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: P01BD51

Indication	Malaria Code ICD11: 1F4Z
INN	Sulfadoxine + pyrimethamine
Type de médicament	Chemical agent
Type de liste	Liste de base (EML) (EMLc)
Additional notes	For intermittent preventive treatment of malaria in infants
Formulations	Oral > Solid: 250 mg + 12.5 mg tablet (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	Sulfadoxine + pyrimethamine
DrugBank	Sulfadoxine, Pyrimethamine

Recommandation du comité d'experts

The Expert Committee recommended listing of sulfadoxine + pyrimethamine 250 mg + 12.5 mg fixed-dose combination tablet on the core list of the EMLc for the new indication of intermittent preventive treatment (of malaria) in infancy (IPTi) on the basis of demonstrated efficacy and acceptable safety, and in alignment with WHO malaria guideline recommendations. The Expert Committee noted the lack of evidence of the impact of the use of SP-IPTi on antimicrobial resistance, and encouraged further assessment and monitoring in this regard within programme delivery.

Contexte

The application requested listing of sulfadoxine + pyrimethamine fixed-dose combination tablet on the core list of the EMLc for the new indication of intermittent preventive treatment (of malaria) in infancy (IPTi). Sulfadoxine + pyrimethamine 500 mg + 25 mg tablets are currently included on the EML and EMLc for use in combination with artesunate 50 mg for the curative treatment of malaria.

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.

Bénéfices

The application presented the findings of a pooled analysis of six randomized, placebo-controlled trials in 7930 infants that investigated the efficacy and safety of IPTi with sulfadoxine + pyrimethamine (IPTi-SP) in four African countries with moderate to high transmission of malaria, when administered to infants at the time of routine vaccination according to the WHO Expanded Programme on Immunization (EPI) (2). From the pooled analysis, the combined estimate of protective efficacy of IPTi-SP against clinical malaria in infants aged up to 1 year of age was 30.3% (95%CI 19.8% to 39.4%, p<0.0001). IPTi-SP was also associated with protective efficacy in infants up to 1 year of age for anaemia (21.3% (95%CI 8.3% to 32.5%, p=0.002)), all-cause hospital admissions (22.9% (95%CI 10.0% to 34.0%, p=0.001)), and hospital admissions associated with malaria parasitaemia (38.1% (95%CI 12.5% to 56.2%, p=0.007)).

Torts

SP for intermittent preventive treatment in infancy is generally well tolerated. Studies showed no evidence of any adverse effects of SP-IPTi on infants' serological responses to vaccines (e.g. DTP, polio, hepatitis B, Haemophilus influenzae B, yellow fever or measles). A rebound effect in terms of greater susceptibility to malaria after termination of SP-IPTi, although reported in some studies, was not found in the pooled analysis, where the pooled estimate of protective efficacy of IPTi-SP against clinical malaria for the potential rebound period was 9.5% (95%CI 0.3% to 17.8%, p=0.044) (2). Surveillance of molecular markers of SP resistance should accompany SP-IPTi, in particular the distribution and prevalence of Pfdhps 540 mutations, which is a surrogate measure of SP efficacy. Use pf IPTi-SP is contraindicated in individuals with known hypersensitivity to pyrimethamine, sulfonamides and related compounds and infants receiving a sulfa-based medication for treatment or prophylaxis, including co-trimoxazole (trimethoprim–sulfamethoxazole), which is widely used as prophylaxis against opportunistic infections in HIV-infected infants.

Preuves supplémentaires

A 2011 systematic review of the cost and the cost-effectiveness of malaria interventions found that the median financial cost of IPTi-SP for protecting one person for one year was US$ 0.60 (range US$ 0.48 to US$ 1.08) (3). A study by Conteh et al of the cost-effectiveness of IPTi in sub-Saharan Africa found the cost per malaria episode averted for IPTi-SP was very low, US$ 1.36 to US$ 4.03 based on trial specific data (US$ 0.68 to US$ 2.27 on pooled analysis). The authors concluded that IPTi delivered with the EPI was a highly cost-effective intervention against clinical malaria (4).

Rapport coût/efficacité

No information was provided in the application.

Directives de l'OMS

A 2010 WHO policy recommendation on IPTi-SP recommends the coadministration of SP-IPTi with DTP2, DTP3 and measles immunization to infants, through routine EPI in countries in sub-Saharan Africa, in areas with moderate-to-high malaria transmission (i.e. annual entomological inoculation rates ≥10), and where parasite resistance to SP is not high – defined as a prevalence of the pfdhps 540 mutation of ≤50% (5). This recommendation was not re-evaluated during the guideline development process for the 2015 WHO Guidelines for the treatment of malaria (3rd edition). The same recommendation is included in the 2015 Guidelines, however the quality of evidence was not formally assessed (6).

Disponibilité

A paediatric formulation of sulfadoxine + pyrimethamine 250 mg + 12.5 mg is currently under assessment by the WHO Prequalification Programme. The administered dose of IPTi-SP depends on the weight of the child: ■ Children weighing less than 5 kg should be given 125 mg sulfadoxine and 6.25 mg pyrimethamine. ■ Children weighing 5 kg or more should be given 250 mg sulfadoxine and 12.5 mg pyrimethamine.

Autres considérations

The successful implementation of SP-IPTi requires that national malaria control and EPI programmes work together. WHO, working with UNICEF developed an implementation guide which provides the necessary technical and operational information and

tools for country-level policy-makers and programme managers to decide on how to include SP-IPTi with immunization services (7). In areas where SP-IPTi is implemented each child will be given SP three times in their first year of life when they receive routine vaccinations as follows: ■■ First SP-IPTi dose (SP-IPTi1) when DTP2/Penta2 (or combo) vaccination is given (i.e. 8-10 weeks of age) ■ Second SP-IPTi dose (SP-IPTi2) when DTP3/Penta3 (or combo) vaccination is given (12-14 weeks of age) ■ Third SP-IPTi dose (SP-IPTi3) at the time of measles vaccination (nine months) The exact timing of the doses may vary according to the national immunization schedule for DTP and measles vaccination.

1. World Malaria Report 2018. Geneva: World Health Organization; 2018. Available from https://apps.who.int/iris/bitstream/handle/10665/275867/9789241565653-eng.pdf?ua=1, accessed 29 September 2019.
2. Aponte JJ, Schellenberg D, Egan A, Breckenridge A, Carneiro I, Critchley J et al. Efficacy and safety of intermittent preventive treatment with sulfadoxine-pyrimethamine for malaria in African infants: a pooled analysis of six randomised, placebo-controlled trials. Lancet. 2009;374(9700):1533–42.
3. White MT, Conteh L, Cibulskis R, Ghani AC. Costs and cost-effectiveness of malaria control interventions--a systematic review. Malar J. 2011;10:337.
4. Conteh L, Sicuri E, Manzi F, Hutton G, Obonyo B, Tediosi F et al. The cost-effectiveness of intermittent preventive treatment for malaria in infants in Sub-Saharan Africa. PLoS One. 2010; 5(6):e10313.
5. WHO Policy recommendation on Intermittent Preventive Treatment during infancy with sulphadoxine-pyrimethamine (SP-IPTi) for Plasmodium falciparum malaria control in Africa. Geneva: World Health Organization; 2010. Available from https://www.who.int/malaria/news/WHO_policy_recommendation_IPTi_032010.pdf, accessed 29 September 2019.
6. 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?ua=1&ua=1, accessed 29 September 2019.
7. Intermittent preventive treatment for infants using sulfadoxine-pyrimethamine (SP-IPTi) for malaria control in Africa: Implementation Field Guide. Geneva: World Health Organization; 2011. Available from https://apps.who.int/iris/bitstream/handle/10665/70736/WHO_IVB_11.07_eng.pdf, accessed 29 September 2019.