

ADVANTAGES OF INJECTABLE ARTESUNATE FOR SEVERE MALARIA

WHO RECOMMENDED TREATMENT



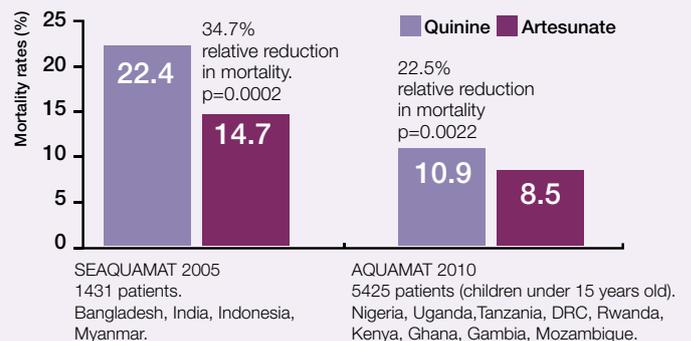
Severe malaria is a medical emergency and is fatal if untreated. Every year an estimated 655,000 people die of malaria, 86% of whom are children under the age of 5. As death from severe malaria often occurs within hours of admission to a hospital or clinic, it is essential that patients receive effective treatment as soon as possible. The WHO strongly recommends injectable artesunate over quinine for the treatment of severe *P. falciparum* malaria in both children and adults¹.

Injectable artesunate can save more lives than quinine

Clinical evidence from two large-scale, multi-centre trials in South East Asia (SEAQUAMAT)² and Africa (AQUAMAT)³ showed a reduction in the risk of death using injectable artesunate compared to quinine. If used throughout Africa, injectable artesunate could save up to an additional 195,000 lives each year⁴.

This equates to saving one extra life for every 41 children treated. This life-saving benefit of artesunate for severe malaria derives from its rapid ability to kill the parasite across all its life stages unlike quinine which is slower and stage-specific, mainly affecting the mature blood stage⁵.

Artesunate substantially reduces mortality from severe malaria compared to quinine



Treatment with artesunate is cost-effective

Although the average cost of injectable artesunate is currently higher than quinine (\$3.3 vs. \$1.3), overall costs are found to be equivalent. Cost analysis from the trials in Asia and Africa show that if total costs are considered (in particular the cost of administering the drugs and management of side-effects) artesunate is found to be cost-effective.⁶

“ For over a century, quinine administered by injection has been the best treatment available for treating severe malaria, but thanks to the development of the artemisinin compounds, we now have a safer and much more effective treatment. ”

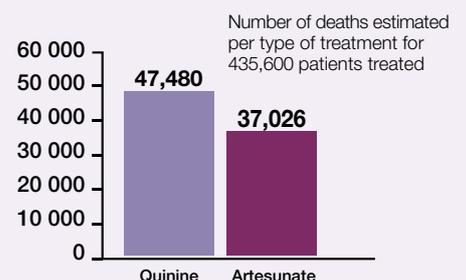
Prof Nick White

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Case study

The comparative benefits of injectable artesunate relative to quinine in the treatment of severe malaria are significant. A case study was prepared based on a hypothetical country with an average of 435,600 cases of severe malaria treated each year in health facilities, among which half are children

under 5 years of age. The anticipated total cost of treatment would be \$2,909,460.⁶ The clinical studies showed that the expected mortality rate would be 28,2% higher with quinine compared to artesunate.³ Therefore artesunate can save 10,454 additional lives (5,05% of the treated population).



➤ Artesunate is better tolerated than quinine and has fewer severe side effects

Clinical trials show that artesunate produces fewer life-threatening side-effects than quinine, with fewer recorded incidences of low blood sugar (hypoglycaemia), and anaemia. Furthermore, quinine can induce potentially serious hyperinsulinaemic hypoglycaemia, especially during pregnancy and cardiotoxicity. Quinine IM is also painful and locally toxic.⁸

➤ Injectable artesunate is easier to administer than quinine

Injectable artesunate is simpler to administer, with the treatment delivered in five minutes. Due to risk of cardiotoxicity, intravenous quinine administration needs rate-controlled infusion⁹ over four hours, three times a day, accompanied by cardiac monitoring if possible. A study examining malaria deaths showed that one in four patients had received incorrect dosing.¹⁰

➤ Current production levels of injectable artesunate ensure continuity of supply

There is currently more than sufficient supply of injectable artesunate to meet demand. The present WHO pre-qualified supplier has reported excess capacity.

The many advantages of injectable artesunate justify its adoption in line with WHO recommendations. This will need sustained support from national health ministries, WHO, malaria partnerships, manufacturers and donors.

- 1 World Health Organization. Guidelines for the treatment of malaria, Second edition(2010): www.who.int/malaria/publications/atoz/mal_treatchild_revised.pdf
- 2 Dondorp A *et al.* South East Asian Quinine Artesunate Malaria Trial (SEAQUAMAT) group: Artesunate versus quinine for treatment of severe falciparum malaria: a randomised trial. *The Lancet*. 366(9487): 715-725 (2005).
- 3 Dondorp A *et al.* Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial. *The Lancet*. 376(9753):1647-57 (2010).
- 4 Médecins Sans Frontières. Malaria: Making the Switch (2011):www.msf.org/shadomx/apps/fms/fms-download.cfm?file_uid=27E406A3-2B31-4C64-8D47-6EB733128EDF&siteName=msf
- 5 White NJ., The parasite clearance curve, *Malaria Journal* 10:278 (2011).
- 6 Lubell *et al.* Cost-effectiveness of parenteral artesunate for treating children with severe malaria in sub-Saharan Africa. *Bulletin, World Health Organization* (2011).
- 7 «Major clinical trial prompts call for change to treatment guidelines for severe malaria worldwide», Media release from Wellcome Trust, 6 Nov. 2010.
- 8 White NJ *et al.* Severe hypoglycemia and hyperinsulinemia in falciparum malaria. *N Engl J Med* 309:61–66 (1983).
- 9 World Health Organization. Severe and complicated malaria. *Trans R Soc Trop Med Hyg* 84 (suppl 2): 1–65 (1990).
- 10 Mehta Z *et al.* Malaria deaths as sentinel events to monitor healthcare delivery and antimalarial drug safety. *Trop Med Int Health* 12:617–28 (2007).

Supporting governments in the use of injectable artesunate

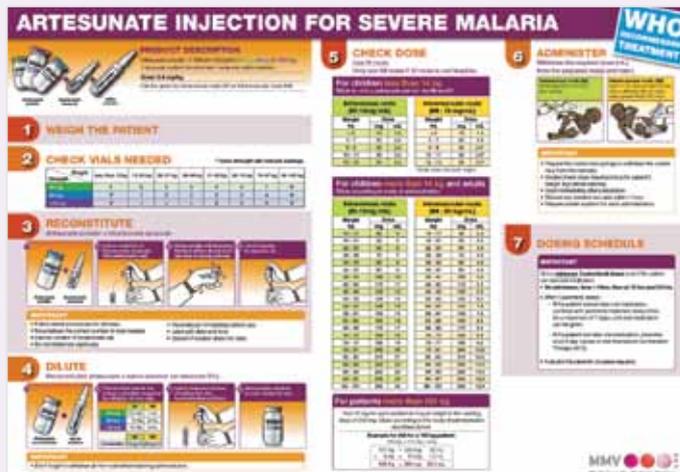
User-friendly pack

At present, only injectable artesunate 60mg has been prequalified by the WHO. To simplify its use, a new combi-pack including a saline vial should be soon on the shelves.



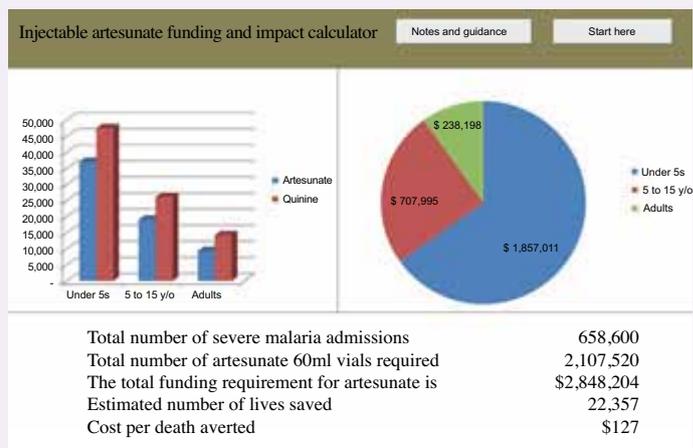
Job-Aid

MMV, with key partners, has developed a poster for health workers to facilitate the preparation and administration of the treatment. This material is available at www.mmv.org/access-delivery.



Funding calculator

MMV and MORU (Mahidol-Oxford Tropical Medicine Research Unit) have developed a calculator to estimate funding requirements and health impact in terms of estimated number of lives saved from injectable artesunate. This Excel-based calculator is available at www.mmv.org/access-delivery. The calculator is easy to use and allows country stakeholders to update the model with individual country data.



Injectable artesunate saves more lives