WHO-PQ RECOMMENDED SUMMARY OF PRODUCT CHARACTERISTICS

This summary of product characteristics focuses on uses of the medicine covered by WHO's Prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information from stringent regulatory authorities.[*]

The medicine may be authorised for additional or different uses by national medicines regulatory authorities.

[*]https://extranet.who.int/prequal/sites/default/files/document_files/75%20SRA%20clarification_Feb2017_newtempl.pdf

1. NAME OF THE MEDICINAL PRODUCT

[MA123 trade name]†

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soft gelatin rectal capsules contains 100 mg artesunate

3. PHARMACEUTICAL FORM

Soft gelatin rectal capsules

Teardrop-shaped, opaque off-white soft gelatin rectal capsules. They contain a white to off white oily mass

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

[MA123 trade name] is to be used as pre-referral treatment for suspected or proven severe malaria in children less than 6 years of age, where complete treatment of severe malaria or obtaining a single dose of intramuscular artesunate injection is not possible. The patient should be immediately referred to a facility where accurate diagnosis and comprehensive treatment with effective antimalarials can be instituted.

Consideration should be given to official treatment guidelines for malaria (e.g. by WHO).

4.2 Posology and method of administration

Limitations of use:

- [MA123 trade name] should not be used for patients aged 6 years and over
- [MA123 trade name] should not be used to prevent malaria
- [MA123 trade name] is for severe malaria only, and should not be used for the treatment of uncomplicated malaria

Paediatric population less than 6 years

This medicine is recommended for pre-referral treatment as a single dose of 10 mg/kg bodyweight.

[MA123 trade name] should be given rectally as soon as a presumptive diagnosis of severe malaria has been made, while the patient is being transferred to the nearest health clinic or hospital. In practice, the following dose of [MA123 trade name] may be given:

Patient weight	***Number of (100 mg) rectal capsules***
Up to 10 kg	1 rectal capsule
Up to 20 kg	2 rectal capsules

When referral is not possible

Repeat the dose of artesunate capsule every 12 hours if referral has still not been possible until the child can tolerate oral medication, then start a 3-day treatment course with an appropriate Artemisinin-based Combination Therapy (ACT) to ensure complete cure of the infection.

Severe febrile illness

For community health workers and in places with limited diagnostic capacity for severe malaria, the WHO algorithm for giving rectal artesunate for pre-referral treatment of severe febrile illness in children less than 6 years described below should be followed.

† Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

▪ **if fever AND** ▪ Convulsions or ▪ Unusually sleepy or unconscious or ▪ Not able to drink or feed anything or ▪ Vomits everything	**Give rectal artesunate capsule (100 mg)** ▪ Age 2 months up to 3 years - 1 rectal capsule ▪ Age 3 years to less than 6 years – 2 rectal capsules

Hepatic or Renal impairment

Dose adjustment is not necessary in patients with hepatic or renal impairment (see sections 4.4 and 5.2).

Method of administration

[MA123 trade name] is to be used by the rectal route only.

[MA123 trade name] should be inserted in the rectum with the rounded end first. Administration should be started as soon as a presumptive diagnosis of severe malaria is made, unless the referral time is less than 6 hours. Treatment should be followed as soon as possible by transfer to a hospital.

Care should be taken to be sure that the rectal capsule is retained after insertion. Especially in young children, the buttocks should be held together for about 10 minutes to prevent expulsion of the artesunate rectal capsule. In the event that the dose is expelled from the rectum within 30 minutes of insertion, a repeat dose should be inserted.

Patients and their guardians should be informed that [MA123 trade name] does not cure malaria and that urgent further management of the patient will be necessary; immediate steps should be taken by the guardians of the patient to transport the patient to the nearest health care facility for confirmation of diagnosis and further management, including curative antimalarial therapy.

4.3 Contraindications

Hypersensitivity to artesunate or related artemisinin derivatives or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Referral of patient

[MA123 trade name] is intended for use as stand-by emergency treatment for malaria to enable the patient to reach a facility without complications for complete diagnosis and treatment. Consequently, there should be strong emphasis on proceeding to the nearest facility; referral is important both to complete the treatment of malaria and to diagnose any other underlying life-threatening infection.

Absorption

Absorption of artesunate may be reduced in patients with diarrhoea. If rectal capsules are used in patients with diarrhoea, the patient should be closely monitored. An additional dose of [MA123 trade name] should be administered per rectum if the initial rectal capsule is expelled within 30 minutes.

4.5 Interaction with other medicinal products and other forms of interaction

Artesunate is rapidly and extensively converted to dihydroartemisinin (DHA), the active metabolite, primarily by plasma and erythrocyte esterases. DHA elimination is also rapid (half-life approximately 45 minutes) and the potential for drug-drug interactions appears limited. In vitro drug-interaction studies have demonstrated minimal effects of artesunate on cytochrome P450 isoenzymes. Few clinical drug-drug interaction studies have been performed. An increase in plasma concentrations of artesunate was observed

with nevirapine and a reduced plasma concentration of dihydroartemisinin was observed when artesunate is given with ritonavir.

4.6 Fertility, pregnancy and breastfeeding

Not applicable.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Note: This product is intended only for children less than 6 years. Some of the data on undesirable effects were obtained in studies which included older children and adults.

Hospital-based clinical trials

Table 1 shows the most frequently reported adverse reactions observed in children who received a 10 mg/kg single dose regimen of artesunate rectal suppositories in hospital studies. Adverse reactions identified in clinical trials included treatment emergent adverse events, defined as events that appeared or worsened after the start of treatment. In children the most frequently reported adverse reactions were headache, convulsions and vomiting.

Table 1: Common Adverse Reactions in Paediatric Patients Treated in Hospital in Clinical Trials with the 10 mg/kg regimen of Artesunate Suppositories

System Organ Class	Preferred term	Rectal Artesunate 10 mg/kg (n=143)
Gastrointestinal disorders	Vomiting	4.2% (n=6)
Nervous system disorders	Headache Convulsions	3.5% (n=5) 2.1% (n=3)

One death occurred in a 3-year-old patient with moderately severe malaria treated with artesunate rectal dose of 11.5 mg/kg. Death was attributed to iatrogenic fluid overload, but it was also noted that the patient's serum dihydroartemisinin levels were higher (2002 ng/mL at 2 hours; 977 ng/mL at 4 hours) than the mean levels from similar age paediatric patients (653 ± 353 at 2 hours; 397 ± 545 at 4 hours).

Community-based clinical trials

Study 13 was a large trial in Bangladesh, Ghana and Tanzania (2 sites) conducted in conditions in which rectal artesunate is most likely to be used, i.e. resource-limited community settings (see section 5.1). 11778 of the children studied were 6 years old or younger. 5902 of these received a single 100 mg dose of rectal artesunate, and 5876 received placebo. Collection of safety data was limited, and consisted mostly of mortality and neurological serious adverse events, thus overlapping with the study's primary efficacy endpoints. Data concerning other AEs were not collected systematically.

No clear safety signal was evident in Study 13 in children aged 6 years and younger.

Of 7709 young children in the modified intent-to-treat population who survived the index malaria episode (3940 artesunate, 3824 placebo), 47 children had neurological sequelae not involving sciatic nerve damage, including 21 children treated with artesunate and 26 treated with placebo.

Assessment of safety was bolstered by examination of the sub-population with negative malaria smears, including 1839 patients who received artesunate suppositories, and 1889 patients who received placebo.

Table 2: Treatment-observed sequelae and malaria (placebo) associated sequelae, in patients with and without malaria				
Children ≤ 72months				
Patients with malaria (n=7028) or parasitology unknown (n=1022)				
System Organ Class	**Artesunate N=4063**		**Placebo N=3987**	
Nervous system disorders				
Altered behaviour	4	0.10%	4	0.10%
Ataxia			1	0.03%
Convulsions	1	0.02%	2	0.05%
Decortication	1	0.02%		
Delirium			1	0.03%
Gait abnormal	4	0.10%	2	0.05%
Hemiparesis	7	0.17%	8	0.20%
Hemiplegia			1	0.03%
Inability to sit unsupported	1	0.02%		
Lower extremity weakness	1	0.02%		
Monoparesis			1	0.03%
Strabismus			1	0.03%
Tremor			1	0.03%
Total	19		22	
Special senses				
Tinnitus/Hearing decreased	1	0.02%	3	0.08%
Vision abnormal	1	0.02%	1	0.03%
Total	2		4	
Malaria + unknown parasitology total	21		26	
Patients without malaria (n=2618) or with prior antimalarial injection(n=1110)				
System Organ Class	**Artesunate N=1839**		**Placebo N=1889**	
Nervous system disorders				
Altered behaviour			1	0.05%
Brain syndrome acute	1	0.05%		
Cerebral palsy	1	0.05%		
Delirium	1	0.05%		
Gait abnormal	1	0.05%		
Hemiparesis	8	0.44%	4	0.21%
Hemiplegia			2	0.11%
Lower extremity weakness	2	0.11%	2	0.11%
Monoparesis			1	0.05%
Paraparesis			1	0.05%
Regression in development	1	0.05%		
Total	15		11	
Special senses				
Speech disorder	1	0.05%		
Tinnitus/Hearing decreased	1	0.05%	2	0.11%
Vision abnormal	3	0.16%		
Total	5	0.27%	2	0.11%
Non-malaria + prior injection total	20		13	

Total	41		39	

There is no clear evidence of neurotoxicity in humans for single-dose rectal artesunate. Intravenous/intramuscular formulations of artesunate have shown adverse events of dizziness, light-headedness, headache, insomnia, and tinnitus.

Reporting of suspected adverse reactions

Health care providers are asked to report adverse reactions that may be linked to a medicine, to the marketing authorisation holder, or, if available, to the national reporting system. Reports of suspected adverse reactions to a medicine are important for the monitoring of the medicine's benefits and risks.

4.9 Overdose

Experience of acute overdose with artesunate is limited. A case of overdose has been documented in a 5 year-old child who was inadvertently administered rectal artesunate at a dose of 88 mg/kg/day over 4 days, representing a dose more than 7-fold higher than the highest recommended artesunate dose. The overdose was associated with pancytopenia, melena, seizures, multi-organ failure and death.

Treatment of overdose should consist of general supportive measures.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antimalarial, ATC code: P01BE03

Mechanism of action

Artesunate is a hemisuccinate derivative of dihydroartemisinin, which is itself formed by the reduction of artemisinin. Artemisinin is a sesquiterpene lactone endoperoxide extracted from qinghao (sweet wormwood, *Artemisia annua L.*), a plant which has been used for centuries in traditional Chinese medicine.

The mechanism of action of the artemisinins likely involves cleavage of the internal endoperoxide bridge through reaction with haem within the infected erythrocyte, thereby generating free radicals which alkylate vital parasite proteins. However, artemisinins have also been reported to inhibit an essential parasite calcium adenosine triphosphatase.

The artemisinins are distinguished from other antimalarials by their ability to kill all erythrocytic stages of the malaria parasite, including the relatively inactive ring stage and late schizonts, as well as the gametocytes responsible for malaria transmission. Artesunate and other artemisinins are the most rapid acting of the antimalarials, and they have also been shown to enhance splenic clearance of infected erythrocytes by reducing cytoadherence.

In vitro, dihydroartemisinin (DHA), the active metabolite of artesunate, exhibits similar potency against chloroquine-resistant and chloroquine-sensitive clones of *P. falciparum.*

Artesunate and the other artemisinins are essentially inactive against extra-erythrocytic forms, sporozoites, liver schizontes or merozoites.

Clinical efficacy and safety

Note: This product is intended only for children up to age 6 years. Some of the data below was obtained in studies which included older children and adults.

Hospital-based studies

Three controlled, open-label, clinical studies in Thailand, Malawi and South Africa evaluated artesunate suppositories given as a single 10 mg/kg dose for the first 24 hours of treatment, to hospitalised children and adults with confirmed moderately severe malaria. Control arms were treated with oral or IV artesunate in the

study in Thailand, and quinine in the two studies in Malawi and South Africa. After 24 hours all patients were given definitive antimalarial therapy using either sulfadoxine/pyrimethamine (Africa) or a combination of oral artesunate with mefloquine (Asia).

Table 3 shows the percentage of patients in each study who required no additional rescue therapy during the first twenty-four hours, and whose parasite counts at 24 hours fell to less than 10% of the baseline parasite count. The proportions of patients successfully meeting this endpoint were greater for those receiving artesunate rectal suppositories than those receiving parenteral quinine and similar for rectal, oral or IV artesunate-treated patients.

Table 3. Proportion of patients who received a single dose of rectal artesunate and who did not receive additional rescue antimalarial therapy and achieved >90% reduction of their baseline parasite count at 24 hours

Study Site (Regimen)	Artesunate suppositories	Comparator
Paediatric (1 - 15 years)		
Thailand (Rectal Artesunate vs Oral Artesunate)	31/41 (75.6%)	10/14 (71.4%)
Malawi (Rectal Artesunate vs Parenteral Quinine)	74/84 (88.1%)	3/22 (13.6%)

Recrudescence rates during the first 28 days were highest in the Malawian study, where sulfadoxine/pyrimethamine was used as definitive therapy. Recrudescence was infrequent in the South African study where sulfadoxine/pyrimethamine was used as definitive therapy and was not observed in the study in Thailand, where a combination of mefloquine and oral artesunate was used for definitive therapy. As shown in Table 4, during the Malawian study, recrudescence was observed earlier and more often in patients initially treated with artesunate suppositories than those initially treated with quinine. By 28 days post-enrolment, 45.3% of subjects receiving artesunate suppositories had recrudesced while 22.7% of the parenteral quinine-treated patients recrudesced by this time point, a finding noted only in the Malawi study.

Table 4. Cumulative Recrudescence Rates of Malaria in the Malawi Clinical Trial

		7 days post treatment	14 days post treatment	28 days post treatment
Artesunate Suppositories N=84	Positive smear	14 (16.3%)	25 (29.1%)	39 (45.3%)
	Missing data*	15 (17.4%)	20 (23.3%)	28 (32.6%)
Parenteral Quinine N=22	Positive smear	0 (0.0%)	2 (9.1%)	5 (22.7%)
	Missing data*	2 (9.1%)	5 (22.7%)	10 (45.5 %)

* Missing observations were considered negative for malaria since patients who did not return to the only locally available medical site were assumed to be clinically well.

Community-based studies

In a large multi-country study in Bangladesh, Ghana and Tanzania, 17826 patients with suspected severe malaria who could not be treated orally were allocated randomly to an artesunate or placebo suppository, then referred to clinics where injections could be given. (11778 patients were aged 6 years or under.) The primary efficacy endpoint was the number of deaths at day 7-30, based on the modified intent-to-treat analysis set, for patients receiving artesunate suppositories, compared to those receiving placebo. Permanent (i.e. persisting) neurological disability was considered a co-primary efficacy endpoint.

After excluding those with pre-randomisation antimalarial injections or negative blood smears 12,068 patients remained; half were in Africa (where all were aged 6-72 months) and half in Bangladesh (where older patients were also recruited, hospitalisation was rapid and mortality rates were low). The effects on mortality are summarized in Table 5. Mortality was 154/6072 in the artesunate versus 177/5996 in the placebo group. Another 2 artesunate vs 13 placebo were permanently disabled; total dead or disabled 156 artesunate vs 190 placebo.

Rectal artesunate takes 6-12 hours to reduce parasitaemia by 50%. In a post-hoc analysis, there was no reduction in early mortality (57 vs 51 deaths within 6 hours; median 2 hours). Among patients reaching clinic within 6 hours (median 3 hours), pre-referral artesunate had no significant effect on death after 6 hours or permanent disability (70 vs 82).

Among patients whose arrival in clinic was delayed by more than 6 hours, pre-referral rectal artesunate significantly reduced death or permanent disability (29 vs 57). All patients in this group were children under 6 years of age.

In Asia a favourable outcome was observed in young children given rectal artesunate (7 vs 19), but an adverse outcome was seen in older patients (22 vs 9). Thus, in children above 6 years and adults, the current evidence suggests more deaths with treatment. Rectal artesunate suppositories should not be given over age 6years.

Table 5: Effects of treatment on death or permanent disability, subdivided by study site and time taken to reach clinic.

	(a) Risk of death in 0-6 hours (at a median of 2 hours)		**(b) Risk of later death/disability (if survived >6 hours)† REACHED CLINIC IN 0-6 HOURS?**			
	ALL PATIENTS		**YES (at ~3 hours*)**		**NO (~15 hours**)**	
	Artesunate	**Placebo**	**Artesunate**	**Placebo**	**Artesunate**	**Placebo**
Africa: Age 6-72 months						
Handeni, Tanzania	22/726	21/737	15/286	17/292	17/418	33/424
Kilosa, Tanzania	11/1170	6/1169	8/542	11/539	8/617	14/624
Navrongo, Ghana	9/1145	12/1093	19/816	26/798	2/320	5/283
All in Africa	42/3041	39/2999	42/1644	54/1629	27/1355	52/1331
	1.4%	1.3%	2.6%	3.3%	2.0%	3.9%
Chittagong, Asia (by age)						
6-72 months	5/1022	7/988	7/947	19/918	2/70	5/63
School age/adult	9/2009	5/2009	22/1858	9/1879	0/141	0/125
All in Asia	15/3031	12/2997	29/2805	28/2797	2/211	5/188
	0.5%	0.4%	1.0%	1.0%	0.9%	2.7%
TOTAL, Africa & Asia	**56/6072**	**51/5996**	**71/4449**	**82/4426**	**29/1566**	**57/1519**
	0.94%	**0.85%**	**1.6%**	**1.9%**	**1.9%**	**3.8%**

	RR 1.10 (CI 0.75-1.61)	**RR 0.86 (CI 0.63-1.18)**	**RR 0.49 (CI 0.32-0.77)**
	P=0.61	**P=0.35**	**P=0.0013**

† Denominators = numbers alive >6h after entry, subdivided by whether patient reached clinic in 0-6 hours. Time to clinic was recorded in all who died or had neurological damage; otherwise, it was recorded routinely only in Kilosa (Tanzania) and Navrongo (Ghana). For those who did not die in Handeni (Tanzania) and Chittagong (Bangladesh) it was recorded whether they reached a clinic. For this table it is assumed that, if they did, the proportions doing so in 0-6 hours were 50% in Handeni and 95% in Chittagong.

* For those who reached clinic in 0-6 hours and then died after hour 6, median time to arrival was 2 hours in Chittagong and 4 hours in Africa.

** For those still not in clinic after >6 hours who died, the median time to reach clinic (or to death without reaching clinic) was 15 hours

5.2 Pharmacokinetic properties

Pharmacokinetics of Artesunate

There is considerable inter-individual variability in the plasma pharmacokinetics of artesunate (AS) and its principal active metabolite dihydroartemisinin (DHA) in healthy volunteers and patients with malaria.

In a study with 36 healthy male adult volunteers, the following mean (%CV) artesunate and dihydroartemisinin pharmacokinetic parameters were obtained with a single-dose administration of 4 x 100 mg rectal suppositories and 1 x 400 mg rectal suppository:

Table 6: Mean (%CV) PK parameters of AS and DHA in healthy male volunteers

Dose	Artesunate			Dihydroartemisinin		
	Cmax (ng/mL)	Tmax (hours)	AUC(0-t) (ng.h/mL)	Cmax (ng/mL)	Tmax (hours)	AUC(0-t) (ng.h/mL)
4 x 100 mg	293 (76.5)	1.7 (80)	733 (75.8)	442 (52.5)	2.4 (55)	1692 (79.8)
1 x 400 mg	261 (65.4)	3.8 (150)	1053 (130)	399 (60.2)	3.4 (41)	1374 (70.4)

$AUC_{(0-t)}$ represents the area under the plasma concentration versus time curve from time zero (dosing) until the end of the sampling period (24 hours post-dose).

A bioequivalence study was performed with 72 participants; data generated from a total of 69 subjects were utilised for analysis to establish pharmacokinetic parameters and assess bioequivalence.

The arithmetic mean and geometric mean values of the pharmacokinetic variables for artesunate as well as statistical results are summarised in the following table:

Table 7: Mean (± s.d.) PK parameters of AS in Healthy Male Volunteers

Dose	Artesunate		
	Cmax (ng/mL)	Tmax (hours)	AUC(0-t) (ng.h/mL)
1 x 100 mg	100 ± 63	0.92 ± 0.57	142 ± 90

$AUC_{(0-t)}$ represents the area under the plasma concentration versus time curve from time zero (dosing) until the end of the sampling period (10 hours post-dose).

The disposition of artesunate in patients with malaria has not been fully characterised. Dihydroartemisinin (DHA), the principal active metabolite of artesunate, accumulates selectively in parasitised red blood cells via binding to unidentified receptor(s).

General	
	Following rectal administration, artesunate and dihydroartemisinin maximal plasma concentrations are observed after about 0.9 and 1.9 hours.
Absorption	
Oral bioavailability	Not applicable
Food effect	Not applicable
Distribution	
Volume of distribution (mean)	Artesunate: 0.14 – 0.22 L/kg Dihydroartemisinin: 0.8 L/kg
Plasma protein binding *in vitro*	Artesunate: 75% Dihydroartemisinin: 80-90% (primarily albumin) Protein binding decreases at high concentrations
Tissue distribution	Dihydroartemisinin accumulates substantially in *P. falciparum*-infected erythrocytes
Metabolism	
	Extensively hydrolysed mainly by plasma esterases
Active metabolite(s)	Dihydroartemisinin is further metabolised through glucuronidation by UGT1A9 and UGT2B7
Elimination	
Elimination half life	Artesunate: 0.6 hours Dihydroartemisinin: 1.2 hours
Mean systemic clearance	Artesunate: 1 – 3 L/kg/h Dihydroartemisinin: 1.1 L/kg/h (after iv administration)
% of dose excreted in urine	NA*
% of dose excreted in faeces	NA*

*Information not available

Paediatrics

After adjustment for total body weight, systemic clearance of dihydroartemisinin was greater in paediatric patients than in adults, and volume of distribution was larger in paediatric patients than in adult patients. In addition, absorption from a suppository formulation appeared to be faster in paediatric patients compared with adult patients.

In infants less than 6 months of age compared to older children or adults, exposures in infants less than 6 months of age are higher and presumed to be due to immature development of the UGT elimination pathway for DHA.

5.3 Preclinical safety data

General toxicity

Artesunate presents low acute toxicity. After repeated administration of 50 mg/kg/day in rats and 82.5 mg/kg/day in dogs, i.e. approximately 10 and 17 times the proposed maximal therapeutic dose in man,

evidence of toxicity was observed in the haematopoietic organs, the immune system and response, the liver and kidneys.

Genotoxicity

Artesunate did not show any mutagenic or clastogenic potential in in vitro and in vivo tests (Ames, mouse micronucleus).

Carcinogenesis

No studies of the carcinogenic potential of artesunate have been conducted.

Reproductive toxicology studies

Oral artesunate caused dose-dependent fetal toxicity in rats, rabbits, and monkeys, resulting in fetal resorption and abortion, as well as a low incidence of cardiac and skeletal defects. The no-observed-adverse-effect-level (NOAEL) was 12 mg/kg in pregnant monkeys (3- and 7-day exposures) and the no or low adverse effects level was 5-7 mg/kg in pregnant rats or rabbits (12-day exposures), both of which are above the therapeutic dose range (2.4-4.8 mg/kg) and expected duration of exposure for treatment of severe malaria in humans. In rats, the embryo-fetuses were most sensitive from gestational days 9-14; at other times embryotoxicity was significantly reduced. A study of artesunate administered to male rats daily for 6 weeks noted testicular and epididymal lesions, although these lesions did not affect fertility. The lesions were reversible after cessation of treatment.

Safety pharmacology studies

A slight sedative effect, decrease in body temperature, mild natriuretic effect, and a decrease in creatinine clearance were observed with artesunate after single intravenous doses of 200 mg/kg (mice), 450 mg/kg (rats, rabbits and dogs), and following single oral doses of 180 mg/kg in male rats. Beagle dogs administered IV artesunate at 10, 20 and 50 mg/kg for 14 days did not display significant clinical effects, including any signs of neurotoxicity, effects on body weight, ECG abnormalities (including QT interval changes), heart rate, blood pressure, or respiratory rate.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule shell: Gelatin,
Glycerol
Titanium dioxide

Fill blend: Medium-chain triglycerides,
Hard fat

6.2 Incompatibilities

Artesunate suppositories should not be given concomitantly with other rectal medications.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at 25° C (77° F); excursions permitted to 15° to 30° C (59° to 86°F). Avoid excursions over 30°C. Do not freeze.

6.5 Nature and contents of container

Alu – Alu blister

Aluminium foil on aluminium foil blister cards, each containing 2 soft gelatin rectal capsules. Available in a box of 1x2 soft gelatin rectal capsules.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

Any unused product or waste material should be disposed of in accordance with local requirements

7. SUPPLIER

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8. WHO REFERENCE NUMBER (WHO Prequalification Programme)

MA123

9. DATE OF PREQUALIFICATION

19 June 2018

10. DATE OF REVISION OF THE TEXT

October 2025

References

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Section 5.2

FDA-PIL Artesunate available at https://reference.medscape.com/drug/artesunate-342684

Malaria Journal volume 10, Article number: 263 (2011); Review of the clinical pharmacokinetics of artesunate and its active metabolite dihydroartemisinin following intravenous, intramuscular, oral or rectal administration. Morris et al.

Detailed information on this medicine is available on the World Health Organization (WHO) website: https://extranet.who.int/prequal/medicines/prequalified/finished-pharmaceutical-products