Hypromellose

REJECTED

The Expert Committee, after evaluation, declines to list the medicine proposed in the application.
The Model List of Essential Medicines reports reasons that Committee Members have identified for denying listing.

Section: 21. Ophthalmological preparations

EMLc | ATC codes: S01KA02

Indication	Keratoconjunctivitis sicca ICD11 code: 9A79
INN	Hypromellose
Medicine type	Diagnostic agent
List type	Core (EML) (EMLc)
Formulations	Local > Ophthalmological > Solution (eye drops): 0.3%
EML status history	Application rejected in 2023 (TRS 1049)
Sex	All
Age	Also recommended for children
Therapeutic alternatives	carmellose sodium hyaluronate (ATC codes: S01KA01)
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Hypromellose
DrugBank	Hypromellose

Expert Committee recommendation

The Committee noted that dry eye disease was a chronic and progressive condition and a common reason for ophthalmic outpatient visits. Severe dry eye disease, if untreated, can lead to ocular infection and inflammation, corneal abrasions, corneal ulcers and vision loss. Based on the evidence presented, the Committee accepted that hypromellose was a generally safe and effective ocular surface lubricant for reducing the signs and symptoms of dry eye disease for patients with mild to moderate disease. Its effectiveness and safety are comparable to other artificial tears preparations. However, the Committee noted that the available data were limited by the variable definition of dry eye disease applied in published studies and the disease severity examined, and that compliance with treatment was rarely quantified. As a result, the optimal composition, dose, formulation or formulations for artificial tears preparations for the treatment of dry eye disease have not been demonstrated. The Committee also considered that the sight-threatening complications of dry eye disease were primarily associated with severe forms of the condition. Limited evidence was available of the effectiveness of hypromellose for in improving relevant clinical outcomes compared with other artificial tear preparations, including combinations, specifically in patients with severe dry eye disease. The Expert Committee therefore did not recommend inclusion of hypromellose on the EML and EMLc for the treatment of dry eye disease in adults and children.

Background

Artificial tears preparations for the treatment of dry eye disease have not previously been considered for inclusion on the Model Lists.

Public health relevance

Dry eye disease is a multifactorial disease of the ocular surface that is characterized by a loss of homeostasis of the tear film. It is accompanied by ocular symptoms, such as visual disturbance and discomfort (1,2). The negative impact on vision can limit education and work productivity by interfering with patients' daily activities, such as sustained visual attention when reading, writing, driving and using digital display monitors (3,4). Patients with dry eye disease also report psychological concerns and higher levels of anxiety and depression compared with those without dry eyes (5). Risk factors for dry eye disease include age 50 years or older (6,7), female sex (8,9), wearing contract lenses or a history of refractive surgery (10), exposure to environments with low relative humidity and extremes of temperature (10), certain chronic and autoimmune conditions (10,11), medication use (9,12) and prolonged engagement in visual tasks (13,14). Dry eye disease has a global prevalence ranging from about 5% to 50%, corresponding to 385 million to 3.85 billion people worldwide (15). The highest prevalence of dry eye disease has been reported in the WHO's African region, followed by the Eastern Mediterranean Region, South-East Asia Region, Western Pacific Region, European Region, and Region of the Americas (16).

Benefits

A Cochrane systematic review published in 2016 of 43 randomized controlled trials (3497 participants) evaluated the effectiveness of over-the-counter artificial tear applications in treating dry eye disease compared with no treatment, placebo or another class of over-the-counter artificial tears (17). The authors considered participant symptoms (subjective) to be the primary outcome for the review. Secondary outcomes included objective measures of effectiveness (e.g. tests of vision or tear stability). Overall, the review found uncertainty with regard to whether different over-the-counter artificial tears provided similar relief of dry eye disease compared with each other or placebo, with most of the included studies producing contradictory between-group results, or no between-group differences. The quality of the evidence was judged as low due to high risks of bias and poor reporting of outcome measures. The authors concluded that over-the-counter artificial tears may be a safe and effective treatment for dry eye disease, with the literature indicating that most products have similar efficacy. A systematic review published in 2009 of 33 studies (1293 participants) assessed the efficacy of dry eye treatments with artificial tears or ocular lubricants using scoring of rose bengal stains as the outcome measure (18). Mean baseline and 30-day post-treatment scores were calculated, along with the net change and the percentage change in the rose bengal scores. A statistically significant reduction in mean rose bengal scores was observed from baseline to 30-days post-treatment with any type of artificial tears or ocular lubricant from 4.2 (standard deviation (SD) 1.6) to 2.8 (SD 1.2). The net reductions in mean rose bengal scores were −1.1 (SD 0.8) for traditional artificial tears (e.g. hypromellose), −1.2 (SD 0.7) for carbomer gels and −2.1 (SD 0.9) for hyaluronic acid-based products. No significant difference was found between traditional artificial tears and carbomer gels, but there was a significant difference between traditional artificial tears and hyaluronic acid-based products. A multiple analysis of variance (ANOVA) test, comparing outcomes using the different treatments, found no significant difference between the three groups. Across all studies, the overall net reduction in rose bengal staining after 4 weeks of treatment was 33%. The authors noted heavily skewed data for some treatments, so determined a 25% improvement in rose bengal staining scores with 1 month of treatment was more reasonable. No information was provided in the application on what constituted a clinically meaningful improvement. The application also presented brief summaries of findings of individual clinical trials comparing hypromellose artificial tears with other artificial tears, placebo or no treatment (19–27). The outcome assessed to evaluate the effectiveness of hypromellose tears was the relief of dry eye symptoms. Both hypromellose and comparator artificial tears products were generally found to be effective in relieving symptoms of dry eye disease. Most of these studies were included in the above-mentioned Cochrane systematic review (17).

Harms

The application stated that overall the clinical evidence surveyed suggested that hypromellose was generally safe, with occasional transient burning and stinging of the eyes. Similar levels of adverse effects were observed when hypromellose was compared with other types of artificial tears and dry-eye treatments. The Cochrane systematic review found that the use of artificial tears was relatively safe, although not without adverse events. The most common adverse events were blurred vision, ocular discomfort and foreign body sensation (17).

Cost / cost effectiveness

The application stated that hypromellose has been found to be cost-effective in several national studies (not referenced in the application) as it is a relatively cheap and effective treatment with considerable potential to reduce the burden on society from dry

eye disease. In the United Kingdom, the price for a 10 mL bottle of preserved hypromellose 0.3% artificial tears (about 200 drops of 0.05 mL) was reported as US$ 1.79, equivalent to an annual treatment cost of US$ 18.37 assuming average usage of 5.7 drops per day. Similar costs were reported in Singapore and the United States, with a price per bottle of US$ 1.52. Non-preserved and single unit-dose preparations of artificial tears are more costly to manufacture and to purchase. They may be less convenient to use than preserved and bottled preparations (29). In Singapore, the mean unit cost of preservative-containing lubricants was around US$ 5.50, meanwhile that for preservative-free lubricants was US$ 12.96 (30).

WHO guidelines

WHO guidelines for treatment of dry eye disease are not currently available. The 2019 WHO World report on vision recognizes that eye conditions that do not typically cause vision impairment, such as dry eye disease and conjunctivitis, are frequently among the leading reasons for patients to present to eye care services globally, and should not be overlooked (28).

Availability

Artificial tears preparations, including hypromellose, are available on the market globally. They are produced by multiple manufacturers and are often available over the counter.

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