Natamycin

Section: 21. Ophthalmological preparations > 21.1. Ophthalmological preparations > Anti-infective agents

EMLc | Codes ATC: S01AA10

Indication	Infectious keratitis Code ICD11: 9A71
INN	Natamycin
Type de médicament	Chemical agent
Type de liste	Liste de base
Formulations	**Local > Ophthalmological > Suspension:** 5% eye drops
Historique des statuts LME	Ajouté pour la première fois en 2017 (TRS 1006)
Sexe	Tous
Âge	Aussi recommandé pour les enfants
Équivalence thérapeutique	La recommandation concerne ce médicament spécifique
Renseignements sur le brevet	Patents have expired in most jurisdictions Lire la suite sur les brevets.
Wikipédia	Natamycin
DrugBank	Natamycin

Recommandation du comité d'experts

Noting the overall favourable benefit–risk profile of topical natamycin for the treatment of fungal keratitis, the Expert Committee recommended the addition of natamycin ophthalmic suspension 5% to the core list of the EML and EMLc.

Contexte

Natamycin eye drops have not previously been considered for inclusion on the EML. Currently, no topical antifungals for ophthalmic infections are listed.

Pertinence pour la santé publique

Keratitis refers to inflammation of the cornea, which causes ulceration and gradual opacification, initially due to an influx of inflammatory cells and later to fibrosis. Microbial keratitis may be caused by bacteria, fungi, viruses or protozoa (inflammation without infection may be due to chemical injury or autoimmune inflammatory pathology) and is the leading cause of unilateral corneal scarring (1, 2). Corneal abrasions or significant trauma from plant or organic material are the most common predisposing factors (3). Other risk factors include being immunocompromised (including exposure to local or systemic corticosteroids), diabetes, HIV infection, impaired tearing, incomplete eyelid closure and poor hygiene practice in those who use contact lenses. Children are often affected (4). In warm, humid climates, approximately 50% of cases of microbial keratitis are caused by fungi, but in dry, cool climates, 95% of cases are caused by bacteria (5). The proportion of microbial keratitis cases attributable to fungal infections rises with proximity to the Equator (6). An estimated 12 million cases of microbial keratitis occur annually in south-east Asia; the proportion of cases with resultant visual loss or blindness is

unknown. A statistically significant correlation has been found between gross national income (GNI) and etiology of microbial keratitis: fungal keratitis is associated with low-GNI countries (7). In Ugandan children with visual impairment, visual loss after corneal ulceration was responsible for nearly 25% of cases (8). The rate of HIV infection in those presenting with fungal keratitis in United Republic of Tanzania was twice the documented rate in the adult population (9). The annual incidence of microbial keratitis in wearers of contact lenses varies from 1.2 to 1304 per 10 000, depending on the type of lens, overnight use and the quality of lens care (10, 11). The proportion of microbial keratitis cases caused by fungi in contact lens wearers varies from 0.33% to 50% (7).

Bénéfices

The application summarized the findings of seven randomized controlled trials (RCTs) of natamycin compared with alternative treatments for fungal keratitis (12–18). Two trials compared natamycin with chlorhexidine gluconate and found more favourable responses at 5 days, and a greater proportion of patients with healed ulcer at 21 days, for the chlorhexidine-treated groups than the natamycin-treated groups (16, 17). These trials had small sample sizes (n = 60 and n=71) and were therefore probably underpowered for detection of differences. A single study comparing natamycin with econazole found no difference between the two treatments for the outcome measure of healed or healing ulcer at the final visit (risk ratio 0.99; 95% confidence interval 0.8–1.21) (15). Three trials compared topical natamycin 5% with topical voriconazole 1% and measured best corrected spectacle visual acuity (BCSVA) at 3 months as the primary outcome (12–14). A meta-analysis of these trials in a recent Cochrane review suggested that: “there is evidence that natamycin is more effective than voriconazole in the treatment of fungal ulcers” (19). The largest of the three studies, referred to as MUTT1, found a substantial benefit for natamycin compared with voriconazole, particularly for Fusarium spp., which are often the major cause (14).

Torts

The adverse events that have been identified during post-marketing use of natamycin in clinical practice are allergic reaction, change in vision, chest pain, corneal opacity, dyspnoea, eye discomfort, eye oedema, eye hyperaemia, eye irritation, eye pain, foreign body sensation, paraesthesia, and tearing. Clinical trial experience suggests that these events are rare and that topical natamycin is generally well tolerated (14).

Preuves supplémentaires

Six of the seven RCTs identified in the application were included in a recent systematic review and meta-analysis of natamycin for the treatment of fungal keratitis (20). The included trials were all conducted in Asian countries (Bangladesh, China, India) where there is a higher prevalence of fungal keratitis. The authors concluded that natamycin is a preferable treatment choice, particularly in the early stages of Fusarium cases.

Rapport coût/efficacité

The Expert Committee noted the considerable variation in the reported cost of topical natamycin 5% by region as described in the application: Indonesia US$ 4, Peru US$ 140, and United Kingdom £330 per bottle.

Directives de l'OMS

The 2004 Guidelines for the management of corneal ulcer at primary, secondary and tertiary care facilities in the South-East Asia region (WHO regional Office for South-East Asia) recommend natamycin 5% eye drops for treatment of confirmed suppurative keratitis where fungal hyphae are seen on corneal smear (1).

Disponibilité

Topical natamycin has been used extensively for the treatment of fungal keratitis in south Asia and south-east Asia and North America and has recently become the standard of care in the United Kingdom. It is less widely used in Africa and continental Europe where it is not readily available.

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