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

[MA186 trade name] †
Artesunate + Sodium Bicarbonate+ Sodium Chloride

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 [MA186 trade name] is and what it is used for

[MA186 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. [MA186 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 [MA186 trade name]

[MA186 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 [MA186 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 breast-feeding

Pregnancy

Severe malaria is especially dangerous during pregnancy, so if you need treatment with [MA186 trade name] it will be given to you. Use during pregnancy is not expected to cause harm to you or the unborn baby.

Breast-feeding

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

Other ingredients of [MA186 trade name]

Each 2 ml of sodium bicarbonate injection contains 100 mg of sodium bicarbonate, equivalent to 27.4 mg (1.2 mmol) sodium.
Each 10 ml of sodium chloride injection contains 90 mg of sodium chloride, equivalent to 35.4 mg (1.5 mmol) sodium.
This medicine contains 27.4 mg sodium (main component of cooking/table salt) in each ampoule of sodium boicarbonate solution and 35.4 mg sodium in each ampoule of sodium chloride solution this is equivalent to 3% of the recommended maximum daily dietary intake of sodium for an adult.

3. How [MA186 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, [MA186 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 [MA186 trade name]

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

Store below 30°C. Keep the vial and ampoules in the provided carton to protect the product from light. Do not refrigerate or freeze.

The reconstituted and diluted solutions should be stored below 30°C and the total in-use period should not exceed 1 hour.

This medicine must not be used after the expiry date stated on the label after 'EXP'.The expiry date refers to the last day of that month.

This medicine must not be used if you notice visible signs of deterioration or that it is different from the description below.

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 [MA186 trade name] contains

- The active ingredient is 120 mg of artesunate .Artesunate injection has no other ingredients.
  The solvent consists of sodium bicarbonate and water for injection that give a concentration of 50 mg/mL.
  The diluent consists of sodium chloride and water for injection that give a concentration of 9 mg/mL.

What [MA186 trade name] looks like and contents of the pack

Artesunate for injection is a sterile, white, crystalline powder.

120 mg of artesunate are filled into a clear, 15-mL USP type I glass vial, sealed with a grey bromobutyl rubber stopper and an aluminium seal closed with a red-flip-off plastic cap embossed with "1Ipca".

Sodium bicarbonate injection is a sterile clear colourless liquid.

2 mL are filled into a clear USP type I glass ampoule with a white ring around the neck of the ampoule.

Sodium chloride injection is a sterile clear colourless liquid.

10 mL are filled into a clear USP type1 glass ampoule with a white ring around the neck of the ampoule.

Pack size: A small box containing one vial of artesunate powder for injection, one ampoule of sodium bicarbonate injection and one ampoule of sodium chloride injection.

Supplier and Manufacturer

Supplier

Ipca Laboratories Limited
48, Kandivli Industrial Estate
Kandivli (West), Mumbai
Maharashtra, 400067
India
Tel. No.: +91-22-6210 5000
Fax No: +91-22-6210 5105/+91-22-6210 5005
E-mail: ipca@ipca.com

Manufacturer

Ipca Laboratories Limited
P.O. Sejavta, Ratlam 457001
Madhya Pradesh,
India
Phone No.: 91-7412-278000/8099
Fax No.: ()
E-mail: ipca@ipca.com

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

This leaflet was last revised in January 2024.

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

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This information is intended for health care providers only:

[MA186 trade name]

Dose:
Adults and children weighing 20 kg or more:
[MA186 trade name] is administered at a dose of 2.4 mg of artesunate / kg body weight, by intravenous (IV) or intramuscular (IM) injection, at 0, 12 and 24 hours, then once daily until oral treatment can be substituted.

Children weighing less than 20 kg:
[MA186 trade name] is administered at a dose of 3 mg of artesunate / kg body weight, by intravenous (IV) or intramuscular (IM) injection, at 0, 12 and 24 hours, then once daily until oral treatment can be substituted.

[MA186 trade name] should be administered for a minimum of 24 hours (3 doses), regardless of the patient's ability to tolerate oral medication earlier. After at least 24 hours of [MA186 trade name], and when able to tolerate oral medication, the patient should be switched to a complete treatment course of an oral combination antimalarial regimen. Relevant treatment guidelines should be consulted when selecting an appropriate regimen, e.g. those of the WHO.

Preparation
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 or dose in mg = patient's weight in kg x 3 for children weighing less than 20 kg, respectively) and the number of vials of artesunate needed should be determined prior to reconstituting the artesunate powder.

Reconstitution of the artesunate solution
Using a syringe, withdraw 1 mL of the supplied sodium bicarbonate solvent from the ampoule and inject into the vial containing the artesunate powder. Shake the vial for several minutes to mix well 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.

Following reconstitution the solution must be diluted according to the method of injection, as described below.

For intravenous (IV) injection (10 mg/mL)

Using a syringe, add 10 mL of sodium chloride 0.9% for injection to the vial containing the reconstituted artesunate solution. This will yield 12 mL of a solution containing artesunate 10 mg/mL. Shake to mix well, ensuring that the resulting solution is still clear. If the solution appears cloudy or a precipitate is present, it should be discarded.
The volume of the solution required (mL) will be:

Volume (mL) = [dose (mg)] ÷ 10

Withdraw the required volume of artesunate solution from the vial with a syringe and then inject slowly intravenously, over 1-2 minutes.

For intramuscular (IM) injection (20 mg/mL)

Using a syringe, add 4 mL of sodium chloride 0.9% for injection to the vial containing the reconstituted artesunate solution. This will yield 6 mL of a solution containing artesunate 20 mg/mL. Shake to mix well, ensuring that the resulting solution is still clear. If the solution appears cloudy or a precipitate is present, it should be discarded.
The volume of the solution required (mL) will be:

Volume (mL) = [dose (mg)] ÷ 20

Withdraw the required volume of artesunate solution from the vial with a syringe and then inject intramuscularly; the anterior thigh is usually the preferred site for injection. If the total volume of solution to be injected intramuscularly is large, it may be preferable to divide the volume and inject it at several sites, e.g. both thighs.

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