Overview

The World Health Organization (WHO) recommends the programmatic use of two vaccines for the prevention of Plasmodium falciparum malaria in children living in malaria-endemic areas, prioritizing areas of moderate and high transmission. The WHO recommendation, first made for RTS,S/AS01 in October 2021, was updated in October 2023 to include a second malaria vaccine, R21/Matrix-M. Both vaccines are WHO prequalified and eligible for procurement by UNICEF, with financial support for eligible countries from Gavi, the Vaccine Alliance.

More than 28 countries have expressed interest in introducing a malaria vaccine and most are actively moving toward introduction. The rapid pace of adoption of malaria vaccines illustrates the strong demand—projected to be 40 to 60 million doses annually by 2026 and 80 to 100 million doses annually by 2030.

Similarities between the two vaccines point to anticipated similar impact

The similarities between RTS,S and R21—construct, mechanism of action, target population, and delivery strategy—enabled WHO recommendation and prequalification of R21 less than two years after RTS,S. WHO’s review of clinical and other data on R21 also benefited from the evidence on and lessons learned with RTS,S, including during the pilot implementation in Ghana, Kenya, and Malawi.

WHO states that there is no evidence one vaccine performs better than the other; decisions regarding product choice should be based on program characteristics, vaccine supply, and affordability. According to WHO, the two malaria vaccines have been shown to reduce clinical malaria cases by more than half during the 12 months following the initial three doses. They have also been shown to prevent three-quarters of malaria cases when given seasonally (prior to onset of the rainy season in areas of high seasonal transmission).

RTS,S and R21 have both been evaluated within the context of other malaria interventions, including long-lasting insecticide-treated bednets (ITNs), indoor residual spraying, seasonal malaria chemoprevention (SMC), and effective case management. The figure below illustrates the reduction in malaria burden that can be achieved when preventive tools are used together, as seen in a study of RTS,S and SMC conducted in Burkina Faso and Mali (2017–2022). For this reason, WHO recommends that vaccine introduction take place within the context of comprehensive national malaria control plans.

Figure. Reduction of malaria burden using preventive tools.

Source: Paul Milligan, London School of Hygiene and Tropical Medicine; 2023.

WHO considers both malaria vaccines to be safe. Similar to some other childhood vaccines, febrile convulsions within several days of vaccination were observed at a higher rate among children who received RTS,S or R21 than those given control vaccines. The convulsions resolved within several days with no long-term effects.

Looking ahead

As with all new vaccines with limited experience, WHO recommends post-introduction safety monitoring of R21. The Phase 3 trial has been extended by two years to enable collection of additional safety and efficacy data.
Table. Product information for the RTS,S/AS01 (Mosquirix) and R21/Matrix-M (R21 malaria) malaria vaccines (as of December 2023).

<table>
<thead>
<tr>
<th>RTS,S/AS01</th>
<th>Information category</th>
<th>R21/Matrix-M</th>
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<tbody>
<tr>
<td>• Recommended in October 2021. Prequalified in July 2022. Reduction of <em>P. falciparum</em> malaria in young children living in areas where malaria is endemic, prioritizing areas of moderate to high transmission.</td>
<td>Who recommendation, Who prequalification. Indication (per WHO recommendation).</td>
<td>• Recommended in October 2023. Prequalified in December 2023. Reduction of <em>P. falciparum</em> malaria in young children living in areas where malaria is endemic, prioritizing areas of moderate to high transmission.</td>
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<td>Four doses: three doses at least four weeks apart from around 5 months of age and a fourth dose to prolong protection. A fifth dose may be considered where a significant malaria risk remains in children a year after receiving dose 4. Two vials clipped together, reconstituted for two doses. Store at 2–8°C; 24 months shelf life. 9.92 cm³ per dose (in secondary packaging). Good safety profile. Robust safety database (approximately 6 million doses provided in pilot introduction). Associated febrile seizures. Pilot implementation (2019–2023): 2 million children vaccinated. Phase 3 trial (2009–2014) in 11 sites in Africa with low, moderate, high, or seasonal transmission; four years follow-up in 11 sites, seven years in 3 sites. Phase 3 trial (2017–2022) of seasonal malaria vaccination with/without SMC in two sites in Africa, five years follow-up. Approximately US$10 per dose (EUR 9.30), subject to Gavi co-financing policy for malaria vaccines.</td>
<td>Recommended schedule (per WHO; flexibility allowed). Presentation. Cold chain requirements. Safety. Experience (Phase 3 and post licensure). Market pricing (2024) (prices may change, depending on volume, etc.).</td>
<td>• Four doses: three doses at least four weeks apart from around 5 months of age and a fourth dose to prolong protection. A fifth dose may be considered where a significant malaria risk remains in children a year after receiving dose 4. Expected: Single vial (liquid), one or two doses per vial (no reconstitution). Store at 2–8°C; 24 months shelf life. Expected: 7.03 cm³ per dose and 14.06 cm³ per dose (in secondary packaging, depending on presentation). Good safety profile. Tested in a Phase 3 trial (approximately 4,000 children). Associated febrile seizures. Phase 3 trial (ongoing since 2021) in five sites in Africa; data available on 12 and 18 months follow-up in low or low/moderate perennial settings or highly seasonal settings.</td>
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References


