MSF International
Route de Ferney 140
1202 Genève
Tel: +41 22 849 84 00
www.msf.org

A.3 Arpraziquantel

MSF strongly supports the proposal from Merck Healthcare KGaA for the inclusion of arpraziquantel 150 mg dispersible tablet to the Core list in both the WHO Model List of Essential Medicines (EML) and the WHO Model List of Essential Medicines for Children (EMLc), for treatment of schistosomiasis in children.
Currently, the EML and EMLc include three dosages form of praziquantel: 150 mg tablet, 500 mg tablet and 600 mg scored tablet.

Schistosomiasis, also known as bilharzia, is a parasitic disease caused by parasitic flatworms (blood flukes) of the genus *Schistosoma*. The disease primarily affects people in poor communities in tropical and subtropical areas, particularly in rural agricultural, peri-urban regions, regions where people are infected through their skin in lakes and rivers used for daily activities. The parasite infects either the liver and intestines, or the uro-genital systems. After a few years, the infection results in liver fibrosis, severe digestive hemorrhages, or painful urogenital lesions, and possibly bladder cancer. Schistosomiasis in children is associated with significant morbidity, including impaired growth and development, cognitive impairment, reduced physical fitness, malabsorption, anemia, urogenital and liver disease, hepatosplenic dysfunction and hemorrhages, and increased severity of other infections.

According to WHO, of the 78 countries considered endemic for schistosomiasis, only 50 countries have populations requiring preventive chemotherapy. The total number of people in need of preventive chemotherapy globally in 2023 was 253.8 million, of which 135 million were school-aged children and 50 million preschool-aged children. Data reported in 2023 from 33 countries for treatment of school-aged children and from 20 countries for the treatment of adults show that about 90 million people received preventive chemotherapy for schistosomiasis globally, which is equivalent to 56% global coverage for school-aged children and 12% for adults at risk.

The implementation of large-scale preventive chemotherapy using praziquantel has led to a significant decrease in schistosomiasis-related deaths, with annual fatalities dropping from 200,000 to approximately 20,000. This represents a 90% reduction in mortality over the years, highlighting the substantial impact of preventive treatment on public health. According to 2022 “WHO Guideline on control and elimination of human schistosomiasis”, praziquantel is recommended for preventive chemotherapy of schistosomiasis in adults and school-aged children at a single dose of 40 mg/kg. However, delivering this treatment to preschool-aged children poses significant challenges due to the size of the tablets currently available on the market in addition to their bitter taste, necessitating alternative solutions.

Arpraziquantel has been developed specifically for preschool-aged children (3 months to 6 years) and represents an option for addressing the mentioned gap for approximately 50 million preschool-aged children in schistosomiasis-endemic regions.

Arpraziquantel is the biologically active enantiomer R-(-)-praziquantel of praziquantel and shares the same mechanism of action as praziquantel. It is indicated for the treatment of schistosomiasis caused

by *Schistosoma mansoni (S. mansoni)* or *Schistosoma haematobium (S. haematobium)* in children aged 3 months to 6 years. The recommended target doses are 50 mg/kg body weight as a single dose for *S. mansoni* infection and 60 mg/kg body weight as a single dose for *S. haematobium* infection. Arpraziquantel's efficacy and safety were assessed through phase II and III clinical trials involving 442 children aged 3 months to 6 years. The trials demonstrated exceptional cure rates, with no parasite eggs detected in stool or urine samples several weeks post-treatment. Specifically, cure rates were close to or above 90% for both *S. mansoni* (at a 50 mg/kg dose) and *S. haematobium* (at a 60 mg/kg dose).

In December 2022, the European Medicines Agency (EMA) validated the regulatory application for arpraziquantel under the EU-M4all framework, a mechanism for high-priority medicines destined for non-EU markets. This validation confirmed the completeness of the submission, triggering a scientific review focused on safety, efficacy, and manufacturing quality. The Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion on the 15th of December 2023, concluding that the benefits of arpraziquantel outweigh its risks for preschool-aged, marking a critical step forward in making this life-saving treatment accessible to children under 6 years.

MSF would like to draw the attention of the Expert Committee to the following points:

- Access to praziquantel, the only available drug for preventive chemotherapy for schistosomiasis continues to be inadequate to cover the 253.8 million individuals across 50 countries in the Africa region that require preventive chemotherapy. While medicine donation is available for school-age children, a significant gap for the treatment of adults, women of childbearing age, and preschool children remains. The inclusion of a 150 mg dispersible tablet, a child-friendly formulation of arpraziquantel will allow the delivery of treatment to children aged 3 months to 6 years old and will serve as a basis for National Essential Medicines Lists and increase interest in paediatric formulations. The inclusion may therefore attract sufficient manufacturing capacity, encourage local registrations, and ultimately improve accessibility.

- Arpraziquantel will not be provided through donation programs. Therefore, ensuring access to this medicine requires collaboration with potential donors and health ministries in endemic countries to make it freely available for treating affected children. WHO has set ambitious targets to eliminate schistosomiasis as a public health concern by 2030. Achieving this goal necessitates treating all at-risk communities, including young children aged 3 months and older. MSF advocates for the inclusion of arpraziquantel in the current praziquantel donation program.

- In October 2024, to support national and global efforts to increase access to and the affordability of care and treatment of neglected tropical diseases, WHO invited manufacturers of medicinal products for treatment of neglected tropical diseases to submit an Expression of Interest for product evaluation to the WHO Prequalification Unit including arpraziquantel 150 mg and 300 mg scored dispersible tablet, preferably orodispersible tablet.

Considering all these elements, MSF encourages the 25th Expert Committee on the Selection and Use of Essential Medicines to include arpraziquantel 150 mg dispersible tablet in the Core List of both WHO Model List of Essential Medicines and the WHO Model List of Essential Medicines for Children, for treatment of schistosomiasis in children aged 3 months to 6 years.

Daniela Garone, ID specialist and DTM&H
International Medical Coordinator
Médecins Sans Frontières | International Office
Rue de l'Arbre Bénit 46 | 1050 Brussels | Belgium
+32 2 474 75 06
Skype danielagarone
Mobile: +32 47872385
http://www.msf.org/

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