GUIDELINES FOR THE TREATMENT OF MALARIA IN MALAWI 6th Edition, January 2025

Main editor

National Malaria Control Programme

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Sections

1. Foreword

GUIDELINES FOR THE TREATMENT OF MALARIA IN MALAWI

6th Edition, January 2025

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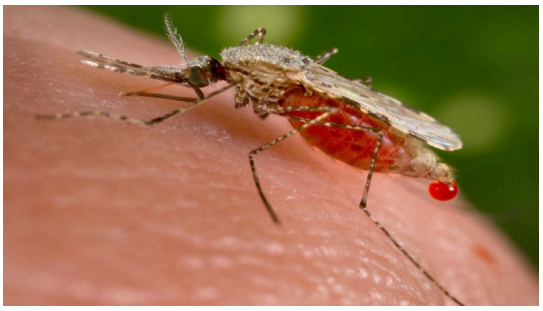


Malaria continues to be the leading cause of morbidity and mortality in Africa, particularly in children under five years of age. In Malawi, it is the commonest cause of outpatient visits, hospitalization, and death. Malaria is also a development problem as it has a serious socioeconomic impact on families and the nation, through loss of work, school absenteeism and high levels of expenditure on malaria treatment, especially those with low socio-economic status.

Organized malaria control efforts started in 1984 with the establishment of the National Malaria Control Programme (NMCP) to spearhead and coordinate responses to malaria by both Malawi Government and the development partners.

In 2007, the Ministry of Health (MoH) through the NMCP changed its national malaria treatment policy from Sulfadoxine-Pyrimethamine (SP) to Artemether-Lumefantrine- (LA), an artemisinin-based combination therapy (ACT), following significant scientific evidence of malaria parasite resistance to SP.

Malawi has been monitoring the effectiveness of ACTs through routine therapeutic efficacy studies (TES) conducted at sentinel sites. In 2016, the efficacy of LA remained high at 98.9% and ASAQ 99.1%, however in 2020, the efficacy rate for LA dropped to 91.2% and that of Dihydroartemisininpiperaquine (DP) was 99.7%. Based on these results, MoH adopted Dihydroartemisininpiperaquine (DP) as an additional first line treatment for malaria while maintaining ASAQ as a second line.

Partial resistance to artemisinin has emerged in several African Countries, although not yet documented in Malawi. To mitigate ACT resistance in countries with a high burden of malaria, WHO recommends introduction of multiple first line therapies (MFT). The MoH has adopted use of MFT for malaria and currently recommends use of DP and LA as part of MFT for uncomplicated malaria.

There is substantial evidence globally showing significant malaria mortality reduction if parenteral artesunate is used in the management of severe malaria compared to quinine. Artesunate has also been shown to significantly reduce the incidences of convulsions, coma and hypoglycaemia developing in hospitalized severe malaria patients. In line with the current WHO recommendation, the MoH has adjusted the dose of injectable artesunate in children <20 kgs.

2. About the guidelines

2.1 Scope and purpose of the guidelines

These guidelines provide national recommendations for the diagnosis, management and treatment of malaria in Malawi across all levels of the health system. The document covers uncomplicated malaria, severe malaria, malaria in pregnancy (including intermittent preventive treatment in pregnancy), post-discharge malaria continuum of care, and selective antimalarial chemoprophylaxis for high-risk groups.

The purpose of this guideline is to standardise malaria care, ensure consistent clinical practice, and support healthcare workers in delivering effective, safe and context-appropriate malaria management in line with national policy and international standards.

2.1.1 Overall objectives of the guideline

The objectives of this guideline are to:

- Ensure prompt and accurate diagnosis of malaria at all levels of care.
- Provide clear and standardised treatment protocols for uncomplicated and severe malaria.
- Improve the management of malaria in pregnancy, including preventive strategies.
- Reduce malaria-related morbidity and mortality, particularly among vulnerable populations such as children under five and pregnant women.
- Mitigate the emergence and spread of antimalarial drug resistance through appropriate use of therapies.
- Strengthen continuity of care, including post-discharge preventive strategies.
- Support implementation of national malaria control policies, including multiple first-line therapies.

2.1.2 Expected health benefits

Implementation of this guideline is expected to:

- Reduce deaths due to severe malaria.
- Improve treatment success rates for uncomplicated malaria.
- Decrease complications such as severe anaemia, cerebral malaria and hypoglycaemia.
- Improve maternal and neonatal outcomes related to malaria in pregnancy.
- Reduce recurrent severe malaria through post-discharge preventive strategies.
- Enhance rational use of antimalarial medicines and delay the development of resistance.
- Strengthen equitable access to effective malaria treatment across Malawi.

2.1.3 Health questions covered by the guideline

This guideline addresses the following key health questions:

1. How should suspected and confirmed malaria be diagnosed at different levels of care?
2. What is the recommended management and treatment for uncomplicated malaria?
3. How should treatment failure be managed?
4. What are the recommended treatment for severe malaria?
5. How should malaria be managed in pregnancy, including intermittent preventive treatment?
6. What post-discharge strategies reduce recurrence and mortality following severe malaria?
7. Which high-risk groups should receive antimalarial chemoprophylaxis, and which regimens are recommended?

2.2 Target audience

The recommendations are intended to support both point-of-care clinical decision-making and national-level policy formulation in the context of evolving antimalarial drug resistance patterns.

This guideline is intended for clinicians (including medical officers, clinical officers, medical assistants, and nurses), pharmacy and laboratory personnel, Health Surveillance Assistants, the National Malaria Control Programme, Ministry of Health, district health management teams, procurement and supply chain units, and the Pharmacy and Medicines Regulatory Authority in Malawi, to support evidence-based antimalarial policy and clinical decision-making in the context of emerging drug resistance.

2.3 Stakeholder involvement

2.3.1 Who developed the guideline

This guideline was developed by the Ministry of Health (MoH) of Malawi through the National Malaria Control Programme (NMCP), which leads and coordinates malaria control efforts in collaboration with relevant stakeholders and development partners. The NMCP, established in 1984, has been responsible for guiding national malaria policy, including treatment strategies informed by therapeutic efficacy studies conducted at sentinel sites across the country. The recommendations outlined in this guideline reflect national surveillance data, emerging evidence on antimalarial drug resistance, and alignment with current World Health Organization (WHO) recommendations to ensure effective, context-specific malaria prevention and management in Malawi.

For uncomplicated malaria, the recommendations were developed using rigorous, evidence-based methods aligned with the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach to ensure transparency, consistency, and trustworthiness. This work was undertaken as part of the MARC-SE (Mitigating Antimalarial Resistance in Southeast Africa) consortium, in collaboration with the MAGIC Evidence Ecosystem Foundation. Methodological support was provided by Per Olav Vandvik (Principal Investigator), Prashanti Eachempati (Senior Researcher), and Valerie Rainthaler (Research Assistant).

The underpinning systematic reviews and evidence synthesis were conducted by the team from the University of Cape Town, led by Karen Barnes and colleagues, including Jonathan Gwasupika, Daniel Yilma, and Marilyn Solomons, together with the MAGIC Evidence Ecosystem Foundation team, including Prashanti Eachempati, Per Olav Vandvik, and Gordon Guyatt. These processes ensured that recommendations were informed by the best available evidence and presented in a structured, transparent manner to support decision-making across different levels of care.

2.3.1.1 Composition of the Guideline Development Group

A multidisciplinary guideline development group was convened, bringing together clinicians, paediatricians, public health specialists, malaria programme managers, pharmacists, epidemiologists, and other technical experts. The group reviewed national therapeutic efficacy data, emerging evidence on antimalarial drug resistance, and current World Health Organization (WHO) recommendations to ensure that the guidance reflects both global standards and the local epidemiological context.

Where applicable, recommendations were informed by structured evidence review processes, while other sections were developed through panel discussions and expert consensus.

2.3.1.2 Funding

We acknowledge:

Global Fund – *The Global Fund to Fight AIDS, Tuberculosis and Malaria*

PMI – U.S. President's Malaria Initiative

PATH – Program for Appropriate Technology in Health

WHO – World Health Organization

MLW – Malawi-Liverpool-Wellcome Programme

MARC-SE – Mitigating Antimalarial Resistance Consortium – South East Africa (This project (GA N° 101103076) is supported by the Global Health EDCTP3 Joint Undertaking and its members.)

TWG- All Members of the Technical Working Group

2.3.1.3 Conflict of interest

The authors declare that they have no conflicts of interest.

2.4 Methods and processes

Methods for the development of recommendations for the treatment of uncomplicated malaria

These recommendations were updated February 2026 due to emerging resistance in Malawi. The update was performed in collaboration with the MARC SE-Africa consortiIum https://www.marcse-africa.org/ and MAGIC Evidence Ecosystem Foundation and included updated systematic reviews.(Gwasupika et al. 2026; Yilma et al. 2026)

MARC-SE Africa plays a central role in generating, collating, and translating evidence on antimalarial drug resistance to inform timely policy and practice across countries in Southern and East Africa, providing technical support to national malaria programmes and facilitating evidence-informed responses to emerging resistance threats. Within this framework, MAGIC contributed methodological leadership in evidence synthesis, GRADE assessment, and the translation of evidence into actionable recommendations, including the development of structured evidence summaries and support for implementation into policy and practice. Through its role in linking evidence to decision-making processes, MAGIC ensured that emerging data could be rapidly synthesised, contextualised, and incorporated into guideline recommendations, thereby strengthening the responsiveness and transparency of the guideline development process .

The recommendatiIons were developed using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach. GRADE provides a systematic and transparent framework for developing trustworthy clinical guidelines. The process involved identifying and reviewing the most relevant and up-to-date systematic reviews and evidence syntheses, critically appraising the evidence, and assessing the certainty of the evidence across key domains: risk of bias, inconsistency, indirectness, imprecision and publication bias.

Details of the systematic reviews used to update the guideline:

To inform comparative efficacy, we used an up-to-date systematic review and meta-analysis conducted by Gwasupika et al. (2026). The review included only randomised controlled trials comparing Artemether-Lumefantrine (LA) with alternative artemisinin-based combination therapies for uncomplicated *Plasmodium falciparum* malaria in sub-Saharan Africa. From 2,639 records identified through electronic database searches, 46 studies met the inclusion criteria. The treatment comparisons comprised LA versus dihydroartemisinin–piperaquine (DP) (n=17) and LA versus artesunate–amodiaquine (ASAQ) (n=36). The primary outcomes were PCR-corrected and uncorrected treatment failure. Effect estimates were synthesised and presented in Summary of Findings tables (see Section 5.3.1 and 5.4.1). This evidence was reviewed by the guideline panel and used to inform the certainty of evidence assessments.

To inform safety and tolerability, we used an up-to-date systematic review and meta-analysis conducted by Yilma et al. (2026), which included only randomised controlled trials comparing DP and ASAQ with LA for uncomplicated *Plasmodium falciparum* malaria. The review assessed key safety outcomes, including symptomatic hepatotoxicity (inferred from elevated bilirubin and elevated aspartate aminotransferase [AST]), and symptoms of anaemia inferred from a drop in haemoglobin. For DP versus LA, the evidence included two studies for elevated bilirubin (n=2), one study for elevated AST (n=1), and two studies for haemoglobin drop (n=2). For ASAQ versus LA, the evidence included two studies for elevated bilirubin (n=2), two studies for elevated AST (n=2), and five studies for haemoglobin drop (n=5). Effect estimates were synthesised and presented in the corresponding Summary of Findings tables (Sections 5.3.1, and 5.4.1). This evidence was reviewed by the guideline panel and used to inform the certainty of evidence assessments.

Evidence to Decision factors:

In addition to assessing the certainty of evidence, the Malawi MoH guideline panel explicitly considered the balance of benefits and harms, patient values and preferences, resource use, feasibility, acceptability and equity implications within the Malawian context. Recommendations were formulated following structured deliberations and documented decision-making processes to enhance transparency and reproducibility. This approach aligns with internationally recognised standards for guideline development, including those used by the World Health Organization and other global health agencies.

Methods for the development of recommendations for severe malaria, malaria in pregnancy (including intermittent preventive treatment in pregnancy), post-discharge malaria continuum of care, and selective antimalarial chemoprophylaxis

These recommendations were developed through expert consensus. These sections were informed by available scientific evidence, national therapeutic efficacy data, World Health Organization guidance, and clinical and programmatic experience. However, a formal GRADE evidence-to-decision process was not undertaken for these areas. Recommendations in these sections were formulated through structured discussions within the guideline development group.

The overall process aimed to ensure that the guideline is evidence-informed, contextually appropriate, transparent in its methods, and responsive to national malaria control priorities.

2.5 Reading guide

1. The Recommendations

Recommended (Green)

A strong recommendation is given when there is high-certainty evidence showing that the overall benefits of the intervention are clearly greater than the disadvantages. This means that all, or nearly all patients will want the recommended intervention.

Not recommended (Red)

A strong recommendation against the intervention is given when there is high-certainty evidence showing that the overall disadvantages of the intervention are clearly greater than the benefits. A strong recommendation is also used when the examination of the evidence shows that an intervention is not safe.

Conditional recommendation (Yellow)

A conditional recommendation is given when it is considered that the benefits of the intervention are greater than the disadvantages, or the available evidence cannot rule out a significant benefit of the intervention while assessing that the adverse effects are few or absent. This recommendation is also used when patient's preferences vary.

Conditional recommendation against (Orange)

A conditional recommendation is given against the intervention when it is judged that the disadvantages of the intervention are greater than the benefits, but where this is not substantiated by strong evidence. This recommendation is also used where there is strong evidence of both beneficial and harmful effects, but where the balance between them is difficult to determine. Likewise, it is also used when patient's preferences vary.

Only in research settings (Orange)

An "only in research settings" recommendation is given when there is insufficient evidence to determine if an intervention is either beneficial or harmful. When an "only in research" recommendation is given, the panel recommends that the intervention should only be considered in a randomised trial with appropriate ethical approval. In any other circumstance, intervention is not recommended.

Consensus recommendation (Dark blue)

A consensus recommendation can be given for or against an intervention. This type of recommendation is used when there is not enough evidence to give an evidence-based recommendation but the panel still regards it as important to give a recommendation.

Good practice statement (Pale blue)

Good practice statements are recommendations made by the panel where an evidence review has not been conducted. These recommendations are often about how care is provided, or additional information that may be useful to health professionals, rather than which interventions are the most effective.

Implications for research (Orange)

A recommendation with implications for research identifies opportunities for future research to contribute to an identified gap in the available evidence.

2. Supporting information

Additional information is presented immediately below each recommendation to provide context for the recommendation. In addition, the following sections may appear below each guideline to provide specific types of information:

Research Evidence: A summary of the research evidence found to support the recommendation and an assessment of the certainty of the evidence. Assessment of certainty of the evidence and the evidence-to-decision framework used for these guidelines is based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Evidence to decision: A brief description of additional considerations used to inform the recommendation, including the balance of beneficial and harmful effects, certainty of evidence, patient preferences and values, equity, resources, feasibility and acceptability of the recommendation.

Rationale: Description of how the above elements were weighted in relation to each other and resulted in the current recommendation's direction and strength.

Practical information: Practical information regarding the intervention or recommendation, and information on any specific considerations for different population groups.

References: Reference list for the recommendation.

Feedback: If you are logged in as a user, you can comment here on specific recommendations.

2.6 How to cite

National Malaria Control Programme, Community Health Sciences Unit. *Guidelines for the Treatment of Malaria in Malawi.* 6th ed. Lilongwe, Malawi; 2025.

3. Summary of Recommendations

Recommendations for treating uncomplicated malaria (updated February 2026)

Clinical question: What are the first-line and second-line treatments for uncomplicated Plasmodium falciparum malaria in Malawi?

Key recommendations:

- **Lumefantrine-Artemether–(LA) or Dihydroartemisinin–Piperaquine (DP)** are both recommended as first-line treatments for uncomplicated malaria, implemented through a multiple first-line therapy (MFT) strategy. Under the MFT approach, DP is introduced in selected geographic areas (including Nkhata Bay, Nkhotakota and Lilongwe), while AL continues to be used elsewhere as it's therapeutic efficacy remains high.(97%)
- **Artesunate–amodiaquine (ASAQ)** is recommended as the second-line treatment for patients with treatment failure following LA or DP.

As detailed in the methods (section 2.4), these updated recommendations are based on the best available evidence and a GRADE assessment of the certainty of evidence, with explicit consideration of benefits and harms, values and preferences, and system-level implementation considerations.

Understanding the recommendation

The strong recommendation to use both LA or DP as first-line treatments reflects the adoption of a multiple first-line therapy (MFT) strategy at the national programme level. By multiple first-line therapies, we refer to the use of alternative first-line treatments, whereby either AL or DP is administered depending on the geographical area or site-specific allocation. This strategy is intended to maximise population-level benefit, delay the emergence and spread of antimalarial drug resistance, and ensure efficient use of limited health-system resources. The recommendation is driven by system-level considerations such as affordability, supply-chain capacity, and feasibility of implementation rather than by uncertainty in the effectiveness of the treatments.

The strong recommendation to use artesunate–amodiaquine (ASAQ) as a treatment option reflects its effectiveness, and long-standing programmatic experience across multiple endemic settings.

Note: Detailed information on dosing, treatment duration, and formulations by age and weight is provided in the relevant sections (5.3.1, 5.4.1) of the guideline and should be consulted when prescribing.

Recommendations for treating severe malaria

Clinical question: What is the recommended treatment for severe malaria in Malawi?

Key recommendations:

- **Parenteral artesunate** is recommended as the first-line treatment for severe malaria in adults and children.
- Once the patient can tolerate oral medication, treatment should be completed with a full course of an effective **oral artemisinin-based combination therapy.**
- **At community level**, when severe malaria is suspected, administer **rectal artesunate immediately** and refer urgently.(For children)
- **At health-centre level**, use **intramuscular artesunate** if IV access is not available.
- If IM artesunate is unavailable or contraindicated, use **intramuscular quinine (in the thigh, not the buttock)**.
- If no IM therapy is available, **rectal artesunate may be used in children under 6 years** as a temporary pre-referral measure.
- **In the In-pateint setting, parenteral artesunate** is recommended. If parenteral artesunate is unavailable or contraindicated, **parenteral quinine** is recommended as an alternative.
- Post-discharge malaria continuum of care (PDMCC) is recommended to be administered for three consecutive months, beginning two weeks after discharge for children initially treated with artemether–lumefantrine (AL) and four weeks after discharge for those treated with dihydroartemisinin–piperaquine (DP), and to be delivered through either health facility or community-based models in accordance with national guidance.

As outlined in the Methods section these recommendations are not informed by a formal evidence synthesis using the GRADE framework or by Summary of Findings tables

Understanding the recommendation:

Severe malaria is a medical emergency requiring prompt initiation of parenteral treatment. These consensus based recommendations align with World Health Organization guidance and are intended to reduce mortality and severe complications across all levels of care.

Note: Detailed information on dosing, treatment duration, and formulations by age and weight is provided in the relevant sections (6.2) of the guideline and should be consulted when prescribing.

Recommendations for malaria in pregnancy

Clinical question
What are the recommended approaches for the management of malaria in pregnancy in Malawi?

Key recommendations
- **Uncomplicated malaria in pregnancy (Prevention)**
  - Sulfadoxine–pyrimethamine (SP) is recommended for intermittent preventive treatment of malaria in pregnancy (IPTp), with pregnant women receiving at least three doses starting after the first trimester, in accordance with national policy.
- **Uncomplicated malaria in pregnancy**
  - Dihydroartemisinin–piperaquine (DP) and lumefantrine–artemether (LA) are safe for use in all trimesters of pregnancy.
  - All pregnant women with uncomplicated malaria should be treated with DP or LA.
- **Severe malaria in pregnancy**
  - Parenteral artesunate is recommended as the first-line treatment for severe malaria in pregnancy.
  - Once the patient is able to tolerate oral medication, treatment should be completed with a full course of an effective oral antimalarial, as specified in the guideline.
- **Prevention in pregnancy**
  - Intermittent preventive treatment in pregnancy (IPTp) with sulfadoxine–pyrimethamine is recommended as part of routine antenatal care.

As outlined in the Methods section these recommendations are not informed by a formal evidence synthesis using the GRADE framework or by Summary of Findings tables

Understanding the recommendation
In the Malawi guideline, the consensus recommendations for malaria in pregnancy align closely with those for the general population. Evidence reviewed by the guideline panel supports the safety and effectiveness of dihydroartemisinin–piperaquine (DP) and lumefantrine–artemether (LA) in all trimesters of pregnancy. As a result, DP and LA are recommended for the treatment of uncomplicated malaria in pregnant women, with an emphasis on early initiation of therapy to reduce maternal and fetal complications.

For severe malaria in pregnancy, prompt treatment with parenteral artesunate is prioritised because of its proven mortality benefit.

Recommendations for selective anti-malarial chemoprophylaxis

Clinical question
Should high-risk individuals receive antimalarial chemoprophylaxis to prevent malaria?

Key recommendations
- We recommend **selective antimalarial chemoprophylaxis for high-risk groups** and non-immune individuals travelling to or residing in malaria-endemic areas, using one of the following regimens as appropriate: **doxycycline, mefloquine, atovaquone–proguanil, chloroquine (where effective) combined with proguanil, or proguanil with weekly chloroquine.**
- Appropriate counselling on adherence, recognition of fever, and **additional preventive measures** such as **insecticide-treated bed nets** should be provided.

As outlined in the Methods section these recommendations are not informed by a formal evidence synthesis using the GRADE framework or by Summary of Findings tables

Understanding the recommendation

High-risk groups have reduced immunity, impaired splenic function, underlying medical conditions, or no prior exposure to malaria, placing them at greater risk of severe disease and complications. Chemoprophylaxis is recommended (consensus based recommendation) to reduce the risk of infection, severe illness, and malaria-related mortality.

4. Introduction

This document has been developed to provide a clear guidance on the management of uncomplicated and severe malaria in Malawi. It also serves as a concise reference for health workers managing malaria in the country.

In 2007, the Ministry of Health introduced Lumefantrine-Artemether (LA) as the first-line treatment and Artesunate-Amodiaquine (ASAQ) as the second-line treatment for uncomplicated malaria. The introduction of these drugs was in line with the WHO recommendation to use artemisinin-based combination therapies (ACT) to improve the malaria treatment outcomes. Since then, Malawi has monitored the effectiveness of ACTs through routine therapeutic efficacy studies (TES) conducted at sentinel sites. In 2016, the efficacy of LA remained high at 98.9% and ASAQ 99.1%, however in 2020, the efficacy rate for LA dropped to 91.2% and that of DihydroartemisininPiperaquine (DP) was 99.7%. Based on these results, MoH adopted DP as an additional first line treatment for malaria while maintaining ASAQ as a second line drug.

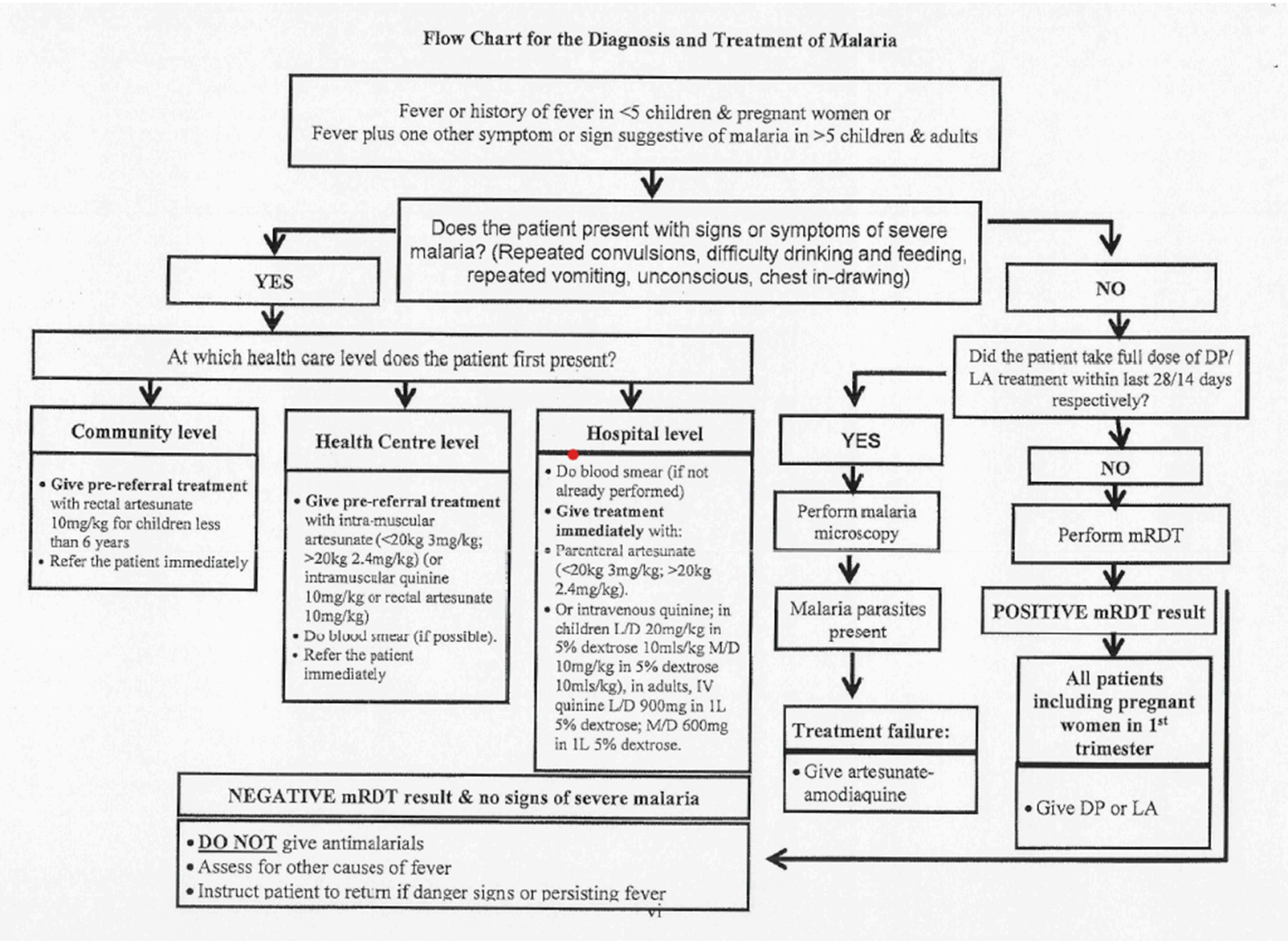
Partial resistance to artemisinins has emerged in several African Countries, although not yet documented in Malawi. While partial resistance alone does not lead to failure of ACT treatment, additional resistance to partner drugs like lumefantrine would jeopardize the effectiveness of ACTs. To mitigate ACT resistance in countries with a high burden of malaria, the WHO recommends introduction of multiple first line therapies (MFT). MFT entails use of two or more effective antimalaria drugs in a population for treatment of uncomplicated malaria, either at the same time or in rotation. The rationale of MFT is to expose the parasite population to different antimalarials to prevent or delay the emergence or spread of resistance. The MoH has adopted use of MFT for malaria and currently recommends use of DP and LA as part of MFT for uncomplicated malaria. However, in an event LA efficacy rate drops below 90%, another ACT shall be recommended.

This edition also introduces a recommendation aimed at enhancing access to malaria treatment among school-going children, who continue to bear a high malaria burden. This is to be achieved through the implementation of the Learner Treatment Kit (LTK) program in primary schools, which enables trained teachers to provide timely diagnosis and treatment of uncomplicated malaria during school hours.

Since 2010, the MoH has banned the manufacturing, importation and use of oral artemisinin-based monotherapies in Malawi. However, the use of parenteral and rectal artesunate monotherapies are recommended for treatment of severe malaria and community pre-referral Management respectively.

The MoH recommends use of parenteral artesunate as definitive treatment for severe malaria at rural, community, district and central hospitals. At the health centre level, intramuscular (IM) artesunate is the recommended pre-referral treatment.However, IM quinine may be used when IM artesunate is not available or is contraindicated. *IM quinine should be administered in the thigh, not in the buttocks.* Rectal artesunate is recommended for children < 6 years as pre-referral treatment of severe malaria at the community level.

To improve patient outcomes from severe malaria and severe anaemia (commonly caused by malaria), MoH has adopted the WHO recommended post discharge malaria continuum of care (PDMCC). This strategy aims to prevent another malaria infection among children living in moderate to high transmission areas after they are discharged from the hospital with high risk for readmission and death. Using an ACT to provide PDMCC to children discharged from the hospital with severe anaemia has been shown to significantly reduce mortality among this cohort (Okell et al, 2023). The MoH recommends the use of DP as a drug of choice in post discharge malaria continuum of care (PDMCC) in under 5 children discharged with diagnosis of severe malaria and or severe Anaemia (which is a targeted, small number of children)(Phiri, Kamija S et al. 2024).


Flow Chart for the Diagnosis and Treatment of Malaria
Fever or history of fever in <5 children & pregnant women or
Fever plus one other symptom or sign suggestive of malaria in >5 children & adults
Does the patient present with signs or symptoms of severe malaria? (Repeated convulsions, difficulty drinking and feeding, repeated vomiting, unconscious, chest in-drawing)
YES
NO
At which health care level does the patient first present?
Community level
• Give pre-referral treatment with rectal artesunate 10mg/kg for children less than 6 years
• Refer the patient immediately
Health Centre level
• Give pre-referral treatment with intra-muscular artesunate (<20kg 3mg/kg; >20kg 2.4mg/kg) (or intramuscular quinine 10mg/kg or rectal artesunate 10mg/kg)
• Do blood smear (if possible).
• Refer the patient immediately
Hospital level
• Do blood smear (if not already performed)
• Give treatment immediately with:
• Parenteral artesunate (<20kg 3mg/kg; >20kg 2.4mg/kg).
• Or intravenous quinine; in children L/D 20mg/kg in 5% dextrose 10mls/kg M/D 10mg/kg in 5% dextrose 10mls/kg), in adults, IV quinine L/D 900mg in 1L 5% dextrose; M/D 600mg in 1L 5% dextrose.
Did the patient take full dose of DP/ LA treatment within last 28/14 days respectively?
YES
NO
Perform malaria microscopy
Malaria parasites present
Treatment failure:
• Give artesunate-amodiaquine
Perform mRDT
POSITIVE mRDT result
All patients including pregnant women in 1st trimester
• Give DP or LA
NEGATIVE mRDT result & no signs of severe malaria
• DO NOT give antimalarials
• Assess for other causes of fever
• Instruct patient to return if danger signs or persisting fever

5. UNCOMPLICATED MALARIA

This section on **Uncomplicated Malaria** includes the case definition, diagnostic approaches, and recommended treatment strategies. It outlines first-line management with artemisinin-based combination therapy (ACT), guidance on managing treatment failure, and concludes with a Learner Treatment Kit to support practical application.

5.1 Case Definition

This section presents two case definitions of malaria: **suspected malaria** and **confirmed malaria.**

5.1.1 Suspected Malaria

Malaria should be suspected in any under five children or pregnant women who present with fever (or history of fever) and in over five children and adults with fever or history of fever plus one other symptom or sign suggestive of malaria. The health care personnel in this case must try to clinically exclude other common causes of fever, such as tonsillitis, chest infections, abscess, urinary tract infection, and otitis media.

5.1.2 Confirmed Malaria

A malaria case is confirmed by demonstration of asexual forms (trophozoite stage) of the parasite in the thick or thin peripheral blood film or by a positive malaria rapid diagnostic test (mRDT) result in the presence of fever or history of fever. Clinically, malaria falls into two categories- uncomplicated and severe, depending on degree of symptoms. However, clinical diagnosis in uncomplicated malaria is not recommended; a confirmatory test should always be performed.

5.2 Diagnosis of malaria

Microscopy remains the gold standard for the diagnosis of malaria. All suspected malaria cases should be confirmed using either mRDT or microscopy. However, MoH recommends the use of mRDT to diagnose uncomplicated malaria. Based on the type of mRDT used in Malawi (HRP2), and the fact that PfHRP2 antigens can remain in blood circulation for not less than two weeks after effective treatment, it is recommended that all suspected severe malaria cases and treatment failures should only be confirmed using microscopy.

A patient who presents with symptoms of malaria and positive parasitological tests (microscopy or mRDT) but with no features of severe malaria is defined as having uncomplicated malaria [refer section 2 page 8 for severe malaria]. For uncomplicated malaria, treatment should only be given to those patients who test positive.

5.2.1 Malaria Rapid Diagnostic Tests (mRDTs)

All suspected uncomplicated malaria cases at all levels of the health care delivery system should be tested using an approved mRDT prior to initiating treatment. (Refer to national malaria diagnostic guidelines).

Advantages of mRDTs:

(1) They provide a quick result;
(2) They are less expensive than microscopy;
(3) Their use is readily taught.
(4) They are accurate.
(5) They don't require power to be used.

Disadvantages of mRDTs:

(1) They continue to be positive in patients who have recently (within two weeks) been treated with effective anti-malarial medicines;
(2) They cannot indicate parasite density or species.
(3) Cannot be stored for future reference.

MoH recommends WHO pre-qualified brands of mRDTs to be used in Malawi. New mRDTs brands are selected for national use every 4-5 years after field-testing to determine user friendliness, field performance of individual test (sensitivity and specificity) and heat stability under Malawi's conditions. (Refer to the national diagnostic guidelines for further information).

5.2.2 Microscopy

Microscopy remains the gold standard for the diagnosis of malaria in Malawi. However, as the capacity for microscopy is limited, microscopy will be used for the following purposes:

1. To confirm malaria diagnosis in all patients suspected with severe malaria

2. To monitor treatment progress in all severe malaria cases receiving either parenteral artesunate or parenteral quinine

3. To confirm first-line treatment failures before second-line treatment is used

4. To identify malaria parasite species

5. To assess malaria parasite densities

6. To confirm uncomplicated malaria cases where mRDT is not available or microscopy capacity and resources are readily available

7. To diagnose malaria in an event that mRDT is negative but there is a high suspicious index of malaria caused by other species

For microscopic diagnosis of malaria, thick and thin blood films are required, and Giemsa stain is to be used. Thick films are recommended for parasite detection and quantification and are used to monitor response to treatment. Thin films are recommended for species identification. In Malawi, approximately 96.3% of malaria infections are due to *P. falciparum* (MIS 2021).

The following microscopy results will be reported on the laboratory result form:

- Presence or absence of parasites (or no malaria parasite seen-NMPS)
- Species of malaria parasite seen
- Stage of the parasite

Parasite density i.e., **Number of parasite counted × 8000/(µl)/Number of WBCs counted**

(see Table 1.1 below for correct interpretation)

Table 1.1: Correlation between parasite density per micro-litre (µl) of blood and percentage of red blood cells parasitized

Parasites per micro-litre (µl) of blood	% of red blood cells parasitized
40 – 400 parasites ring stage per µl	0.001 – 0.01%
401 – 4000 parasites ring stage per µl	0.01 – 0.1%
4001 – 40000 parasites ring stage per µl	0.1 – 1%
40001 – 400000 parasites ring stage per µl	1 – 10%

5.3 Treatment of Uncomplicated Malaria

Proper history and physical examination are important in the management of malaria. For uncomplicated malaria, treatment should only be given to those patients who test positive. MoH recommends the use of MFT in the treatment of uncomplicated malaria. Currently, DP and LA are part of MFT in Malawi. The clinical objectives of treating uncomplicated malaria are to cure the infection as rapidly as possible and prevent progression to severe disease. 'Cure' is defined as elimination of all parasites from the body. The public health objectives are to prevent onward transmission of the infection to others and to prevent the emergence and spread of resistance to antimalarial drugs.

First-line Treatment [Artemisinin Combination Therapy]
Artemisinin based Combination Therapy [ACT] is a combination of rapidly acting artemisinin derivative with a longer acting drug [more slowly eliminated partner drug]. The artemisinin component rapidly clears parasites from the blood [reducing parasite numbers by a factor of 48-hr asexual cycle] and is also active against the sexual stages of parasite that mediate onward transmission to mosquitoes. The longer acting partner drug clears the remaining parasite and provides protection against resistance to artemisinin derivative. Partner drugs with longer elimination half-life also provides a period of post treatment prophylaxis.

Note. Artemisinin Combination treatments should be used to treat malaria in pregnant women in the first trimester of pregnancy except where the other partner drug is contraindicated as in Artesunate + SulphadoxinePyrimethamine (SA+SP)

5.3.1 Recommendation for multiple first-line therapy (MFT) for uncomplicated falicparum malaria (updated February 2026)

For patients with uncomplicated malaria

Strong recommendation

We recommend Dihydroartemisinin–Piperaquine (DP) or Lumefantrine-Artemether (LA) as part of a MFT strategy

- *By multiple first-line therapies, we refer to the use of alternative first-line treatments, whereby either AL or DP is administered depending on the geographical area or site-specific allocation. (See rationale)*
- *Different dosages apply for children, adolescents and adults (see practical info)*

Practical info

Dihydroartemisinin Piperaquine (DP)

DP is one of the two first line treatments for uncomplicated malaria in Malawi. The dosing regimen currently recommended by the manufacturer provides adequate exposure to piperaquine and excellent cure rates (>95%), except in children < 5 years, who have 3 times risk of treatment failure because of lower plasma piperaquine concentrations. Children weighing < 25kg should receive at least 2.5 mg/kg dihydroartemisinin and 20mg/kg piperaquine to achieve the same exposure as persons > 25kg. DP should be given once a day for three days.

Table 1.2: Dihydroartemisinin and Piperaquine dosing

BODY WEIGHT	PRESENTATION	DAY-1	DAY-2	DAY-3
< 8kg	Dihydroartemisinin 20mg + Piperaquine 160mg (DP-20mg/160mg)	1 tab a day	1 tab a day	1 tab a day
8kg to < 11kg	Dihydroartemisinin 30mg + Piperaquine 240mg (DP 30mg/240mg)	1 tab a day	1 tab a day	1 tab a day
11kg to < 17kg	Dihydroartemisinin 20mg + Piperaquine 160mg (DP-20mg/160mg)	2 tab a day	2 tab a day	2 tab a day
17kg to < 25kg	Dihydroartemisinin 30mg + Piperaquine 240mg (DP-30mg/240mg)	2 tab a day	2 tab a day	2 tab a day
25kg to < 36kg	Dihydroartemisinin 40mg + Piperaquine 320mg (DP-40mg/320mg)	2 tab a day	2 tab a day	2 tab a day

Adult dose:

BODY WEIGHT	STRENGTH	DAY-1	DAY-2	DAY-3
36kg to < 60kg	Dihydroartemisinin 60mg + Piperaquine 480mg (DP-60mg/480mg)	2 tab a day	2 tab a day	2 tab a day
60kg to < 80kg	Dihydroartemisinin 80mg + Piperaquine 640mg (DP-80mg/640mg)	2 tab a day	2 tab a day	2 tab a day
>80kg	Dihydroartemisinin 80mg + Piperaquine 640mg (DP-80mg/640mg)	2 and half tab a day	2 and half tab a day	2 and half tab a day

DP comes in fixed dose combinations of tablets, and dispersible tablets, containing varying amounts of dihydroartemisinin and piperaquine for specific weight bands. Malawi uses the following fixed dose combinations:

• DP 20 mg/160 mg Dispersible (3 Blister Pack Tablets) – for pediatrics
• DP 40 mg/320 mg Dispersible (3 Blister Pack Tablets) – for pediatrics

• DP 60 mg/480 mg Non Dispersible (6 Blister Pack Tablets) – for adults
• DP 80 mg/640 mg Non Dispersible (6 Blister Pack Tablets) – for adults

On the market, there are multiple formulations including DP 30mg/240mg Dispersible (3 Blister Pack Tablets) – for paediatrics, which can be used if available in Malawi.

If certain DP fixed dose combinations are not available in Malawi, some weight bands (8–11kg, >80kg) will need to split tablets in order to achieve satisfactory drug levels.

Cautions with DP include risk of prolonged QT interval and risk of possible arrhythmias although less than quinine. It is not necessary to perform an electrocardiogram before providing DP but should not be used in patients with congenital QT prolongation or on medications that prolong the QT interval. Dihydroartemisinin exposure is lower in pregnant women and piperaquine is eliminated more rapidly in pregnant women, but as this does not affect the primary efficacy, no dosage adjustment is recommended for pregnant women. Malnourished children are at increased risk for treatment failure, they should be monitored closely.

Lumefantrine-Artemether [LA]

Lumefantrineartemether is one of the two first line treatments for uncomplicated malaria in Malawi. Lumefantrine-artemether is an ACT and comes in "fixed-dose combinations". Each tablet of either dispersible or regular LA contains artemether, a synthetic derivative of artemisinin, (20 mg) and lumefantrine (120 mg). Lumefantrine-artemether has a high clinical and parasitological cure rate and produces rapid gametocyte clearance.

Lumefantrine-artemether comes in two oral formulations. These are 1) dispersible LA [LA (D)], 2) non-dispersible LA [LA (ND)]. There are two forms of LA (ND); these are regular tablets and double strength LA [LA (DS)] tablets. LA (ND) should be used in older children weighing 25 kg or more and adults. LA (D) should be used in children weighing less than 25 kg. Table 1.3 below presents the dosing schedule for non-dispersible and dispersible LA.

Table 1.3: Dosage schedule for dispersible Lumefantrine-Artemether (LA)

Body Weight in kg (age in years)	Day 1 Start dose	Day 1 8 hrs.	Day 2 AM	Day 2 PM	Day 3 AM	Day 3 PM
LA (D) <15 kg (<3)	1	1	1	1	1	1
LA (D) 15 – <25 kg (3 – <9)	2	2	2	2	2	2

Table 1.4: Dosage schedule for non-dispersible lumefantrine-artemether (LA)

Body Weight in kg (age in years)	Day 1 AM	Day 1 PM	Day 2 AM	Day 2 PM	Day 3 AM	Day 3 PM
LA (ND) 25 – <35 kg (9 – <14)	3	3	3	3	3	3
LA (ND) ≥35 kg (>14)	4	4	4	4	4	4

Most of the reported events associated with LA have been mild, and most studies have shown no indications of cardiotoxicity. However, the manufacturer of LA recommends avoiding medications that prolong the QT interval, including antimalarials such as quinine, should be used cautiously following administration of LA. There is decreased blood concentration of LA in patients who are receiving rifampicin therefore their response to treatment should be monitored more closely and their full adherence ensured. There should be an interval of 8 hours between the last dose of artesunate and the first dose of LA. Similarly, the interval between the last dose of quinine and the first dose of LA should be 12 hours. The following are some of the commonly reported side effects for lumefantrine-artemether: dizziness, abdominal pain, palpitations, myalgia, arthralgia, headache, and skin rash.

Dispersible Lumefantrine-Artemether

Dispersible lumefantrine-artemether is a tablet formulation recommended for babies and children weighing less than 25 kg or less than 9 years of age. The dispersible tablets of LA are specially formulated to disintegrate rapidly when put in water. They come in 6x1 and 6x2 blister packs and are available in all Government and CHAM health facilities, as well as all community village clinics. Pharmacologically, LA (D) is similar to LA (ND). LA (D) is cherry flavoured and sweetened to mask the bitter taste of lumefantrine. This makes it more acceptable to children. The other advantage of LA (D) is that it is easy to prepare, as it does not require crushing.

The treatment regimen for LA (D) is six doses (twice per day for three days) according to the body weight or age. The second dose is given 8 hours after the first dose, thereafter doses are given after every 12 hours. Table 1.3 above presents the dosing schedule for dispersible LA.

It is recommended that each dose of LA should be taken with food to optimize absorption. Milk has been shown to improve the absorption of the lumefantrine component of the combination. The dose should be repeated if the medicine is vomited within 30 minutes of ingestion.

Evidence to decision

Benefits and harms

Substantial net benefits of the recommended alternative

Compared with lumefantrine-artemether (LA), dihydroartemisinin–piperaquine (DP) reduces the risk of treatment failure, assessed using both PCR-corrected (recrudescence) and PCR-uncorrected (recurrence) outcomes. However, LA continues to demonstrate high therapeutic efficacy (approximately 97%) in many settings, indicating that it remains a highly effective first-line option.

DP probably has little to no difference in adverse events (symptomatic hepatotoxicity and symptoms of anaemia) compared with AL.

Certainty of the evidence

High

Based on an up-to-date systematic review of randomised controlled trials (Gwasupika et al., 2026), high-certainty evidence demonstrates that dihydroartemisinin–piperaquine (DP) reduces the risk of treatment failure, including both recurrence and recrudescence, compared with artemether–lumefantrine (AL). This conclusion is informed by a comprehensive meta-analysis of 46 trials (n≈46 studies identified from 2,639 records), including 17 trials directly comparing DP with AL, with PCR-corrected and uncorrected treatment failure as primary outcomes.

To inform safety and tolerability, we used an up-to date systematic review and meta-analysis (Yilma et al., 2026) restricted to randomised controlled trials comparing DP with AL for uncomplicated *Plasmodium falciparum* malaria. Moderate-certainty evidence indicates that DP probably has little to no difference in symptomatic hepatotoxicity outcomes (elevated bilirubin and AST) compared with AL. In contrast, for symptoms of anaemia (inferred from haemoglobin reduction), the certainty of evidence is low, and DP may have little to no difference compared with AL. The evidence base includes a small number of trials contributing to each outcome (e.g., two studies for elevated bilirubin, one for elevated AST, and two for haemoglobin drop), evaluating symptomatic hepatotoxicity (bilirubin and AST) and symptoms of anaemia inferred from haemoglobin reduction.

Values and preferences

No substantial variability expected

From an individual patient perspective, patients and caregivers are likely to place a high value on reducing treatment failure, given the clinical, financial, and social burden associated with recurrent malaria and retreatment.

At the health-system level, decision-makers must also value affordability, sustainability of supply, and the ability to maintain high treatment coverage across the population. The panel judged that these system-level values appropriately modify how individual-level benefits are implemented at scale

Resources

Important negative issues

Resource considerations played an important role in shaping implementation decisions.
Dihydroartemisinin–piperaquine (DP) is approximately four times more costly than artemether–lumefantrine (AL), and nationwide replacement would have substantial budgetary implications.

Equity

No important issues with the recommended alternative

The panel considered whether geographic targeting of DP could raise equity concerns. Given the continued high efficacy of AL and the need to preserve programme sustainability, the panel judged that the current strategy is unlikely to result in meaningful inequities in health outcomes in the short term.
Ongoing therapeutic efficacy monitoring and periodic reassessment were emphasised to ensure equitable access as resistance patterns, epidemiology, and resources evolve.

Acceptability No important issues with the recommended alternative

Both DP and AL were judged acceptable to patients and healthcare workers. At the programme level, acceptability is influenced by procurement costs, supply-chain reliability, and operational feasibility, supporting phased and geographically targeted implementation of DP.

Feasibility No important issues with the recommended alternative

Implementation of DP was judged feasible when introduced in selected areas within the existing health system. Nationwide replacement of AL with DP was considered less feasible at present due to financial and logistical constraints, despite DP's superior efficacy.

Rationale

The adoption of Multiple First-line Therapies (MFT) is primarily driven by the need to delay the emergence and spread of antimalarial drug resistance. When a single artemisinin-based combination therapy (ACT) is used as the sole first-line treatment, it exerts uniform selective pressure on *Plasmodium falciparum* populations, increasing the likelihood that resistant parasites will be selected and transmitted. By contrast, deploying two or more ACTs concurrently distributes drug pressure across different partner drugs, thereby reducing the probability that resistance to any single regimen will dominate. MFT aims to preserve the therapeutic efficacy of existing ACTs, prolong their useful lifespan, and safeguard treatment outcomes in high-burden settings.

The rationale for offering AL to certain regions in Malawi, rather than DP which shows higher therapeutic efficacy, is that Dihydroartemisinin–piperaquine (DP) is more costly than artemether–lumefantrine (AL), and nationwide replacement would have substantial budgetary implications and is therefore not feasible.

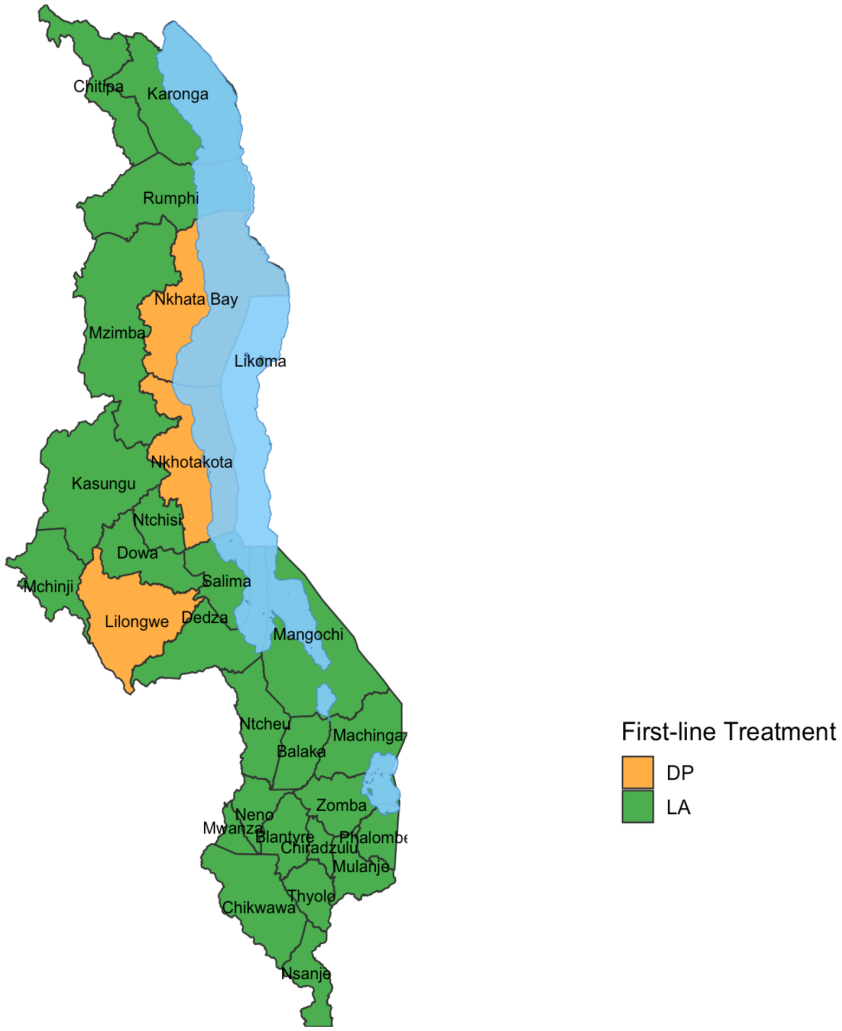
In line with the adopted MFT approach, DP has been strategically introduced in selected geographic areas where the cases are high (meaning higher pressure on drugs and resistance to occur), while AL continues to be used elsewhere, supported by high therapeutic efficacy (approximately 97%, according to MARC SE annual country report).

The panel judged that this approach balances maximising population-level benefits, delaying the emergence of drug resistance, and ensuring efficient use of limited resources.

Implementation

DP will be strategically introduced in selected geographic areas (including Nkhata Bay, Nkhotakota, and Lilongwe) while AL continues to be used elsewhere.

Districts Implementing Dihydroartemisinin–Piperaquine (DP) vs. Artemether–Lumefantrine (LA)



Clinical question/ PICO

Population: People with uncomplicated falciparum Malaria
Intervention: Dihydroartemisinin–Piperaquine (DP)
Comparator: Lumefantrine-Artemether

Outcome Timeframe	**Study results and measurements**	**Comparator** LA	**Intervention** DP	**Certainty of the evidence** (Quality of evidence)	**Summary**
Treatment failure (Recurrence)	Odds ratio 0.22 (CI 95% 0.13 — 0.37) Based on data from 3,106 participants in 17 studies. (Randomized controlled)	**234** per 1000 Difference:	**63** per 1000 **171 fewer per 1000** (CI 95% 196 fewer — 132 fewer)	**High** 1	Dihydroartemisinin–Piperaq (DP) reduces treatment failure compared to Lumefantrine-Artemether (LA).
Treatment failure (Recrudescence)	Odds ratio 0.25 (CI 95% 0.13 — 0.48) Based on data from 2,991	**56** per 1000	**15** per 1000	**High** 2	Dihydroartemisinin–Piperaq (DP) reduces treatment failure compared to

Outcome Timeframe	**Study results and measurements**	**Comparator** LA	**Intervention** DP	**Certainty of the evidence** (Quality of evidence)	**Summary**
	participants in 17 studies. (Randomized controlled)	Difference:	**41 fewer per 1000** (CI 95% 48 fewer — 28 fewer)		Lumefantrine-Artemether (LA).
Adverse Event (Symptomatic hepatotoxicity inferred from elevated bilirubin)	Odds ratio 0.63 (CI 95% 0.1 — 3.86) Based on data from 800 participants in 2 studies. (Randomized controlled)	4 per 1000 Difference:	3 per 1000 **1 fewer per 1000** (CI 95% 4 fewer — 11 more)	**Moderate** Rated down one level due to serious imprecision and indirectness [3]	Dihydroartemisinin–Piperaq (DP) probably has little or no difference in symptomatic hepatotoxicity compared with Lumefantrine-Artemether (LA).
Adverse event (Symptomatic hepatotoxicity inferred from elevated aspartate aminotransferase (AST))	Odds ratio 1.12 (CI 95% 0.26 — 4.76) Based on data from 807 participants in 1 studies.	4 per 1000 Difference:	4 per 1000 **0 fewer per 1000** (CI 95% 3 fewer — 15 more)	**Moderate** Rated down one level due to serious imprecision and indirectness [4]	Dihydroartemisinin–Piperaq (DP) probably has little or no difference in symptomatic hepatotoxicity compared with Lumefantrine-Artemether (LA).
Adverse event (Symptoms of anaemia as inferred from drop in haemoglobin (<7 g/dL))	Odds ratio 0.92 (CI 95% 0.6 — 1.42) Based on data from 1,938 participants in 2 studies.	26 per 1000 Difference:	24 per 1000 **2 fewer per 1000** (CI 95% 10 fewer — 11 more)	**Low** Rated down one level due to serious risk of bias and one level for serious imprecision and indirectness [5]	Dihydroartemisinin–Piperaq (DP) may have little or no difference in symptoms of anaemia compared with Lumefantrine-Artemether (LA).

1. **Inconsistency: no serious. Indirectness: no serious.** Uncorrected PCR is a surrogate outcome that does not distinguish reinfection from recrudescence. The similar and clinically important effects (OR 0.26 uncorrected; 0.45 corrected) support a robust benefit of DP, so we did not rate down for indirectness.. **Imprecision: no serious. Publication bias: no serious.**
2. **Inconsistency: no serious. Indirectness: no serious.** Corrected PCR is a diagnostic tool and a strong surrogate for recrudescence and hence we do not consider rating down. **Imprecision: no serious. Publication bias: no serious.**
3. **Inconsistency: no serious. Indirectness: serious.** Symptomatic hepatotoxicity is inferred from elevated bilirubin which is a surrogate outcome. **Imprecision: serious.** A threshold of 10/1000 has been considered. Based on this threshold, the CI crosses the threshold. **Publication bias: no serious.**
4. **Inconsistency: no serious. Indirectness: serious.** Symptomatic hepatotoxicity inferred from elevated aspartate aminotransferase (AST) which is a surrogate outcome. **Imprecision: serious.** A threshold of 10/1000 has been considered. Based on this threshold, the CI crosses the threshold. . **Publication bias: no serious.**
5. **Risk of Bias: serious.** High risk of bias studies dominate (78.2%). **Inconsistency: no serious. Indirectness: serious.** Symptoms of anaemia are inferred from drop in haemoglobin (<7 g/dL) which is a surrogate outcome. **Imprecision: serious.** A threshold of 10/1000 has been considered. Based on this threshold, the CI crosses the threshold. . **Publication bias: no serious.**

5.4 Treatment Failure and second line treatment

Treatment failure is the persistence of signs and symptoms of malaria in a patient with a positive blood film for malaria parasites after three days of completing a recommended first-line treatment taken in full dosage. Treatment failure is not always due to drug resistance.

Treatment failure should be suspected if symptoms persist or the patient clinically deteriorates within 3 to 14 days for LA and 3 to 28 days for DP after initiation of drug therapy.

Causes of real or apparent treatment failure may include:

• Unreported poor adherence to treatment
• Drug resistance
• Inadequate drug exposure due to:
o Unrecognized incorrect dosage
o Vomiting within one hour of administration
o Unusual pharmacokinetic properties in an individual
• Misdiagnosis
• Counterfeit or defective drug
• Drug-drug interaction

Note: If the patient develops symptoms and has a positive blood smear after 14 or 28 days [need to check the data substantiating the 14 days] of initiation of therapy where there has been prior clearance of symptoms and/or parasites, this should be considered as a new infection and be treated with the first-line drug.

• If, after 14 or 28 days, adherence, or dosage is found to have been incorrect, then 'treatment failure' is excluded and the primary treatment should be repeated correctly.

• If, however, treatment failure is confirmed, the patient should be treated with the second-line treatment (artesunate-amodiaquine), according to the recommended dosing schedule.

Second-line Treatment
Second-line treatment should be used in the following conditions:

1. Treatment failures within 14 or 28 days of initial treatment with LA or DP
2. All patients with contraindications or intolerance to LA or DP

5.4.1 Recommendation for second line of treatment (Updated February 2026)

For patients with uncomplicated malaria

Strong recommendation

We recommend Artesunate–amodiaquine (ASAQ) as the second-line treatment for patients with treatment failure following Lumefantrine-Artemether–(LA) or Dihydroartemisinin–Piperaquine (DP).

Different dosages apply for children, adolescents and adults (see practical info)

Practical info

Artesunate-Amodiaquine (ASAQ)
The recommended second-line treatment for uncomplicated malaria in Malawi is artesunate–amodiaquine (ASAQ). It is available in fixed-dose combinations with tablets containing 25 mg/67.5 mg, 50 mg/135 mg and 100 mg/270 mg of artesunate and amodiaquine, respectively. The recommended total treatment dose per day is 4 mg/kg/day of artesunate and 10 mg/kg/day of amodiaquine given once a day for 3 days. Do not give Artesunateamodiaquine in HIV positive patients who are taking zidovudine, cotrimoxazole and efavirenz. Instead give quinine and clindamycin.

Table 1.5: Dosage schedule for fixed combination dose of artesunate-amodiaquine

Body Weight (kg)	Age	Daily dose for 3 days artesunate-amodiaquine	Preparation strength per tablet
< 8.9	2 – 11 months	1 tablet	25 mg/67.5 mg
9.0 – 17.9	1 – 5 years	1 tablet	50 mg/135 mg

Body Weight (kg)	Age	Daily dose for 3 days artesunate-amodiaquine	Preparation strength per tablet
18.0 – 35.9	6 – 13 years	1 tablet	100 mg/270 mg
≥ 36	14 years old and above	2 tablets	100 mg/270 mg

NOTE: Confirmed treatment failures with ASAQ should be treated with quinine and doxycycline for seven days if not contraindicated. For children under 8 years, give oral quinine and clindamycin.

For children weighing less than 5kg with treatment failure to LA or DP, they should be given ASAQ.

MoH recommends Pharmacy and Medicines Regulatory Authority (PMRA) to conduct post marketing surveillance every quarter.

Evidence to decision

Benefits and harms

Substantial net benefits of the recommended alternative

The Summary of Findings tables present the effects of the interventions on outcomes important to patients. Compared with lumefantrine-artemether (LA), artesunate–amodiaquine (ASAQ) reduces the risk of treatment failure, assessed using both uncorrected and corrected PCR. The reduction in recrudescence was considered particularly important, as it reflects improved parasite clearance following treatment rather than protection against reinfection alone. These benefits are particularly relevant in the context of second-line treatment, where effective parasite clearance after failure of initial therapy is critical.

Compared with LA, ASAQ may increase symptoms of anaemia as inferred from drop in heamoglobin, while showing little or no difference in hepatotoxicity.

Certainty of the evidence

High

To inform comparative efficacy, we used an up-to-date systematic review and meta-analysis conducted by Gwasupika et al. (2026), which included randomised controlled trials comparing artemether–lumefantrine (AL) with alternative artemisinin-based combination therapies for uncomplicated *Plasmodium falciparum* malaria in sub-Saharan Africa. From 2,639 records identified through electronic database searches, 46 studies met the inclusion criteria, including 36 trials comparing artesunate–amodiaquine (ASAQ) with AL. The primary outcomes were PCR-corrected and uncorrected treatment failure. High-certainty evidence demonstrates that ASAQ reduces the risk of treatment failure, including both recurrence and recrudescence, compared with AL. The panel considered this high-certainty evidence sufficient to support ASAQ as an effective option where first-line therapy has failed or cannot be used.

To inform safety and tolerability, we used an up-to-date systematic review and meta-analysis conducted by Yilma et al. (2026), restricted to randomised controlled trials comparing ASAQ with artemether–lumefantrine (AL). The review assessed key safety outcomes, including symptomatic hepatotoxicity (inferred from elevated bilirubin and aspartate aminotransferase [AST]) and symptoms of anaemia inferred from haemoglobin reduction. For ASAQ versus AL, the evidence included two studies for elevated bilirubin, two studies for elevated AST, and five studies for haemoglobin drop.

Moderate-certainty evidence indicates that ASAQ probably has little to no difference in hepatotoxicity outcomes compared with AL. In contrast, for symptoms of anaemia, low-certainty evidence suggests that ASAQ may increase symptoms of anaemia compared with AL.

Values and preferences

No substantial variability expected

In situations where first-line treatment is ineffective or not tolerated, the panel judged that patients would value access to an alternative treatment with demonstrated effectiveness in reducing treatment failure. No important variability in values and preferences across populations or regions was anticipated.

Resources

No important issues with the recommended alternative

Resource considerations were relevant to decision-making. ASAQ is a long-established artemisinin-based combination therapy, and its use is generally associated with lower acquisition costs than some newer alternatives.

Equity

No important issues with the recommended alternative

The panel judged that the use of ASAQ as a second-line treatment is unlikely to raise equity concerns, as access would be determined by clinical indication (treatment failure or intolerance) and ensuring availability of an effective second-line option was considered supportive of equitable malaria care.

Acceptability

No important issues with the recommended alternative

The panel judged that ASAQ is likely to be acceptable to patients and healthcare workers, given its long history of use in malaria treatment globally and familiarity within similar settings.

No major acceptability concerns were anticipated that would limit its use as a second-line option.

Feasibility

No important issues with the recommended alternative

The panel judged that implementation of ASAQ as a second-line treatment is feasible within the existing malaria treatment infrastructure.

Rationale

Artesunate–amodiaquine (ASAQ) is recommended as second-line treatment following failure of artemether–lumefantrine (AL) or dihydroartemisinin–piperaquine (DP) because it provides an effective artemisinin-based combination therapy (ACT) with a different partner drug, thereby reducing the risk of cross-resistance. While artesunate ensures rapid parasite clearance, amodiaquine has a distinct resistance and pharmacokinetic profile compared with lumefantrine and piperaquine, making it a suitable alternative when failure of those regimens is suspected. Switching to ASAQ avoids re-exposure to the same partner drug that may have contributed to treatment failure and helps distribute selective drug pressure across different ACTs. This approach supports resistance containment, preserves the efficacy of available therapies, and ensures continued effective management of uncomplicated *Plasmodium falciparum* malaria.

Clinical question/ PICO

Population: People with uncomplicated falciparum Malaria
Intervention: ASAQ
Comparator: AL

Outcome Timeframe	**Study results and measurements**	**Comparator** AL	**Intervention** ASAQ	**Certainty of the evidence** (Quality of evidence)	**Summary**
Treatment failure (Recurrence)	Odds ratio 0.45 (CI 95% 0.32 — 0.62) Based on data from 5,872 participants in 35 studies. (Randomized controlled)	**159** per 1000 Difference:	**78** per 1000 **81 fewer per 1000** (CI 95% 102 fewer — 54 fewer)	**High** 1	Artesunate-Amodiaquine (ASAQ) reduces the risk of treatment failure compared to Artemether–Lumefantrine (AL).
Treatment failure (Recrudescence)	Odds ratio 0.58 (CI 95% 0.42 — 0.82) Based on data from 5,548 participants in 34 studies.	**42** per 1000	**25** per 1000	**High** 2	Artesunate-Amodiaquine (ASAQ) reduces the risk of treatment failure (recrudescence) compared

Outcome Timeframe	**Study results and measurements**	**Comparator** AL	**Intervention** ASAQ	**Certainty of the evidence** (Quality of evidence)	**Summary**
	(Randomized controlled)	Difference:	**17 fewer per 1000** (CI 95% 24 fewer — 7 fewer)		to Artemether–Lumefantrine (AL).
Adverse Event (Symptomatic hepatotoxicity inferred from elevated bilirubin)	Odds ratio 0.57 (CI 95% 0.13 — 2.51) Based on data from 943 participants in 2 studies. (Randomized controlled)	5 per 1000 Difference:	3 per 1000 **2 fewer per 1000** (CI 95% 4 fewer — 7 more)	**Moderate** Due to serious indirectness [3]	Artesunate-Amodiaquine (ASAQ) probably has little or no difference in symptomatic hepatotoxicity compared with Artemether–Lumefantrine (AL).
Adverse event (Symptomatic hepatotoxicity inferred from elevated aspartate aminotransferase (AST))	Odds ratio 0.58 (CI 95% 0.13 — 2.61) Based on data from 1,046 participants in 2 studies. (Randomized controlled)	4 per 1000 Difference:	2 per 1000 **2 fewer per 1000** (CI 95% 3 fewer — 6 more)	**Moderate** Due to serious indirectness [4]	Artesunate-Amodiaquine (ASAQ) probably has little or no difference on symptomatic hepatotoxicity compared with Artemether–Lumefantrine (AL).
Adverse event (Symptoms of anaemia as inferred from drop in haemoglobin (<7 g/dL))	Odds ratio 1.4 (CI 95% 1 — 1.99) Based on data from 2,538 participants in 5 studies.	28 per 1000 Difference:	39 per 1000 **11 more per 1000** (CI 95% 0 fewer — 26 more)	**Low** Rated down one level for serious risk of bias and one level for serious imprecision and indirectness [5]	Artesunate-Amodiaquine (ASAQ) may increase symptoms of anaemia compared with Artemether–Lumefantrine (AL).

1. **Inconsistency: no serious. Indirectness: no serious.** Uncorrected PCR is a surrogate outcome that does not distinguish reinfection from recrudescence.The similar and clinically important effects (OR 0.50 uncorrected; 0.58 corrected) support a robust effect of ASAQ, so we did not rate down for indirectness. **Imprecision: no serious. Publication bias: no serious.**
2. **Inconsistency: no serious. Indirectness: no serious.** Corrected PCR is a diagnostic tool and a strong surrogate for recrudescence and hence we do not consider rating down. **Imprecision: no serious. Publication bias: no serious.**
3. **Inconsistency: no serious. Indirectness: serious.** Symptomatic hepatotoxicity is inferred from elevated bilirubin which is a surrogate outcome. **Imprecision: no serious.** A threshold of 10/1000 has been considered. Based on this threshold, the CI does not cross the threshold. .
4. **Inconsistency: no serious. Indirectness: serious.** Symptomatic hepatotoxicity is inferred from elevated AST which is a surrogate outcome.. **Imprecision: no serious.** A threshold of 10/1000 has been considered. Based on this threshold, the CI does not cross the threshold. . **Publication bias: no serious.**
5. **Risk of Bias: serious.** High risk of bias studies dominate (65%). **Inconsistency: no serious. Indirectness: serious.** Symptoms of anaemia are inferred from drop in haemoglobin (<7 g/dL) which is a surrogate outcome. . **Imprecision: serious.** A threshold of 10/1000 has been considered. Based on this threshold, the CI crosses the threshold. . **Publication bias: no serious.**

References

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5.5 LEARNER TREATMENT KIT

LTK is a school-based malaria case management intervention implemented as part of the basic first aid kit for school going children. It is an intervention provided by trained teachers during the school operational hours.

The aim is to increase access to malaria diagnosis and treatment. Historically pregnant women and under five children have been the most at-risk groups to malaria infection. Malaria control interventions have been targeting these vulnerable groups. However, recent studies have shown a high malaria burden among school going children. Studies in Zomba and Karonga conducted in 2015 and 2022 respectively demonstrated a high prevalence rate of malaria among the school going children (60% in Zomba and 58% in Karonga). In view of these developments, the MOH recommends the use of available effective first line treatments for implementation of LTK interventions in primary schools. It is one way of expanding case management through prompt and effective treatment to avert malaria complications.

Teachers are trained for five days on how to effectively test and treat only uncomplicated malaria cases. Following the training, they are equipped with mRDTs, first line antimalarial drugs and reporting tools. For detailed information on LTK, refer to the National LTK operational guide.

6. SEVERE MALARIA

This section consists of three main components: **case definition and diagnosis**, **treatment of severe malaria**, and **post-discharge malaria continuum of care (PDMCC)**.

6.1 Case Definition and Diagnosis

Severe malaria is defined as malaria due to *P. falciparum* infection that is sufficiently serious to be an immediate threat to life. Severe malaria is most often caused by *P. falciparum*, especially in Africa. However, other species of malaria parasites can cause severe symptoms. It is a medical emergency, which requires hospitalization. Most severe malaria occurs in children under 5 years of age. However, some adults are also at risk of severe disease, including:

- Malawians returning from long stay (at least one year) in a non-malarious country.
- Expatriates from non-malarious countries
- Pregnant women
- Splenectomised individuals
- Immunocompromised patients

Although most children with malaria have fever or history of fever, the fever may be variable in patients who have progressed to severe malaria. Children with suspected severe malaria should be examined for other conditions (e.g. pneumonia, meningitis) as a possible cause of their symptoms. If these diseases are found, they should be managed accordingly. If severe malaria is diagnosed in the out-patient settings, treatment should be commenced, and the patient referred immediately to a hospital for further evaluation and management.

The health worker should regard a patient as having severe malaria if he or she has one or more (mostly seen in combination) of the following conditions:

Table 2.1: Clinical manifestations and some laboratory findings

Clinical manifestations	Some laboratory findings
• Respiratory distress (acidotic breathing)	• Severe anaemia: (Hb<5 g/dl) (i.e. Hb<5 g/dl or Hct<15 %)
• Impaired level of consciousness (cerebral malaria)	• Hypoglycaemia: (<2.5 mmol/l or <45 mg/dl; adults <3.8 mmol/l or <70 mg/dl)
• Repetitive convulsions	• Hyperlactataemia (lactic acidosis) (blood lactate >4 mmol/l)
• Shock (weak pulse, cold extremities)	• Electrolyte imbalance (hyponatraemia <135 mmol/l)
• Hypovolaemia	• Acute kidney injury (serum creatinine >265 µmol/l or more than 1.4 mg/dl)
• Spontaneous bleeding (mouth, nose, skin, eyes)	• Haemoglobinuria
• Pulmonary oedema	
• Prostration	
• Excessive or persistent vomiting	
• Extreme pallor	
• Jaundice (yellowish coloration of eyes)	
• Little or no urine output (think about acute kidney injury)	
• Very dark coloured urine	

NOTE: A patient with any of the above features must be treated urgently as a case of severe malaria. Patients with hyperparasitaemia: (40,000 – 400,000/µl or ring stage ≥5% of RBCs) who do not have any of these indicators of severe disease should be admitted for observation. Treat with first-line antimalarial (LA or DP).

The most common and important complications of *P. falciparum* infection in children are cerebral malaria, severe anaemia, respiratory distress (acidosis) and hypoglycaemia. The differences between severe malaria in adults and in children are shown in Table 2.2 below.

Table 2.2: Different presentations of Severe Malaria between Adults and Children

Sign or symptom	Adults	Children
Duration of illness	5–7 days	1–2 days
Resolution of coma	2–4 days	1–2 days
Neurological sequelae	Uncommon	Common
Jaundice	Common	Uncommon
Pre-treatment hypoglycaemia	Less common	Common
Pulmonary oedema	Uncommon	Rare
Acute respiratory distress syndrome	Common	Rare
Acute kidney injury	Common	Common
CSF opening pressure	Usually, normal	Usually raised
Respiratory distress (acidosis)	Common	Common
Bleeding/clotting disorders	Uncommon	Rare
Invasive bacterial infection (co-infection)	Uncommon	Common

6.2 Treatment of Severe Malaria

Severe malaria is a medical emergency and as such treatment should begin immediately, whether the patient presents at the community level, health centre, or at a hospital. The commencement of life-saving therapy must not be delayed.

6.2.1 Pre-referral Treatment of Severe Malaria

When severe malaria is suspected at the community level, pre-referral treatment should be initiated immediately with rectal artesunate and the patient should be referred to the nearest health facility for further evaluation and management. Refer to **Table 2.3**.

At the health centre level, intramuscular (IM) artesunate is the recommended pre-referral treatment. However, intramuscular quinine – administered in the thigh, not the buttock – may be used when IM artesunate is not available or is contraindicated. If neither IM therapy is available, rectal artesunate should be used only to children below the age of 6 years. Personnel at health centres should refer any patient with suspected severe malaria to a hospital for further evaluation and management.

6.2.1.1 Recommendation for pre-referral treatment at the community Level

For patients with severe malaria

Consensus recommendation

Rectal artesunate is recommended at the community level as immediate pre-referral treatment for children with suspected severe malaria, followed by urgent referral to the nearest health facility for further evaluation and definitive management.

6.2.1.1.1 Rectal Artesunate

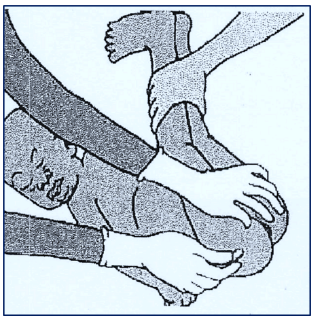
For children: One or more artesunate suppositories inserted in the rectum should be given immediately and followed as soon as possible by definitive therapy for severe malaria at a hospital. The buttocks should be held together for 10 minutes to ensure retention of the rectal dose, especially in young children. **Table 2.3** shows the recommended pre-referral doses of artesunate suppositories for children aged < 6 years. If referral is not possible within 12 hours, a second dose of rectal artesunate should be administered at 12 hours after

the initial dose. Thereafter rectal artesunate may be given every 24 hours. However, this treatment is suboptimal, and every effort should be made to refer the patient as soon as possible.

Table 2.3: Initial (pre-referral) Dosage of Artesunate Suppositories for Children Aged <6 Years

Age (Months)	Weight (Kg)	Artesunate dose (mg)	Regimen (single dose)
6 months to < 3 years	5 to < 10	100	One 100 mg suppository
> 3 years to 6 years	11 to 20	200	Two 100 mg suppositories

Figure 2.1: Insertion of rectal suppository



Here are 4 easy steps to insert a suppository:

- Put on a new pair of gloves (i.e., not used before)
- Ask the caregiver to hold the child for you in the position shown
- Insert the suppository, the larger rounded side first, pushing it with one of your fingers. Hold child's buttocks together for 10 minutes or so to make sure that the suppository is not expelled
- Dispose of the gloves so that they cannot be reused

6.2.1.2 Recommendation for pre-referral treatment at the health centre level

For patients with severe malaria

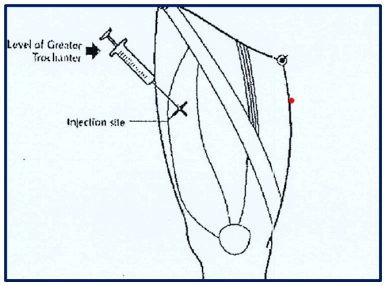
Consensus recommendation

Intramuscular (IM) artesunate is recommended as the medicine of choice for pre-referral treatment of severe malaria at the health centre level. If IM artesunate is unavailable or contraindicated, IM quinine should be administered in the thigh (not the buttock). If neither IM artesunate nor IM quinine is available, rectal artesunate should be used in children under 6 years of age; rectal artesunate is contraindicated in children over 6 years. All patients should be referred immediately to a hospital for further evaluation and definitive management.

6.2.1.2.1 Intramuscular Artesunate

The recommended dose of IM artesunate for infants and children whose body weight is <20 kg should be 3 mg/kg (0.15 ml/kg). For children weighing 20 kg and above, and adults the dosage should be 2.4 mg/kg (0.12 ml/kg) body weight. Artesunate should be given by intramuscular injection into the upper-outer quarter of anterior thigh and **should not be injected into the buttocks**.

Figure 2.2: Administration of Intramuscular Injections



To prepare IM artesunate, weigh the patient and determine the number of vials needed for treatment, according to Table 2.4 below.

Table 2.4: Number of Required Vials for Parenteral Artesunate by Body Weight

Weight	60 mg vials required	120 mg vials required
< 20 kg	1	1
20 kg – 50 kg	2	1
51 kg – 75 kg	3	2
> 75 kg	4	2

Each 60 mg vial of injectable artesunate must be reconstituted with **1 ml of sodium bicarbonate**. Dilute the artesunate-bicarbonate mixture with **2 ml of 5% dextrose solution or normal saline (0.9% Sodium Chloride)** to produce a **20 mg/ml solution**. In case you have **120 mg vial of injectable artesunate**, reconstituted with **2 ml of sodium bicarbonate**. Dilute the artesunate-bicarbonate mixture with **4 ml of 5% dextrose solution or normal saline (0.9% Sodium Chloride)** to produce a **20 mg/ml solution**.

In case you have **single solvent injectable artesunate**, the following steps must be followed: reconstitute artesunate powder with sodium bicarbonate ampule to produce a concentration **20 mg/ml** for IM and IV administration. Withdraw the appropriate volume in a syringe (**children <20kgs, give 3 mg x body weight in kg, and children >20kg and adults, give 2.4 mg x body weight in kg)/10 mg/ml**) for intramuscular injection, rounding to the next whole number in milliliters.

Table 2.5: Number of Required Vials for Parenteral single solvent Artesunate

Strength	60 mg vials required	120 mg vials required
Sodium bicarbonate and Arginine volume (ml)	3	6
Artesunate concentration	20 mg/ml	20 mg/ml

Administration of pre-referral IM artesunate should be followed as soon as possible by definitive therapy for malaria at a hospital. If referral is not possible within **12 hours**, a second dose of IM artesunate should be administered at **12 hours** after the initial dose. If referral is still not possible after **24 hours**, a third dose of IM artesunate should be given.

6.2.1.2.2 Intramuscular Quinine

Intramuscular quinine should be used for pre-referral treatment of severe malaria in instances where IM artesunate is either unavailable or contraindicated. The recommended dose of IM quinine is **10 mg (0.2 ml) per kg body weight**.

To administer intramuscular quinine, use a **10 ml sterile syringe** to draw **5 ml of sterile water for injection**, then into the same syringe draw up **300 mg (1 ml)** from an ampoule of quinine. The syringe now contains **50 mg of quinine per ml**. Withdraw the appropriate volume and administer into the **upper outer thigh**. If the volume to be injected exceeds **3 ml**, give half into each thigh. An example of body weights and dosing (ml) for IM quinine is given in **Table 2.6 below**.

Table 2.6: Sample Dosages of IM Quinine by Body Weight

Body weight	Quinine (ml)
Under 5 kg	1.0 ml
5.1 – 7.5 kg	1.5 ml
7.6 – 10.0 kg	2.0 ml
10.1 – 12.5 kg	2.5 ml
12.6 – 15.0 kg	3.0 ml
15.1 – 17.5 kg	3.5 ml
17.6 – 20.0 kg	4.0 ml
20.1 – 22.5 kg	4.5 ml
22.6 – 25.0 kg	5.0 ml
25.1 – 27.5 kg	5.5 ml
27.6 – 30.0 kg	6.0 ml

Administration of pre-referral IM quinine should be followed as soon as possible by definitive therapy for malaria at a hospital. If referral is not possible within **12 hours**, a second dose of IM quinine should be administered **12 hours after the initial dose**. If referral is still not possible after **24 hours**, a third dose of IM quinine should be given.

6.2.2 Management of Severe Malaria in the in-Patient Setting

6.2.2.1 The 8-8-8 schedule

The health worker should consider following the 8-8-8 schedule (described in Boxes 1-3 below) in the management of patients with severe malaria.

Box 1: Take 8 Immediate Measures

1.Start resuscitation, particularly maintenance of a patent airway and breathing.
2.Establish IV line.
3.Make thick and thin blood smear on the same slide for immediate malaria parasite count
(if microscopy is not available, an mRDT may be useful to indicate whether malaria infection is present or not. It is not recommended to use both mRDT and microscopy).
4.Assess for severe dehydration (lethargy, sunken eyes, dry mouth and reduced skin turgor).
Assess patient's fluid requirements and correct accordingly.
5.Control fever if the axillary temperature is 38 °C or above:
Tepid sponge, fanning, and oral paracetamol (10 mg/kg every 6–8 hours)
or rectal paracetamol (15 mg/kg every 4 to 6 hours).
6.Manage convulsions:
Maintain airway and breathing, treat with:

1. rectal diazepam (0.5 mg/kg), or
2. slow IV diazepam (0.3 mg/kg, maximum 10 mg in an adult), or
3. paraldehyde (0.2 ml/kg IM or 0.4 ml/kg rectal).
   Remember to correct any hypoglycaemia or hyperpyrexia in a convulsing patient.

7.Detect and treat hypoglycaemia:
Hypoglycaemia can be induced by high parasitaemia, fasting and quinine therapy and can recur, especially in pregnant women and children.

1. Children:
   If blood glucose is ≤2.5 mmol/l (≤45 mg/dl) in well-nourished children or ≤3 mmol/l (≤54 mg/dl) in severely malnourished children:
   give 5 ml/kg of 10% glucose IV slowly over 3–5 minutes, recheck after 30 minutes and repeat if still low.
2. Adults:
   If blood glucose is ≤3.8 mmol/l (≤70 mg/dl), give 50 ml of 50% dextrose IV stat slowly over 3–5 minutes and recheck after 30 minutes.

8.If there is no test for blood glucose, treat as if the patient is hypoglycaemic.
9.Start intravenous or intramuscular artesunate.
Dosage schedule is provided in section 2.2.2.2 below.
If intravenous or intramuscular artesunate is unavailable, use intravenous or intramuscular quinine.

Box 2: Look for and Deal with the Following 8 Complications

1. Shock
If cold peripheries, delayed capillary refill >3 seconds, fast weak pulse, or systolic BP <50 mmHg in children 1–5 years or <80 mmHg in >5 years, suspect Gram-negative septicaemia.
•Take blood samples for culture.
•Give parenteral broad-spectrum antimicrobials.
•Correct fluid disturbance by giving a bolus of 10 ml/kg Ringer's lactate over 1 hour; may repeat boluses until a maximum of 40 ml/kg has been given.
•Then consider blood transfusion and continue with maintenance fluids as follows:
- Children <10 kg: 4 ml/kg/hour
- Children 10–20 kg: 40 ml/hour plus 2 ml/kg for each kg over 10 kg
- Children >20 kg: 60 ml/hour plus 1 ml/kg for each kg over 20 kg

•Give oxygen if possible.

2. Altered consciousness and/or convulsions
Check for hypoglycaemia, hyperpyrexia, and *subtle* seizures.
In a comatose patient, seizures may be subtle, e.g. flickering of eyelids, mouth or fingers; unusual repetitive movements (rhythmical cry, abnormal breathing, or "pedalling" of legs).
•If seizure is suspected, treat as in Item 6 of Box 1.

3. Severe anaemia
Assess the need for blood transfusion.
•Assess degree of pallor (palms of hands and mucous membranes).
•Assess danger signs: respiratory distress, altered consciousness, shock, and hyperparasitaemia.
Note:
The decision to transfuse should not be based on laboratory values alone, but on full clinical assessment.
•All patients with PCV <12% or Hb <4 g/dl should be transfused regardless of clinical state.
•Patients with danger signs may be transfused even if PCV 13–18% or Hb 4–6 g/dl.

4. Blood transfusion
•Transfuse packed red cells in most cases.
•In shock or severe acidosis, use whole blood.
•Volume transfused: 20 ml/kg.

5. Metabolic acidosis (deep, fast breathing)
Exclude or treat hypoglycaemia, hypovolaemia, and Gram-negative septicaemia.
•Give isotonic saline 20 ml/kg rapidly, or screened whole blood 10 ml/kg if PCV <18% or Hb <6 g/dl.
•Rule out lactic acidosis.

6. Spontaneous bleeding or coagulopathy
If underlying malnutrition, hepatic obstruction, bile salt excretion defects, or prolonged fasting (>3 days):
•Transfuse screened fresh whole blood.
•Give Vitamin K 10 mg IV slowly once daily for 3 days.
•For children: 2–3 mg/day IV slowly.
Vitamin K should not be given routinely to all severe malaria patients with bleeding; weigh risks and benefits.
Serious adverse events include hypotension, breathing difficulty, bradycardia, or anaphylaxis.
•Acute pulmonary oedema:
- Prevent by avoiding over-hydration.
- Treatment: sit patient upright, give oxygen, stop IV fluids if due to over-hydration, give diuretic (furosemide IV 40 mg in adults; 0.5–1 mg/kg/dose in children).

•Acute respiratory distress syndrome:
- Supportive treatment ± ventilation.

7. Acute kidney injury
Detect by monitoring fluid balance.
•Identify and correct dehydration or hypovolaemia.
•Maintain strict fluid balance.
•Consider peritoneal dialysis if oliguria persists beyond a few days.

Note:
Many children recover from severe anaemia with antimalarial drugs alone.
Because of the risk of blood transfusion (HIV, hepatitis), transfuse **only if essential** for recovery.

Box 3: Monitor the Following 8 Observations
Where possible, use Critical Care Pathways (CCPs).
1.Level of consciousness
Monitor using a coma score (see annex).
2.Vital signs
Record every 4 hours: temperature, pulse, respiration, and blood pressure.
3.Fluid balance
Monitor urine output and intake volumes (IV and oral). Watch for signs of fluid overload, including puffy eyes, chest crepitations, and elevated jugular venous pressure.
4.Increasing anaemia
Look for pallor and signs of heart failure, including increasing liver size.
5.Occurrence of convulsions
Manage as described in Item 2 of Box 2.
6.Blood glucose
Measure every 4 hours while the patient is unconscious and whenever convulsions occur.
7.Haemoglobin (Hb) / Packed Cell Volume (PCV)
Measure at least daily, or more frequently if anaemia is suspected.
8.Functional ability
Assess the ability to suck, drink, eat, sit, and walk as measures of overall strength and recovery.

Educate the patient and relatives about home prevention of malaria. Counselling should be provided after the patient has recovered.

6.2.2.2 Recommendation for severe Malaria in the In-patient setting

For patients with severe malaria

Consensus recommendation

For the definitive treatment of severe malaria in the In-pateint setting, parenteral artesunate is recommended. If parenteral artesunate is unavailable or contraindicated, parenteral quinine is recommended as an alternative.

6.2.2.2.1 Severe Malaria Treatment with Parenteral Artesunate

Intravenous (IV) artesunate is the treatment of choice for the management of severe malaria. Artesunate may also be administered intramuscularly if intravenous bolus administration is not feasible.

- For **children weighing <20 kg**, give artesunate **3 mg/kg body weight**.
- For **children weighing ≥20 kg and adults**, give artesunate **2.4 mg/kg body weight** IV or IM on admission (at 0 hour), then repeat at **12 hours and 24 hours**, and thereafter **once daily** for not more than **six days**.

Once the patient can tolerate oral treatment and **at least 24 hours of parenteral artesunate** has been administered, discontinue parenteral therapy and commence a full course of **lumefantrine–artemether (LA)** or **dihydroartemisinin–piperaquine (DP)**.
There should be an **interval of at least 8 hours** between the last dose of artesunate and the first dose of LA or DP.

Artesunate is supplied as a powder of artesunic acid and must be dissolved in **5% sodium bicarbonate** to form sodium artesunate. The solution is then diluted in approximately **5% dextrose**.

When administered intramuscularly, artesunate should be injected into the **upper-outer quarter of the anterior thigh**. **Artesunate or quinine should never be injected into the buttocks.**

The solution should be **freshly prepared immediately prior to administration** and **must not be stored**.

Preparation and Administration of Parenteral Artesunate

To prepare IV artesunate, weigh the patient and determine the number of vials required for treatment according to **Table 2.6**.

Table 2.7: Number of Required Vials for Parenteral Artesunate by Body Weight

Body weight	60 mg vials required	120 mg vials required
<20 kg	1	1
20–50 kg	2	1
51–75 kg	3	2
>75 kg	4	2

T**able 2.8: Use of 30 mg, 60 mg, and 120 mg vials of injectable artesunate to minimise wastage**

Intramuscular (IM) Route

Body weight	Vials required	Dose (ml)
1–6 kg	1 × 30 mg	1 ml
7–25 kg	1 × 60 mg	2–3 ml
26–33 kg	1 × 30 mg + 1 × 60 mg	4 ml
34–50 kg	1 × 120 mg	5–6 ml
51–58 kg	1 × 30 mg + 1 × 120 mg	7 ml
58–75 kg	1 × 60 mg + 1 × 120 mg	8–9 ml
76–83 kg	1 × 30 mg + 1 × 60 mg + 1 × 120 mg	10 ml
84–100 kg	2 × 120 mg	11–12 ml

Intravenous (IV) Route

Body weight	Vials required	Dose (ml)
1–10 kg	1 × 30 mg	1–3 ml
11–25 kg	1 × 60 mg	4–6 ml
26–37 kg	1 × 30 mg + 1 × 60 mg	7–9 ml
39–50 kg	1 × 120 mg	10–12 ml
51–62 kg	1 × 30 mg + 1 × 120 mg	13–15 ml
63–75 kg	1 × 60 mg + 1 × 120 mg	16–18 ml
76–87 kg	1 × 30 mg + 1 × 60 mg + 1 × 120 mg	19–21 ml
91–100 kg	2 × 120 mg	22–24 ml

Preparation of Injectable Artesunate

Each **60 mg vial** of injectable artesunate must be reconstituted with **1 ml of sodium bicarbonate**.

- For **intravenous (IV) bolus injection**, dilute the artesunate–bicarbonate mixture with **5 ml of 5% dextrose solution or normal saline (0.9% sodium chloride)** to produce a **10 mg/ml solution**.

If using a **120 mg vial** of injectable artesunate:

- Reconstitute with **2 ml of sodium bicarbonate**.

- For **IV bolus injection**, dilute the artesunate–bicarbonate mixture with **10 ml of 5% dextrose solution or normal saline (0.9% sodium chloride)** to produce a **10 mg/ml solution**.

6.2.2.2.2 Severe Malaria Treatment with Parenteral Quinine

Parenteral quinine should be used for the treatment of severe malaria **only when parenteral artesunate is not available or is contraindicated**.

Quinine Treatment in Children
Intravenous quinine should be administered as follows:

- **Initial (loading) dose:**
  Give **20 mg (quinine salt) per kg body weight**, diluted in **10 ml/kg of 5% dextrose or half-strength Darrow's solution**, and **infuse over 3–4 hours**.
- **If the patient has already received quinine for the current illness:**
  Do **not** give a loading dose.
  Instead, give **10 mg/kg**, diluted as above, and infuse over **3–4 hours**.
- **Subsequent doses:**
  Give **10 mg/kg every 12 hours**, with each infusion administered over **3–4 hours**.
- **Between quinine doses:**
  Continue **5% dextrose or half-strength Darrow's IV fluids** at **10 ml/kg**, infused over **3–4 hours**.

Stop intravenous quinine as soon as the child is able to take food and fluids orally **and** has received **at least 24 hours of parenteral quinine**.
Begin age- or weight-appropriate oral treatment with **lumefantrine-artemether (LA) or dihydroartemisinin-piperaquine (DP) 12 hours after the last dose of quinine**.

Note: Quinine dosing intervals should be calculated **from the start of the IV infusion**, not from the end.

Quinine Treatment in Adults
If the adult patient **can be weighed**, administer intravenous quinine **using the same weight-based regimen as for children**.

If the patient **cannot be weighed**, administer intravenous quinine as follows:

- **First dose:**
  Give **900 mg** diluted in **1 litre of 5% dextrose or half-strength Darrow's solution**, infused over **3–4 hours**.
- **Subsequent doses:**
  Give **600 mg** diluted in **1 litre of 5% dextrose or half-strength Darrow's solution** every **12 hours**, infused over **3–4 hours**.
- **Between doses:**
  Continue IV fluids (5% dextrose, half-strength Darrow's solution, or Ringer's lactate) at **10 ml/kg infused over 3–4 hours**, with a **maximum total fluid volume of approximately 3 litres per 24 hours** to avoid fluid overload.

Stop intravenous quinine as soon as the patient can take food and fluids orally and has received **at least 24 hours of parenteral quinine**.
Start **LA or DP 12 hours after the last dose of quinine**.

Important Safety Note
LA or DP must only be started at least 12 hours after the last dose of quinine, in order to **reduce the risk of cardiotoxicity**.

6.3 Post-Discharge Malaria Continuum of Care (PDMCC)

Post-Discharge Malaria Continuum of Care (PDMCC) refers to the **continuous administration of a full antimalarial treatment course at regular intervals** for **children under five years of age** who are discharged from hospital following **severe malaria or severe anaemia**.

Recent studies conducted in **Malawi and other settings** have shown that **within six months after hospital discharge for severe anaemia or malaria**, these children have a **five-fold increased risk of readmission or death** due to the same conditions. PDMCC aims to reduce this high post-discharge vulnerability.

6.3.1 Recommendation for Post-discharge malaria continuum of care (PDMCC)

For patients with severe malaria

Consensus recommendation

Post-discharge malaria continuum of care (PDMCC) is recommended to be administered for three consecutive months, beginning two weeks after discharge for children initially treated with artemether–lumefantrine (AL) and four weeks after discharge for those treated with dihydroartemisinin–piperaquine (DP), and to be delivered through either health facility or community-based models in accordance with national guidance.

6.3.2 Implementation of PDMCC

The PDMCC treatment is provided over a period of **three consecutive months**:

- Treatment begins **two weeks after discharge** for children who were discharged on **lumefantrine-artemether (LA)**.
- Treatment begins **four weeks after discharge** for children who were discharged on **dihydroartemisinin-piperaquine (DP)**.

The **World Health Organization (WHO)** recommends the use of post-discharge malaria continuum of care in these children to reduce the risk of **readmission and death**. Evidence shows that PDMCC is highly effective, reducing:

- Severe malaria by **87%**,
- Severe anaemia related to malaria by **89%**, and
- Readmissions and deaths by **70%**.

In view of this strong evidence and in line with WHO recommendations, the **Ministry of Health (MOH)** recommends implementation of the PDMCC intervention in Malawi. With the adoption of **DP as the first-line treatment policy**, the MOH recommends the use of **DP for PDMCC** as the continuation-of-care regimen.

Delivery Models for PDMCC

PDMCC is delivered using **two models**:

1. **Health facility model**
   - Delivered through nearby **hospitals or health centres**
   - PDMCC is provided by **clinicians and nurses**
2. **Community model**
   - Delivered through **village clinics**
   - PDMCC is provided by **integrated Community Case Management (iCCM) providers** using updated iCCM tools

For detailed operational guidance, refer to the **Malaria Case Management Participant's Manual** and **iCCM training manuals**.

7. MALARIA IN PREGNANCY

Pregnancy increases the risk of malaria infection in all women. Malaria during pregnancy can cause **febrile illness and anaemia**, and increases the risk of **maternal and neonatal complications**, including **miscarriage, stillbirth, low birth weight**, and, if left untreated, **maternal and neonatal death**.

Women in their **first and second pregnancies**, as well as **all HIV-infected women**, are at increased risk of the adverse effects of malaria. All pregnant women living in malaria-risk areas should be counselled on **malaria prevention measures** and the importance of **early diagnosis and timely clinical management** using effective antimalarial medicines.

7.1 Intermittent Preventive Treatment of Malaria in Pregnancy (IPTp)

Intermittent Preventive Treatment of malaria in pregnancy (IPTp) is one of the **key malaria prevention strategies** in Malawi.

7.1.1 Recommendation for Intermittent Preventive Treatment of malaria in pregnancy

For preventing malaria in pregnant patients

Consensus recommendation

We recommend intermittent preventive treatment of malaria in pregnancy (IPTp) with sulfadoxine–pyrimethamine (SP), administered as at least three doses starting after the first trimester (from 13 weeks), in accordance with national IpTp policy.

7.1.1.1 Sulfadoxine-Pyrimethamine

IPTp should be administered as follows:

- Begin IPTp from **13 weeks of gestation**
- Administer **three tablets of SP** at each scheduled antenatal care visit
- Doses should be given **at least four weeks apart**
- SP should be administered as **directly observed therapy (DOT)**
- The **last dose of SP can be safely taken at the time of delivery**
- SP may be taken **with food or on an empty stomach**

Note:
HIV-positive women receiving **cotrimoxazole prophylaxis** should **not receive SP**.

Benefits of Receiving at Least Three Doses of SP
Receiving at least three doses of SP during pregnancy has the following benefits:

- Increases **mean birth weight**
- Reduces the number of **low-birth-weight infants**
- Reduces **placental parasitaemia**
- Reduces **maternal parasitaemia**

Although IPTp significantly reduces the risk of malaria during pregnancy, **clinical malaria episodes can still occur** in women who have received IPTp. Pregnant women presenting with symptoms suggestive of malaria should therefore be **promptly tested and treated according to national guidelines**.

7.2 Management of Malaria in Pregnancy

As in non-pregnant adults, malaria in pregnancy should be managed according to its clinical presentation, either as an **uncomplicated febrile illness** or as **complicated (severe) malaria.**

7.2.1 Clinical Features of Malaria in Pregnancy

The clinical manifestations of malaria in pregnant women are generally similar to those seen in non-pregnant women.

However, pregnant women are at **increased risk of specific complications**, particularly:

- **Hypoglycaemia**, especially as a consequence of treatment with quinine
- **Anaemia**
- **Pulmonary oedema**

These complications may occur more frequently and can be more severe in pregnancy.

7.2.2 Recommendation for treatment of uncomplicated malaria in pregnancy

For pregnant patients with uncomplicated malaria

Consensus recommendation

We recommend Dihydroartemisinin–piperaquine (DP) or Lumefantrine Artemether (LA) for the treatment of uncomplicated malaria in pregnant women in all trimesters.

In pregnant women with confirmed treatment failure following DP or LA in any trimester, changing treatment to artesunate–amodiaquine (ASAQ) is recommended.

7.2.2.1 LA and DP for Uncomplicated Malaria in Pregnancy

Management of malaria in pregnancy includes:

- Treatment of malaria
- Management of complications
- Management of labour, where applicable

Treatment should be **initiated as early as possible**.

Dihydroartemisinin–piperaquine (DP) and lumefantrine–artemether (LA) are **safe for use in all trimesters of pregnancy**. Therefore, all pregnant women with uncomplicated malaria should be treated with **DP or LA**.

Refer to:

- **Table 1.2** for DP dosing
- **Table 1.3** for LA dosing

Note:
If there is a **confirmed treatment failure** with DP or LA in pregnant women in any trimester, treatment should be changed to **artesunate–amodiaquine (ASAQ)**, as outlined in **Table 1.5**.

7.2.3 Management of Severe Malaria in Pregnancy

In the management of **severe malaria in pregnancy**, special attention must be given to **anaemia, hypoglycaemia, and pulmonary oedema**. These complications occur more frequently in pregnant women and may be life-threatening if not promptly recognised and managed.

Management of complications follows the **same principles as for non-pregnant adults**, as outlined in the **8-8-8 schedule**. However, certain complications require particular vigilance in pregnancy, as detailed below.

Box 4: Management of Complications in Severe Malaria during Pregnancy
(See the 8-8-8 schedule above)
The management of complications in pregnancy is generally the same as for other adults. Complications of particular importance in pregnancy include:
•**Pulmonary oedema**
Careful fluid management is essential. Use diuretics if necessary, provide oxygen where available, and nurse the patient in a semi-upright position.
•**Hypoglycaemia**
Hypoglycaemia should be suspected in any pregnant woman with altered consciousness or seizures. Management should follow the guidance outlined in **Item 2 of Box 2**.
•**Anaemia**
Be prepared for blood transfusion, particularly if the patient is close to delivery. In other situations, indications for transfusion are the same as for non-pregnant patients (see **Box 2**).
•**Acute kidney injury**
This is a particular concern if the patient has had **eclampsia or shock**. Identification and management should follow the guidance in **Box 2, Item 7**.
•**Shock**
Consider concealed haemorrhage, ongoing blood loss, and septicaemia. Pay close attention to fluid requirements. Obtain blood cultures if possible and administer **broad-spectrum antibiotics** in addition to quinine.

7.2.4 Recommendation for treatment of severe malaria in pregnancy

For pregnant patients with severe malaria

Consensus recommendation

We recommend **Parenteral artesunate** for the treatment for severe malaria in **all pregnant women**, regardless of trimester.

7.2.4.1 Parenteral artesunate of severe malaria in pregnancy

Parenteral artesunate is the recommended treatment for severe malaria in **all pregnant women**, regardless of trimester.

Artesunate should be administered at a dose of **2.4 mg/kg body weight**, given intravenously (IV bolus) or intramuscularly (IM) on admission (**0 hour**), then repeated at **12 hours** and **24 hours**, followed by **once daily dosing** thereafter for a maximum duration of **six days**.

Once the patient is clinically stable, able to tolerate oral medication, and has received **at least 24 hours of parenteral therapy**, parenteral artesunate should be discontinued and a **full 3-day course of oral artemisinin-based combination therapy**, either **dihydroartemisinin–piperaquine (DP)** or **lumefantrine–artemether (LA)**, should be commenced.

Alternative Treatment When Artesunate Is Unavailable or Contraindicated
Pregnant women in **all trimesters** may be treated with **parenteral quinine** if artesunate is unavailable or contraindicated.

Quinine should be administered as follows:

- **Loading dose:** 20 mg/kg body weight
- **Maintenance dose:** 10 mg/kg body weight **every 12 hours**

Treatment should continue until the patient can take oral medication and has received **at least 24 hours of parenteral therapy**, after which oral DP or LA should be initiated.

Special Circumstances

- **If the patient cannot be weighed:**
  Start treatment with an infusion of **900 mg quinine in 1 litre of 5% dextrose**.
- **If quinine cannot be given by infusion:**
  Administer **quinine 10 mg/kg by intramuscular injection**.
  Ensure that **10% glucose or 5% glucose** is given before quinine administration to reduce the risk of hypoglycaemia. Care must be taken to avoid fluid overload and **pulmonary oedema**.
- **Blood glucose monitoring:**
  Random blood glucose should be measured **before and after quinine administration**, given the high risk of quinine-induced hypoglycaemia in pregnancy.

Transition to Oral Therapy

Switch to **DP or LA** as soon as the patient is able to tolerate oral medication and has completed **at least 24 hours of parenteral therapy**.

7.3 Specific Messages for Pregnant Women

- Health education for pregnant women should strongly encourage **early attendance at antenatal care (ANC) clinics**, ideally as soon as pregnancy is suspected.
- **All pregnant women presenting with fever** should be promptly **tested for malaria** and treated according to national malaria treatment guidelines.
- **Intermittent Preventive Treatment in pregnancy (IPTp)** should be taken **in conjunction with other acceptable and available malaria preventive measures**, such as use of insecticide-treated nets.
- **Malaria prevention and treatment services provided during ANC** should be considered an **integral component of maternal and child health (MCH) services**, contributing to improved health outcomes for both mother and child.

8. Guide To COMA SCALES

8.1 Assessing Level of Consciousness Using Coma Scales

All patients who fulfil the clinical diagnosis of **severe malaria**, defined as malaria with a **reduced level of consciousness**, should have their level of consciousness assessed using a **coma scale**. This allows monitoring of the patient's clinical status and response to treatment over time.

The choice of coma scale depends on the patient's age:

- The **Blantyre Coma Scale (BCS)** is used for **children under 12 years of age**.
- The **Glasgow Coma Scale (GCS)** is used for **children aged 12 years and older and for adults**.

8.1.1 Blantyre Coma Scale (for children <12 years)

The Blantyre Coma Scale is a **simple and rapid tool** that can be used by any trained health worker. The **maximum score is 5**, which indicates a fully conscious child.

The scale assesses **three responses**:

1. Eye movement
2. Verbal response
3. Best motor response

Each response is scored individually, and the **sum of the three scores gives the total coma score**. The score should be recorded **daily or more frequently**, depending on the clinical condition, to assess response to treatment.

Table 4.1: Blantyre Coma Scale Scoring

Component	Response	Score
Eye movement	Follows (watches mother's face or a coloured object)	1
	Does not follow	0
Verbal response	Appropriate cry	2
	Moan or inappropriate cry	1
	No verbal response	0
Best motor response	Localises painful stimulus*	2
	Withdraws limb from pain	1
	Non-specific or absent response	0
Total score		**0 – 5**

(a) Press knuckles firmly on the patients sternum
(b) Press firmly on the thumbnail bed with side of a horizontal pencil
(c) Press knuckle firmly on the supra-orbital ridge (eyebrow)

Add the scores for each column, to get a total out of 5

The scale can be applied repeatedly to assess improvement or deterioration. Total score for a fully conscious child is 5/5, and for a totally unresponsive child is 0/5

8.2 Glasgow Coma Scale

The Glasgow Coma Scale provides a score in the range of three to 15. Patients with scores of three to eight are usually said to be in a coma. To determine the Glasgow coma score, calculate the score for each section and add the three figures. The scores for adults are outlined in Table 4.2 below. (Note that the minimum possible Glasgow Coma Scale score is 3, while the minimum Blantyre Coma Scale score is zero).

Table 4.2: The Glasgow Coma Scale (for adults and children 12 years and older)

Category	Response	Score
Eyes open	Spontaneously	4
	To speech	3
	To pain	2
	Never	1
Best verbal response	Oriented	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	None	1
Best motor response	Obeys commands	6
	Localizes pain	5
	Withdraws from pain	4
	Flexion to pain	3
	Extension to pain	2
	None	1
Total		**3–15**

9. Selective Antimalarial Chemoprophylaxis

9.1 Risk Groups

The following high-risk groups should be given antimalarial chemoprophylaxis:

- Patients who have had a splenectomy;
- Those taking cytotoxic or immunosuppressive drugs for malignant disease;
- Hyper-reactive malarial splenomegaly (previously known as tropical splenomegaly syndrome)
- Children who have had recurrent severe malaria;
- Individuals with sickle cell disease;
- Visitors from countries where there is no malaria transmission.

9.2 Giving Advice about Malaria Prophylaxis

Emphasize that no prophylaxis is 100% effective. (e.g. "Don't assume the fever could not be malaria, just because you have been taking these tablets.") Advise other measures also (especially to sleep under an insecticide-treated bed net every night and to promptly seek care in the event of a fever).

9.3 Recommendation for antimalarial prophylaxis regimens

For high-risk groups and non-immune individuals travelling to or residing in malaria-endemic areas

Consensus recommendation

Recommendation:

We recommend selective antimalarial chemoprophylaxis for high-risk groups and non-immune individuals travelling to or residing in malaria-endemic areas, using one of the following regimens as appropriate: doxycycline, mefloquine, atovaquone–proguanil, chloroquine (where effective) combined with proguanil, or proguanil with weekly chloroquine. Appropriate counselling on adherence, recognition of fever, and additional preventive measures such as insecticide-treated bed nets should be provided.

9.3.1 Doxycycline 100 mg daily.

- Begin 1–2 days before travel to malaria-endemic areas, continue while in malaria-endemic areas, and daily for 4 weeks after leaving the endemic areas.
- Good for last minute travellers.
- Prophylaxis in all malaria-endemic areas. Give 2.2 mg/kg body weight (maximum 100 mg per day)
- It can cause photosensitivity skin reactions.
- Doxycycline is strongly contraindicated during pregnancy, breastfeeding and in children aged <8 years.

9.3.2 Mefloquine (Lariam) 250 mg weekly.

• Begin taking ≥2 weeks before travel to malaria-endemic areas. Take 1 tablet weekly, on the same day each week while in malaria-endemic areas. Continue taking 1 tablet once a week for another 4 weeks after leaving endemic areas.

• Give 5mg/kg body weight

• Prophylaxis in areas with mefloquine-sensitive malaria. Good choice for long trips because it is taken once a week. Can be used in all trimesters of pregnancy and during breastfeeding. Contraindicated in pilots. Not a good choice for last-minute travellers because drug needs to be started at least 2 weeks before travel

• Some people react badly – headache, insomnia, and feeling of unreality. In very few people there may be serious effects: psychosis, ataxia, convulsions. Therefore, contraindicated in pilots etc. Avoid mefloquine in people with a history of cardiac disease, neurological disease or depression, and in those taking beta blocking drugs. Quite expensive, and not widely available within Malawi.

• There is no evidence that mefloquine is harmful in pregnancy. However, many prefer not to use it during pregnancy.

9.3.3 Atovaquone 250mg-Proguanil 100mg (Malarone-fixed dose combination) one tablet daily.

Begin 1–2 days before travel to malaria-endemic areas, continue while in malaria-endemic areas, and daily for 7 days after leaving the endemic areas.

• Extremely expensive, so suitable only for short-term use.

• It has the advantage (for travellers) that it needs to be taken only once a day and for only one week after exposure ends.

• Prophylaxis in all malaria-endemic areas.

• Available paediatric Atovaquone 62.5mg-Proguanil 25mg.

• Contraindicated in people with severe renal impairment (creatinine clearance <30 mL/min), children weighing <5 kg, women who are pregnant or breastfeeding infants weighing <5kg.

9.3.4 Chloroquine 300 mg (base) (2 tablets) weekly

• If the above options are not possible, chloroquine may now be efficacious in Malawi but should be combined with daily proguanil (see below). *[P falciparum resistance to chloroquine was extensive in Malawi in the 1990s, but is now diminished. Chloroquine causes itching in 40% of black people. Avoid in persons with psoriasis or epilepsy.]*

• Prophylaxis only in areas with chloroquine-sensitive malaria.

• Give 5mg/kg base.

• Take 2 tablets weekly.

• Begin taking 1–2 weeks before travel to malaria-endemic areas, continue the same day each week while in malaria-endemic areas, and weekly for another 4 weeks after leaving the endemic areas.

Note: There is risk of retinal damage if chloroquine is taken every week for more than 5 years. For clients expected to use chloroquine for longer than 5 years, a baseline retinal exam should be conducted at the onset of prophylaxis, and annual exams should be conducted beginning after 5 years of use

9.3.5 Proguanil (Paludrine) 200 mg daily

• Very few problems.

• Mouth ulcers sometimes troublesome.

• Moderately effective.

• Should combine with an additional drug such as weekly chloroquine.

• Chloroquine and proguanil are safe in pregnancy.

9.4 Health Education Messages for Persons Receiving Chemoprophylaxis

Health education should be provided to the individuals at risk and to the general population through the health care workers, PHC system and existing village structures. The chemoprophylactic drug regimen should be explained carefully to all patients or guardians to ensure compliance at home.

10. Monitoring and auditing criteria

Implementation of this guideline will be monitored by the Ministry of Health through the National Malaria Control Programme (NMCP) using routine health information systems, therapeutic efficacy surveillance, supervisory visits, and periodic programme evaluations.

Key indicators include:

- Proportion of suspected malaria cases tested prior to treatment.
- Proportion of confirmed cases receiving recommended first-line therapy.
- Proportion of severe malaria cases treated with parenteral artesunate.
- Coverage of IPTp-SP among eligible pregnant women.
- Proportion of eligible children enrolled in and completing post-discharge malaria continuum of care (PDMCC).
- Availability of recommended antimalarial medicines at facility level.

Therapeutic efficacy studies and resistance surveillance will inform ongoing policy decisions and trigger guideline review where necessary.

For recommendations developed using the GRADE approach and hosted in MAGICapp, version control, evidence updates, and transparent documentation of changes will support continuous monitoring and timely updating of recommendations as new evidence emerges. Implementation data and programme feedback may be used to inform future revisions, ensuring that recommendations remain current, context-appropriate, and responsive to national malaria trends.

The guideline should be reviewed periodically, or earlier if significant changes in drug efficacy, resistance patterns, or WHO recommendations occur.

11. ACRONYMS & ABBREVIATIONS

Acronym	Full form
ACTs	Artemisinin-based Combination Therapies
AIDS	Acquired Immunodeficiency Syndrome
ANC	Antenatal Clinic
ART	Antiretroviral Therapy
ASAQ	ArtesunateAmodiaquine
CCP	Critical Care Pathway
CHAI	Clinton Health Access Initiative
DHS	Director of Health Services
DP	Dihydroartemisininpiperaquine
DOT	Directly Observed Therapy
Hb	Haemoglobin
HIV	Human Immunodeficiency Virus
HRP 2	Histidine Rich Protein 2
IM	Intramuscular
IPTp	Intermittent Preventive Treatment in pregnancy
IV	Intravenous
LA or AL	Lumifantrine Artemether or Artemether-Lumefantrine
LA (D)	Artemether-Lumefantrine- Dispersible
LA (ND)	Artemether-Lumefantrine- Non-dispersible
LTK	Learner Treatment Kit
MCH	Maternal and Child Health
MFT	Multiple First-Line Therapies
MoH	Ministry of Health
MP	Member of Parliament
mRDTs	malaria Rapid Diagnostic Tests
NMCP	National Malaria Control Program
PCV	Packed Cell Volume
PDMCC	Post Discharge Malaria Continuum of Care
PHC	Primary Health Care
PMI	President's Malaria Initiative
Pf	*Plasmodium falciparum*
RA	Rectal Artesunate
RBCs	Red Blood Cells
SD	Standard Diagnostics
SP	SulfadoxinePyrimethamine
TBA	Traditional Birth Attendant
WHO	World Health Organization

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