Amodiaquine + sulfadoxine + pyrimethamine

Statut de médicament essentiel

Section: 6. Anti-infective medicines > 6.5. Antiprotozoal medicines > 6.5.3. Antimalarial medicines > 6.5.3.2. Antimalarial medicines > For chemoprevention

EMLc | Codes ATC: P01BA06 P01BD51

Indication	Malaria Code ICD11: 1F4Z
INN	Amodiaquine + sulfadoxine + pyrimethamine
Type de médicament	Chemical agent
Type de liste	Liste de base (EML) (EMLc)
Formulations	Oral > Solid: 76.5 mg (as hydrochloride) [3] + 250 mg + 12.5 mg [1] dispersible tablets in co-package (EMLc) ; 153 mg (as hydrochloride) [3] + 500 mg + 25 mg [1] dispersible tablets in co-package (EMLc)
Historique des statuts LME	Ajouté pour la première fois en 2019 (TRS 1021)
Sexe	Tous
Âge	Enfants (1 mois - 12 ans)
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	Amodiaquine + sulfadoxine + pyrimethamine
DrugBank	Amodiaquine, Sulfadoxine, Pyrimethamine

Recommandation du comité d'experts

The Expert Committee recommends the addition of co-packaged amodiaquine with sulfadoxine + pyrimethamine to the core list of the EMLc for seasonal malaria chemoprevention in children on the basis of acceptable safety and demonstrated benefits for reducing clinical malaria episodes, serious malaria episodes and reduced rates of mortality and anaemia, and in alignment with WHO malaria guidelines. The Expert Committee noted the lack of evidence of the impact of the use of amodiaquine with sulfadoxine + pyrimethamine for SMC on antimicrobial resistance, and encouraged further assessment and monitoring in this regard within programme delivery.

Contexte

The application requested the addition of co-packaged amodiaquine with sulfadoxine + pyrimethamine to the core list of the EMLc for seasonal malaria chemoprevention (SMC) in children. Amodiaquine and sulfadoxine + pyrimethamine are both listed on the EMLc for use in combination with artesunate for the curative treatment of malaria. These medicines have not previously been considered for use in malaria prophylaxis/ prevention.

Pertinence pour la santé publique

Malaria is one of the leading causes of illness, death and lost economic productivity globally. In 2017, there were an estimated 219 million malaria cases worldwide, the majority of which occurred in the African region (92%, 200 million cases) (1). Of the 435 000 deaths due to malaria globally in 2017, 266 000 (61%) were in children under 5 years of age. Across the Sahel sub-region in Africa,

most childhood morbidity and mortality from malaria occurs during the rainy season, which is generally short. Giving effective antimalarial medicines – at full treatment doses and at appropriate intervals during this period – has been shown to prevent illness and death from malaria in children. The interventions currently recommended by WHO for the control of malaria are use of long-lasting insecticidal mosquito nets and/or indoor residual spraying for vector control, prompt access to diagnostic testing of suspected cases and treatment of confirmed cases with effective artemisinin-based combination therapy. In addition to these, other interventions recommended for specific high-risk groups in areas of high transmission include intermittent preventive treatment in pregnancy (IPTp) and infancy (IPTi). With the changing epidemiology of malaria, there has been a progressive shift from a 'one size fits all' approach to targeting malaria control strategies to specific populations and/ or locations for maximal effectiveness. In line with this approach and on the basis of new evidence, WHO recommends an additional intervention against Plasmodium falciparum malaria: seasonal malaria chemoprevention (SMC). The objective of preventive treatment is to prevent malarial illness by maintaining therapeutic drug levels in the blood throughout the period of greatest risk (2).

Bénéfices

A 2012 Cochrane systematic review of seven trials (12 589 participants) evaluated the effects of seasonal malaria chemoprophylaxis compared with no prophylaxis in children aged 6 years or less living in areas of West Africa with seasonal malaria transmission (3). In three studies, amodiaquine (AQ) and sulfadoxine + pyrimethamine (SP) was administered monthly at full treatment doses, two studies used SP every two months, and one study used SP and artesunate monthly, during the malaria transmission season. In comparison with no chemoprophylaxis, SMC was associated with markedly reduced clinical malaria episodes (rate ratio (RR) 0.26, 95%CI 0.17 to 0.38) and serious malaria episodes (RR 0.17, 95%CI 0.1 to 0.76). SMC may also be associated with a reduction in mortality (RR 0.66, 95%CI 0.31 to 1.39) and a reduction in moderately severe anaemia (RR 0.71, 95%CI 0.52 to 0.98). The findings were consistent in trials in which there was high (>90%) use of insecticide-treated bednets (3).

Torts

AQ + SP are safe and well tolerated when used at the recommended doses and regimens. Both drugs have been used for decades for malaria treatment, and SP is currently used for intermittent preventive treatment of malaria in pregnancy and in infancy. Both AQ and SP are also used in combination with artesunate as artemisinin-based combination therapy, which is used for the treatment of uncomplicated malaria in many endemic countries. In Senegal, where nearly 800 000 treatment courses of SP + AQ within SMC have been given to children, no serious adverse events attributable to these drugs were observed during intensive pharmacovigilance based on spontaneous reporting (4). AQ + SP is generally well tolerated in children. Mild side-effects may occur, of which the most common is vomiting associated with intake of AQ. No serious adverse events attributable to AQ + SP have been reported in trials involving children (5–7). SMC with AQ + SP is contraindicated in children receiving sulfabased medication for treatment or prophylaxis, including sulfamethoxazole + trimethoprim, which is widely used as prophylaxis against opportunistic infections in HIV-infected infants.

Rapport coût/efficacité

Evaluation of the cost of delivering SMC in large field trials shows that the greatest costs are associated with delivering the drugs and the incentives paid to health workers. In Gambia, the cost of SMC delivery by village health workers was estimated to be US$ 1.63 per child per year (9). In Senegal, where SMC was delivered by community health workers paid a daily rate and supervised by the health post nurse, the overall cost at 46 health posts was estimated to be US$ 0.5 per child per month, or approximately US$ 1.50 per child per year (10). The cost of SMC is similar to those of other malaria control interventions (11).

Directives de l'OMS

The 2015 WHO Guidelines for the treatment of malaria recommend SMC with monthly AQ + SP for all children aged less than 6 years during each transmission season in areas with highly seasonal malaria transmission in the sub-Sahel region of Africa (strong recommendation, high quality evidence) (8). The guideline recommendation was informed by the Cochrane systematic review mentioned above (3).

Disponibilité

Co-packaged sulfadoxine + pyrimethamine and amodiaquine tablets are currently available on the market from three

manufacturers and have been prequalified by the WHO Prequalification Programme.

1. World Malaria Report 2018. Geneva: World Health Organization; 2018. Available from https://apps.who.int/iris/bitstream/handle/10665/275867/9789241565653-eng.pdf, accessed 29 September 2019.
2. World Health Organization. WHO Policy Recommendation: Seasonal malaria chemoprevention (SMC) for Plasmodium flaciparum malaria control in highly seasonal transmission areas of the Sahel sub-region in Africa. March 2012. Available from https://www.who.int/malaria/mpac/feb2012/smc_policy_recommendation.pdf, accessed 29 September 2019.
3. Meremikwu MM, Donegan S, Sinclair D, Esu E, Oringanje C. Intermittent preventive treatment for malaria in children living in areas with seasonal transmission. Cochrane Database Syst Rev. 2012(2):CD003756.
4. Cisse B, Ba EH, Sokhna C, JL ND, Gomis JF, Dial Y et al. Effectiveness of Seasonal Malaria Chemoprevention in Children under Ten Years of Age in Senegal: A Stepped-Wedge Cluster-Randomised Trial. PLoS Med. 2016;13(11):e1002175.
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6. Konate AT, Yaro JB, Ouedraogo AZ, Diarra A, Gansane A, Soulama I et al. Intermittent preventive treatment of malaria provides substantial protection against malaria in children already protected by an insecticide-treated bednet in Burkina Faso: a randomised, double-blind, placebo-controlled trial. PLoS Med. 2011;8(2):e1000408.
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8. Guidelines for the treatment of malaria - 3rd edition. Geneva: World Health Organization; 2015. Available from http://apps.who.int/iris/bitstream/10665/162441/1/9789241549127_eng.pdf, accessed 29 September 2019.
9. Bojang KA, Akor F, Conteh L, Webb E, Bittaye O, Conway DJ et al. Two strategies for the delivery of IPTc in an area of seasonal malaria transmission in the Gambia: a randomised controlled trial. PLoS Med. 2011;8(2):e1000409.
10. Pitt C, Ndiaye M, Conteh L, Sy O, Hadj Ba E, Cisse B et al. Large-scale delivery of seasonal malaria chemoprevention to children under 10 in Senegal: an economic analysis. Health Policy Plan. 2017;32(9):1256–66.
11. Seasonal malaria chemoprevention with sulfadoxine-pyrimethamine plus amodiaquine in children: a field guide. Geneva: World Health Organization; 2013. Available from https://apps.who.int/iris/bitstream/handle/10665/85726/9789241504737_eng.pdf, accessed 29 September 2019.