Amitriptyline
Le Comité d'experts, après évaluation, refuse d'inscrire le médicament proposé dans la demande.
La Liste Modèle des Médicaments Essentiels fait état des raisons que les membres du Comité ont identifiées pour refuser l'inscription.
Refusée
Section:
5. Medicines for neurological disorders 5.1. Medicines for central nervous system disorders 5.1.5. Medicines for headache disorders 5.1.5.2. Medicines for migraine prophylaxis
Codes ATC: N06AA09
Indication
Migraine Code ICD11: 8A80.Z
INN
Amitriptyline
Type de médicament
Chemical agent
Type de liste
Liste de base
Formulations
Oral > Solid > tablet: 25 mg
Historique des statuts LME
Demande refusée en 2025 (TRS 1064)
Sexe
Tous
Âge
Adolescents et adultes
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
Amitriptyline
DrugBank
Amitriptyline
Recommandation du comité d'experts
☐
The Expert Committee noted that migraine is a common primary headache disorder characterized by recurrent moderate to severe pain and acknowledged the public health relevance of effective treatments. Migraine is a cause of considerable disability and results in a substantial socioeconomic burden, which is greater for women than for men. Migraine prophylaxis is generally recommended in the presence of at least four migraine days per month and/or when migraine substantially affects quality of life. The Expert Committee noted that several classes of medication are commonly used for migraine prophylaxis, including antidepressants, anticonvulsants, antihypertensives and calcitonin gene-related peptide (receptor) monoclonal antibodies. Currently, the Model Lists include only propranolol for migraine prophylaxis. The Committee noted that there is moderate-certainty evidence that amitriptyline increases the proportion of people who experience a 50% or greater reduction in monthly migraine days. However, amitriptyline was also associated with a greater proportion of patients who discontinued treatment due to adverse events compared with placebo. Furthermore, the Committee noted that very few data exist comparing the efficacy and safety of amitriptyline versus active comparators, e.g. propranolol, other beta-blockers or other prophylaxis interventions. Based on these considerations, the Expert Committee did not recommend the inclusion of amitriptyline on the EML for use in migraine prophylaxis. In the absence of adequate evidence for comparative benefit and safety versus currently listed propranolol, the Expert Committee was unable to determine if amitriptyline has a favourable and meaningful balance of benefits to harms.
Contexte
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Amitriptyline has not previously been evaluated for inclusion on the EML for migraine prophylaxis. It is currently listed for use in the treatment of depression and other common symptoms in palliative care. Propranolol is currently included in the EML for migraine prophylaxis.
Pertinence pour la santé publique
☐
Migraine is a prevalent neurovascular disorder characterized by moderate to severe headache attacks, often accompanied by nausea, vomiting, photophobia/phonophobia and sensitivity to external stimuli (light, noise, odours). Symptoms are disabling and affect participation in life activities, quality of life and productivity (1). In around 25% of people affected, episodes may be preceded by transient focal neurological symptoms – most commonly visual disturbances, less commonly paresthesias, rarely motor or language deficits. The global prevalence of migraine is estimated at 14–15% (more than 1 billion people worldwide), and it is two to three times higher in women than men (2). According to the Global Burden of Disease study 2021, migraine was the fourth highest cause of years lived with disability at level 4 (3). In an analysis of the Global Burden of Disease study 2016, migraine accounted for 45.1 million disability-adjusted life years (4). Around 2–3% of people with episodic migraine (headache on < 15 days/month) transition to more disabling chronic migraine (headache on ≥ 15 days/month of which a majority are with symptoms of migraine) (5). One of the main risk factors for the transition to chronic migraine is poorly managed acute treatment and the overuse of acute medications (6).
Bénéfices
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The application presented the results of a critical re-appraisal and meta-analysis of amitriptyline for migraine

prophylaxis (7). Three studies were included that compared amitriptyline and placebo for migraine prophylaxis (8–10). For efficacy outcome, two trials reported a ≥ 50% reduction in monthly migraine and one trial reported 50% responder rates. Two of the three trials were rated at high risk of bias, due to missing data on outcomes and failure to describe the methods for allocation concealment. In a pooled analysis, there was moderate-certainty evidence that amitriptyline probably increases the proportion of patients who experience ≥ 50% reduction in monthly migraine days (risk ratio 1.60, 95% confidence interval (CI) 1.17 to 2.19; three randomized controlled trials, 389 participants). A subgroup analysis based on risk of bias of the included trials did not indicate a difference between the trials at low and high risk of bias. One cross-over randomized controlled trial compared the efficacy of amitriptyline with propranolol and placebo for migraine prophylaxis in 30 patients over 40 weeks (11). The reported outcome measure was a headache score calculated by multiplying headache hours by pain severity. The arithmetic mean of weekly scores was calculated. Both amitriptyline and propranolol were significantly superior to placebo. No significant difference was observed between amitriptyline and propranolol. Of note, the superiority of amitriptyline over placebo did not correlate with significantly reduced test scores for depression.

Torts

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Adverse effects of amitriptyline are well known and include drowsiness and anticholinergic symptoms (e.g. dry mouth, urinary retention, constipation, tachycardia, blurred vision), weight gain, glaucoma, benign prostatic hypertrophy, and PQ and QT interval prolongation. In the pooled analysis presented in the application, there was moderate-certainty evidence that amitriptyline probably increases the proportion of patients who discontinue treatment due to adverse events compared to placebo (risk difference 0.05, 95% CI 0.01 to 0.10; two randomized controlled trials, 507 participants) (7). The cross-over trial comparing amitriptyline and propranolol did not report safety outcomes (11).

Rapport coût/efficacité

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A 2015 cost–effectiveness analysis investigated interventions for migraine in four low- and middle-income countries including prophylaxis with amitriptyline (12). A population model was run for two scenarios over a lifetime horizon. Scenario 1 reflected the natural history of migraine and scenario 2 represented the population-level impact of each intervention implemented for 10 years. The population included was aged between 18 and 65 years. It was assumed that prophylaxis was only offered to people with three or more migraine attacks per month. Amitriptyline was cheaper than topiramate and more cost-effective than propranolol. The combination of amitriptyline prophylaxis and acute management with acetylsalicylic acid was associated with costs per healthy life year gained of 1649 United States dollars (US$), US$ 1795, US$ 5264 and US$ 773 in China, India, Russian Federation and Zambia, respectively. Costs were lower when treatment was accompanied by consumer education and prescriber training: US$ 959, US$ 957, US$ 3059 and US$ 573 per healthy life year gained, respectively. Using the same modelling framework as the above study, the applicants conducted a cost–effectiveness analysis of amitriptyline versus propranolol. The model assumed an amitriptyline dose of 25 mg daily for the first week, 50 mg daily for the second week and 75 mg daily thereafter, and a propranolol dose of 160 mg daily. Costs per healthy life year gained were US$ 560 for amitriptyline and US$ 887 for propranolol. In this analysis, amitriptyline dominated propranolol (i.e. lower cost and more effective). However, the results are considered highly uncertain due to the poor quality of the efficacy data.

Directives de l'OMS

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WHO guidelines for migraine are not currently available. The application provided a brief summary of recommendations on amitriptyline for migraine prophylaxis from various current national and international clinical guidelines.

Disponibilité

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Amitriptyline has wide globally. Availability in branded and generic forms. In some jurisdictions, its use in migraine prophylaxis is an off-label indication.

Autres considérations

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The Department of Mental Health, Brain Health and Substance Use provided comments on the application. The technical department did not support the inclusion of amitriptyline on the EML for migraine prophylaxis, suggesting that more evidence with clearer outcomes and specific indications for use in particular populations should be required to be considered for inclusion on the EML.

☐ Afficher les références Masquer les références

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