WHO-PQ RECOMMENDED PATIENT INFORMATION LEAFLET

This patient information leaflet 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/pqweb/sites/default/files/documents/75%20SRA%20clarification_Feb2017_newtempl.pdf

Information for the patient

[MA168 trade name] †
Arginine Co-Pack + Artesunate

The warnings and instructions in this leaflet are intended for the person taking the medicine. If you are a parent or carer responsible for giving the medicine to someone else such as a child, you will need to apply the instructions accordingly.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have questions about the medicine, ask your health care provider.
- This medicine is for you only. Do not pass it on to others. It may harm them, even if their illness seems to be the same as yours.
- If you get any side effects, talk to your health care provider.This includes unwanted effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What [MA168 trade name] is and what it is used for

[MA168 trade name] is a medicine used to treat severe malaria in adults and children. It contains the active substance artesunate and is made up into a solution that is injected into a vein or a muscle.

Malaria is caused by infection with a parasite called *Plasmodium*, spread by the bite of an infected mosquito. [MA168 trade name] is used when the malaria is caused by a type of malaria parasite called *Plasmodium falciparum* and only when the infection is severe enough that it cannot be treated with medicines by mouth.

Your health care provider will follow the most recent official guidelines on the use of malaria medicines to select the right medicine for your malaria treatment.

2. What you need to know before you are given [MA168 trade name]

[MA168 trade name] should **not be used** if you are allergic to the active substance or any of the other ingredients of this product (see section 6).

Warnings and precautions

After you have been treated with [MA168 trade name] to bring down the most severe symptoms of your malaria infection, you will need to take malaria medicines by mouth to complete the treatment.

Some people treated with this medicine have developed increased breakdown of red blood cells in the body after treatment has finished, leading to low red blood cell levels within the first month after therapy., This has been seen most often in small children and travelers. Your health care provider may carry out blood tests to check for this for the first few weeks after treatment.

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

Taking other medicines

Please inform the health care provider if the patient is taking or has recently taken any other medicines, including medicines bought without prescription.

Pregnancy and breastfeeding

Pregnancy

Severe malaria is especially dangerous during pregnancy, so if you need treatment with [MA168 trade name] it will be given to you. Use during pregnancy is not expected to cause harm to you or the unborn baby.

Breastfeeding

A small amount of the medicine enters human breast milk, but if you are well enough to breastfeed this is not expected to cause any problems for your baby. However, there is not enough medicine to protect the child from malaria.

3. How [MA168 trade name] is given

Artesunate is given by injection into a vein or into a muscle (usually the muscle of your thigh). The dose is based on your weight. Your health care provider will work out the right dose to give.

Treatment is given for at least a day, until you are well enough to be treated by malaria medicines taken by mouth.

If you have any further questions on the use of this product, ask your health care provider.

4. Possible side effects

Like all medicines, [MA168 trade name] can cause side effects, but not everybody gets them. Some of these may be difficult to detect, and may be similar to effects of the disease itself.

Common side effects (may affect up to 1 in 10 people):

Dizziness, feeling sick, vomiting, light-headedness, headache, sleeplessness, hearing problems or ringing in the ears, slow heart rate (bradycardia), low blood pressure, fever, tiredness, joint and muscle pain, cough, irritated or runny nose, altered taste, abdominal pain, diarrhoea,, rise in liver enzymes (may indicate liver damage), rash, hair loss and pain at injection site.

Uncommon side effects (may affect up to 1 in 100 people):

Anaemia (low red blood cell count, see also below), neutropenia (low numbers of white blood cells which are important to fight infections), increased levels of a substance called bilirubin seen in blood tests, yellowing of eyes or skin (jaundice), reduction in platelets (which are important for blood clotting), severe painful rashes with flu-like symptoms (Stevens-Johnson syndrome), itching, and allergic reactions.

Rare side effects (may affect up to 1 in 1,000 people):

Inflammation of the liver (hepatitis) and inflammation of the pancreas (pancreatitis).

Very rare side effects (may affect up to 1 in 10,000 people):

Severe reduction in red blood cells, tingling sensation and nerve pain.

Not known (frequency cannot be estimated from the available data):

Abnormal electrical activity of the heart.

Anaemia (low red blood cells) may occur within one month after treatment. It has been reported especially in young children and in travelers. If you feel excessively tired, weak or short of breath up to 4 weeks after treatment, inform your health care provider.

Reporting of side effects

If you get a side effect, talk to your health care provider. This includes side effects not listed in this leaflet. You may also be able to report such effects directly to your national reporting system if one is available. By reporting side effects, you can help to improve the available information on this medicine.

5. How to store [MA168 trade name]

Keep this medicine out of the sight and reach of children.

Store in the original packing, below 30℃, until it is ready to be used to create a solution. The reconsitituted solution should be stored below 30℃ and the total in-use period should not exceed one hour.

Protect from light. Do not store in a refrigerator or freezer.

This medicine must not be used after the expiry date stated on the carton, vial or ampoule, after "EXP".

This medicine must not be used if you notice visible signs of deterioration.

Do not throw away any medicines in wastewater or household waste. Ask your health care provider how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What [MA168 trade name] contains

- The active ingredient is 60 mg of artesunate.
- The artesunate injection does not contain any other ingredients.

- The solution for dilution (3mL) contains 8.4 mg of sodium bicarbonate and 20 mg of arginine per mL of solution.
- The other ingredients of the solvent are phosphoric acid (for pH adjustment) and water for injection.
- There is too little sodium in solvent to have any effect, even if you are on a low-sodium diet.

What [MA168 trade name] looks like and contents of the pack

Artesunate 60 mg powder for solution for injection:
White crystalline powder.

Artesunate 60 mg powder for solution for injection is filled in a colourless, transparent type I glass vial (5mL) with a type I grey halogenated butyl rubber stopper, crimped with a blue aluminium-plastic cap.

Sodium bicarbonate 8.4 mg/mL and arginine injection 20 mg/mL solution for dilution:
Clear, colourless liquid.

3mL of sodium bicarbonate 8.4 mg-mL and arginine injection 20 mg/mL solution for dilution are filled in a colourless, transparent type I glass ampoule.

Supplier and Manufacturer

Guilin Pharmaceutical Co., Ltd
No. 43, Qilidian Road, Guilin 541004
Guangxi, China

Tel. No.: +86 773 3675053
Fax No.: +86 773 3675692
Email: ra@guilinpharma.com

For any information about this medicine, contact the local representative of the supplier.

This leaflet was last revised in October 2023.

Detailed information on this medicine is available on the World Health Organization (WHO) website: https://extranet.who.int/pqweb/medicines

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The following information is intended for health care providers only:

Preparation and administration

Because of the instability of artesunate in aqueous solutions, the reconstituted solution must be used within one hour of preparation. Therefore, the required dose of artesunate should be calculated (dose in mg = patient's weight in kg x 2.4 for patients weighing more than 20 kg; or dose in mg = patient's weight in kg x 3 for children weighing less than 20 kg) and the number of vials of artesunate needed should be determined prior to reconstituting the artesunate powder.

When reconstituted correctly, one vial of [MA168 trade name] will yield 3 mL of a solution for intravenous or intramuscular administration (20 mg/mL).

For patients weighing over 25 kg, more than 1 vial of [MA168 trade name] will be needed for each dose. The required number of product packs should be determined as follows:

Patient weight	Number of vials of artesunate (60 mg) needed
up to 25 kg	1
26 to 50 kg	2
51 to 75 kg	3
76 to 100 kg	4

Reconstitution of the artesunate solution

Using a syringe, withdraw 3 ml of the sodium bicarbonate and arginine solvent and inject this into the vial containing the artesunate powder. Gently shake the vial until the powder is completely dissolved and the solution is clear. If the solution appears cloudy or a precipitate is present, it should be discarded. The reconstituted artesunate solution should always be used immediately and discarded if not used within one hour. The end concentration of the solution will be 20 mg artesunate per ml of solvent. Thus, the volume in ml for administration to the patient will be equal to: (desired dose in mg)/20.

Withdraw the required volume of artesunate solution from the vial with a syringe and then administer to the patient by slow intravenous or intramuscular injection over 1-2 minutes.

[MA168 trade name] should **NOT** be administered as an intravenous drip.

Reconstituted vials of artesunate injection and ampoules of the sodium bicarbonate and arginine injection are for single use only. Discard unused portions.

Do not use water for injection for reconstitution of the artesunate powder or for dilution of the resulting solution prior to injection.