = 909) using real-world data from the European Adrenal Insufficiency Registry (EU-AIR) (15). The results showed significantly higher mean total cholesterol (6.3 mmol/L versus 5.4 mmol/L; P = 0.003) and low-density lipoprotein levels (3.9 mmol/L versus 3.2 mmol/L; P = 0.013) in patients receiving prednisolone compared with those receiving hydrocortisone at baseline and at follow-up. Glycated haemoglobin (HbA1c), high-density lipoprotein, triglyceride levels, body mass index, systolic and diastolic blood pressure, and waist circumference were not significantly different between treatment groups.

Cost / cost effectiveness

No cost–effectiveness information was presented in the application. The application reported available prices of prednisolone and hydrocortisone tablets in a variety of settings. In Australia, prednisolone 1 mg tablets cost 16.56 Australian dollars (AU$) for 100 tablets, sufficient for 1 month supply at 3 mg a day. Hydrocortisone 4 mg tablets cost AU$ 42.39 for 100 tablets or AU$ 63.58 a month for a typical dosing regimen. In Pakistan, prednisolone 5 mg tablets cost between 45–110 Pakistani rupees (P Rs) a month. Hydrocortisone costs range from P Rs 252 for generic hydrocortisone to P Rs 5300–10 500 for branded hydrocortisone. In Sri Lanka, prednisolone 5 mg tablets cost between 3 and 14 Sri Lankan rupees (SL Rs) a day. Generic branded hydrocortisone 20 mg tablets (used to deliver divided daily doses) cost between SL Rs 64 and SL Rs 96 a day. In Thailand, prednisolone is reported to be generally more affordable than hydrocortisone, however specific price information was not provided. In the United Kingdom, prednisolone 1 mg tablets cost 0.71 pounds sterling (£) a month at a dose of 1 mg daily, and £2.13 a month at a dose of 3 mg daily. Hydrocortisone 10 mg tablets cost £3.84 a month for a typical dosing regimen, with lower strength tablets available at higher costs.

WHO guidelines

WHO guidelines for the management of adrenal insufficiency are not currently available. The NICE guidelines for adrenal insufficiency include recommendations for the use of prednisolone in children younger than 16 years (if they have stopped growing) and people older than 16 years with primary adrenal insufficiency, congenital adrenal hyperplasia and secondary and tertiary adrenal insufficiency as an alternative glucocorticoid to first-choice hydrocortisone. Prednisolone is not recommended as replacement therapy for adrenal insufficiency in children younger than 1 year. The guidelines also include recommendations for prednisolone dose-tapering and withdrawal which incorporates 1 mg dose reductions to avoid adrenal crisis and glucocorticoid withdrawal syndrome (16).

Availability

Prednisolone 1 mg tablets are available in a limited number of countries, including Australia, New Zealand and United Kingdom. They are reported to be unavailable in Pakistan, Sri Lanka and Thailand and other countries within the Association of Southeast Asian Nations. Prednisone 1 mg tablets are available in Australia and the United States of America.

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