Ivermectin

Essential medicine status ✓

Section: 6. Anti-infective medicines > 6.6. Medicines for ectoparasitic infections

EMLc | ATC codes: P02CF01

Indication	Scabies ICD11 code: 1G74
INN	Ivermectin
Medicine type	Chemical agent
List type	Core
Formulations	Oral > Solid: 3 mg tablet (scored)
EML status history	First added in 2019 (TRS 1021)
Sex	All
Age	Also recommended for children
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Ivermectin
DrugBank	Ivermectin

Expert Committee recommendation

The Expert Committee recommended listing of ivermectin on the core list of the EML and EMLc for the new indication of treatment of scabies. The Committee noted that oral ivermectin treatment is associated with comparable effectiveness to topical therapies and has acceptable safety. The Committee also noted the effectiveness of ivermectin as a public health intervention when delivered via mass drug administration programmes. The Committee considered that the ease of oral administration compared to topical administration may also represent an advantage for patients in terms of compliance.

Background

The application requested listing of ivermectin on the core list of the EML and EMLc for the new indication of treatment of scabies. Ivermectin is currently included on the EML and EMLc as an intestinal anthelminthic and antifilarial treatment. Only topical therapies for scabies (benzyl benzoate and permethrin) are currently included on the Model Lists.

Public health relevance

Scabies is seen in all countries. In many resource-poor settings, prevalence rates of infestation can exceed 20% of the population and the most vulnerable members of society, children (1) and the elderly, are at highest risk. In 2015, the global prevalence of scabies was over 200 million (2). Globally, scabies was responsible for 0.21% of disability-adjusted life-years (DALYs) from all conditions studied by the Global Burden of Disease Study 2015 (2). A major complication of scabies with lasting consequences for health, seen most in resource-poor settings, is symptomatic acute glomerulonephritis (AGN), which was reported in 10% of children in a survey in northern Australia, while 24% had microscopic haematuria (3). AGN was closely linked to skin sores due to streptococcal infection, and scabies was identified as the principal cause. Scabies infestation is also an epidemiological risk factor for rheumatic fever and there is a strong association with scabies-associated streptococcal infections (4). One study has identified a possible link between scabies and bacterial sepsis caused by Staphylococcus aureus in infants in the Gambia (5). Household

economic loss due to scabies is also a major problem in resource-poor communities. A study in rural Mexico indicated that families were spending a significant part of their household income on ineffective topical treatment of scabies (US$ 24) over each 3-month period, impacting the ability to purchase other commodities, including food (6). Scabies in resource-poor environments is therefore both a potential cause of serious morbidity and a source of financial burden. Its high prevalence places a huge burden on stretched health care resources.

Benefits

The application presented the results of a 2018 Cochrane systematic review of 15 studies (1896 participants) comparing topical permethrin, systemic ivermectin or topical ivermectin for treatment of scabies (7). The response to oral ivermectin was found to be equivalent to the response to topical permethrin, two and four weeks after treatment. 200 µg/kg oral ivermectin (was associated with slightly lower rates of complete clearance after one week compared to permethrin 5% cream. Using the average clearance rate of 65% in the trials with permethrin, the illustrative clearance with ivermectin was 43% (RR 0.65, 95%CI 0.54 to 0.78; 613 participants, six studies; low certainty evidence). After two weeks, there was no significant difference (illustrative clearance of permethrin 74% compared to ivermectin 68%; RR 0.91, 95%CI 0.76 to 1.08; 459 participants, five studies; low certainty evidence). In this review, there did not appear to be any advantage in repeated treatments in conventional cases of scabies. Hence treatment with one to three doses of ivermectin or one to three applications of permethrin led to little or no difference in rates of complete clearance after four weeks follow-up (illustrative cures with one to three applications of permethrin 93% and with one to three doses of ivermectin 86%; RR 0.92, 95%CI 0.82 to 1.03; 581 participants, five studies; low certainty evidence). Seven days after treatment with oral ivermectin 200 µg/kg or one application of permethrin 5% lotion, there was little or no difference in complete clearance rates (illustrative cure rates: permethrin 73%, ivermectin 68%; RR 0.93, 95%CI 0.74 to 1.17; 120 participants, one study; moderate certainty evidence). After two weeks, one initial dose of systemic ivermectin compared to one application of permethrin lotion produced similar complete clearance rates (extrapolated cure rates: 67% in both groups; RR 1.00, 95%CI 0.78 to 1.29; 120 participants, one study; low certainty evidence). The application also presented the findings of numerous individual studies of ivermectin versus various topical agents for scabies that supported the comparative effectiveness of oral ivermectin (8–18). The application presented evidence of the effectiveness of ivermectin for treating scabies when delivered through mass drug administration programmes. Studies in Solomon Islands (19, 20), Australia (21), Brazil (22) and Fiji (23) all showed mass drug administration of ivermectin to be an effective public health intervention. There is some evidence from case reports and case series that oral ivermectin (with or without topical scabicides) is effective in the treatment of crusted scabies (24–28). Crusted scabies is a hyper-transmissible form of scabies where patients are infected with very large populations of scabies mites. It is mainly seen in those who are immunocompromised including HIV-infected individuals, transplant recipients and those on high doses immuno-modulating drugs or biologic agents; it may also occur in endemic settings in apparently healthy individuals. It is rare but can cause a major problem with transmission to susceptible populations.

Harms

Evidence for the safety of ivermectin has been evaluated when it was considered for listing on the EML for other indications. In terms of safety of oral ivermectin for treatment of scabies, the Cochrane systematic review reported moderate certainty evidence of no withdrawals due to adverse events in either the oral ivermectin or topical permethrin treatment groups. There was moderate certainty evidence of little or no difference between treatment groups for the proportion of participants who experienced at least one adverse event two weeks after initiation of treatment. After four weeks, ivermectin was associated with a larger proportion of participants with at least one adverse event (RR 1.30, 95%CI 0.35 to 4.83; 502 participants, four studies; low certainty evidence). Most side-effects reported in other studies were transient and mild. Loose stool, fatigue and headache were most frequently reported, and the incidence among the randomized control trials of all side-effects was highest in the studies involving children. When ivermectin is administered to subjects with high Loa loa microfilariaemia, severe adverse reactions such as neurological signs, encephalopathy and coma have been reported (29). In Loa loa endemic countries, potential coinfection with this parasite has to be considered prior to using ivermectin. There were a total of 1656 reports for ivermectin in VigiBase (out of a total of over 14 million reports in the database). Reports in males and females were of similar proportions. The majority of reports were in adults aged 18 years and older. The most commonly reported adverse drug reactions (ADRs) for ivermectin alone and ivermectin co-administered with albendazole included pruritus, headache, dizziness, vomiting, rash, urticarial and diarrhoea. Most reported ADRs were considered to be minor and transient. Safety of ivermectin in pregnant women or children under 15 kg body weight has not been established.

Cost / cost effectiveness

The application stated that no cost-benefit analyses on the use of ivermectin in scabies have been undertaken, but proposes that effective interventions with ivermectin may reduce personal, institutional and governmental expenditure.

WHO guidelines

WHO guidelines on the treatment of skin and oral HIV-associated conditions in children and adults (30) recommend treatment with oral ivermectin (200 µg/ kg) for mild/moderate scabies in HIV-infected children and adults if topical permethrin treatment is not feasible or there is a poor response (Strong recommendation, low quality evidence). The guidelines also recommend two doses of oral ivermectin for treatment of HIV-infected children ≥ 15 kg and adults with severe or crusted scabies.

Availability

Ivermectin has wide market availability. Generic brands are available.

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