Eravacycline

REFUSÉE

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.

Section: 6. Anti-infective medicines > 6.2. Antibacterials > 6.2.3. Reserve group antibiotics

Codes ATC: J01AA13

Indication	Other carbapenem resistant Enterobacterales Code ICD11: MG50.C0
INN	Eravacycline
Type de médicament	Chemical agent
Groupes d'antibiotiques	R RESERVE
Type de liste	Liste complémentaire
Formulations	**Parenteral > General injections > IV:** 50 mg lyophilized powder for injection
Historique des statuts LME	Demande refusée en 2019 (TRS 1021)
Sexe	Tous
Âge	Adolescents et adultes
Équivalence thérapeutique	La recommandation concerne ce médicament spécifique
Renseignements sur le brevet	Lire la suite sur les brevets.
Wikipédia	Eravacycline
DrugBank	Eravacycline

Recommandation du comité d'experts

The Expert Committee did not recommend the addition of eravacycline to the EML. The Committee considered that although eravacycline demonstrates activity against some strains of carbapenemase-producing Enterobacteriaceae, there are some concerns with regard to efficacy, as eravacycline failed to demonstrate non-inferiority compared to levofloxacin in one RCT for cUTI. In addition, the Committee considered that there could be safety concerns, with no long-term safety data currently available. The Committee noted pharmacological similarities between eravacycline and tigecycline, and the reported increased mortality associated with tigecycline in some meta-analyses. The Expert Committee agreed with the EML Antibiotic Working Group's recommendation that eravacycline be classified in the AWaRe Reserve group.

Contexte

The application requested the inclusion of eravacycline on the complementary list of the EML as a last-resort treatment option for infections due to multidrugresistant organisms (MRDOs). Eravacycline had not previously been considered for inclusion on the EML. Eravacycline is a fully synthetic tetracycline antibiotic that has a spectrum of activity similar to tigecycline and maintains its activity in the presence of two common resistance

mechanisms: ribosomal protection and active drug efflux. It retains activity against most ESBL producing Enterobacteriaceae and some strains of carbapenem-resistant Enterobacteriaceae and Acinetobacter baumannii but has limited activity against Pseudomonas aeruginosa (1–4).

Pertinence pour la santé publique

Antibiotic-resistant bacteria are a significant threat to public health, both in HICs as well as LMICs (5–7). A recent study estimated that infections with antibioticresistant bacteria were responsible for approximately 33 000 attributable deaths in Europe in 2015 (5). Fewer data are available for LMICs, but a retrospective study in ten hospitals in India found that resistant pathogens were associated with two to three times higher mortality than infections with susceptible strains after adjusting for several confounders (6). Over the past decade there has been increasing spread of multidrugresistant Gram-negative pathogens such as carbapenemase producing Enterobacteriaceae (8). The Global Antimicrobial Resistance Surveillance System (GLASS) report published in 2018 found high levels of carbapenem resistance in Enterobacteriaceae and non-fermenters in many of the LMICs providing data for the report (6). The 2015 WHO Global action plan on antimicrobial resistance calls for the development of new antimicrobial medicines (7). To provide a framework for this endeavour, in 2017 WHO published a priority list of antibiotic-resistant bacteria (9). “Priority 1: critical” category includes four types of pathogens, all of which are Gram-negative: carbapenem resistant Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacteriaceae; and third-generation cephalosporin-resistant Enterobacteriaceae (10).

Bénéfices

Eravacycline achieved the predefined criteria for non-inferiority compared with ertapenem in one trial and meropenem in another trial in the treatment of cIAI in hospitalized adults (11, 12). A further trial has been conducted in adult patients with cUTI using levofloxacin as comparator, but the results have so far only been published on cinicaltrials.gov (NCT01978938) and eravacycline “did not achieve its primary endpoint of statistical non-inferiority compared to levofloxacin” (13). Like for other tetracyclines, eravacycline use is not recommended in children younger than 8 years and pregnant or breastfeeding women due to the risk of tooth discoloration and enamel hypoplasia. A Phase I multicentre study to assess the pharmacokinetics and safety of intravenous (IV) eravacycline in children aged 8 to 18 years is currently recruiting patients (ClinicalTrials.gov Identifier: NCT03696550).

Torts

In the trials comparing eravacycline to a carbapenem (ertapenem and meropenem respectively) more treatment-emergent AEs were observed in the eravacycline treatment groups (11, 12). The difference was mostly attributable to nausea and phlebitis.

Rapport coût/efficacité

United States: wholesale acquisition cost of US$ 175 per day of treatment (14). No cost-effectiveness data are available.

Directives de l'OMS

There are no available WHO guidelines for the treatment of infections due to MDROs.

Disponibilité

Eravacycline has been approved in the United States and the European Union for the treatment of cIAI in adults.

Autres considérations

Safety concerns exist for tigecycline, a pharmacologically similar agent with a similar spectrum of activity to eravacycline, with an increased risk of mortality compared with other antimicrobials being reported (15–17). The

FDA issued a boxed warning about this risk in 2013 (18). In a separate recommendation made during the meeting, the Expert Committee recommended the removal of tigecycline from the EML and EMLc.

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