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

[MA152 trade name] †

Artesunate Sodium Bicarbonate + Sodium Chloride

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 has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness seem 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 [MA152 trade name] is and what it is used for

[MA152 trade name] contains artesunate and is for preparation of a solution for intravenous or intramuscular injection.
[MA152 trade name] is used for the treatment of severe *falciparum* malaria caused by the parasite *Plasmodium falciparum.*

2. What you need to know before you are given [MA152 trade name]

[MA152 trade name] should not be used if the patient is allergic to the active substance or any of the other ingredients of this product (see section 6).

Warnings and Precautions

After intravenous or intramuscular treatment of the critical phase of the falciparum malaria infection, the patient will need to take oral medication to complete the treatment and avoid relapse.

A reduction of red blood cells within the first month after therapy with artesunate has been reported, particularly in small children and travelers. The health care provider may therefore monitor the patient's blood count in the first weeks after malaria therapy.

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 hazardous during pregnancy, therefore full dose parenteral artesunate treatment should be administered at any stage of pregnancy without delay.

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

Breastfeeding
A small amount of the medicine enters human breast milk, but it will not protect the child from malaria. The health care provider will advise the patient on breast-feeding.

Excipients

This medicinal product contains sodium.

For Intravenous (IV) Injection (10 mg/ml)
This medicinal product contains 31.40 mg (1.365 mmol) sodium per one injection (prepared by dissolving 60 mg artesunate in 1 ml sodium bicarbonate (50 mg/ml) injection and diluting this with 5 ml (9 mg/ml) sodium chloride), is equivalent to 1.6 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

For Intramuscular (IM) Injection (20 mg/ml)
This medicinal product contains 20.77 mg (0.903 mmol) sodium per one injection (prepared by dissolving 60 mg artesunate in 1 ml sodium bicarbonate (50 mg/ml) injection and diluting this with 2 ml (9 mg/ml) sodium chloride), is equivalent to 1.06 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

It is important to consider the contribution of excipients from all the medicines that the patient is taking.

3. How [MA152 trade name] is given

Artesunate may be injected intravenously (into a vein) or intramuscularly (into a muscle).

The duration of treatment is at least one day, and will be determined by the health care provider.

For each dose, a new syringe and injection needle must be used. Further information on the method of administration for the health care professionals is attached to this leaflet.

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

4. Possible side effects

Like all medicines, [MA152 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, ‘flu-like effects (including fever, tiredness, bone and muscle pain), cough, irritated or runny nose, altered taste, abdominal pain, diarrhoea, 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), neutropenia (low white blood cell count), rise in liver enzymes (may indicate liver damage), reduction in platelets (which are important for blood clotting), and allergic reactions.

Rare side effects (may affect up to 1 in 1,000 people):
Inflammation of the liver (hepatitis, with yellowing of eyes and skin) 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):
Anaemia (low red blood cells) may occur within one month after treatment. It has been reported especially in young children and in travellers. If you feel excessively tired, weak or short of breath up to 4 weeks after treatment, inform your doctor or health hcare provider.

Reporting of side effects

If you get any side effects,talk to your health care provider. This includes unwanted effects not listed in this leaflet. If available, you can also report side effects directly through the national reporting system.
By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store [MA152 trade name]

Do not store above 25°C, in a dry place. Keep the vial and ampoules in the provided carton to protect the product from light. Do not refrigerate or freeze. Avoid excursions above 30°C.

For single use only.

The reconstituted and diluted solutions should be stored below 25°C and used within 1 hour.

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

This medicine must not be used after the expiry date stated on the after “EXP -----”.

6. Contents of the pack and other information

What [MA152 trade name] contains

The active ingredient is artesunate powder for injection: No excipient.

The other ingredients of [MA152 trade name] are excipients:
Solvent: Sodium bicarbonate, disodium edetate 0.007%w/v and water for injection
Diluent: Sodium chloride and water for injection

What [MA152 trade name] looks like and contents of the pack

Artesunate powder for injection is filled in a 10ml clear glass vial (USP Type III.) The filled vial is closed with 20mm grey bromobutyl rubber plug and sealed with 20mm chocolate brown flip off aluminium seal.

Sodium bicarbonate injection is filled in a 1ml clear glass ampoule (USP Type I) with a green snap off ring.

Diluent: Sodium chloride injection is filled in a 5ml clear glass ampoule (USP Type I)

Pack size: A carton containing one vial of artesunate powder for injection, one ampoule of sodium bicarbonate injection, one ampoule of sodium chloride injection placed in a plastic tray along with a package insert.

Supplier and Manufacturer

Supplier

Macleods Pharmaceuticals Limited
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For any information about this medicine, contact the supplier:

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Section 6 was updated in May 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:

[MA152 trade name]
Artesunate for injection

Please refer to the Summary of Product Characteristics for full prescribing information.

Posology and method of administration

Dose:
Adults and children weighing 20 kg or more:
[MA152 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:
[MA152 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.

[MA152 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 [MA152 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

1. Using a syringe, withdraw 1 ml of the supplied sodium bicarbonate solvent from the ampoule
2. Inject into the vial containing the artesunate powder.
3. 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.
4. 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.

Dilution for intravenous (IV) injection (10 mg/ml)

1. Using a syringe, add 5 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 10 mg/ml.
2. 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
3. Withdraw the required volume of artesunate solution from the vial with a syringe and then inject slowly intravenously, over 1-2 minutes.

[MA152 trade name] should NOT be administered as an intravenous drip.

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

1. Using a syringe, add 2 ml of sodium chloride 0.9% for injection to the vial containing the reconstituted artesunate solution. This will yield 3 ml of a solution containing artesunate 20 mg/ml.
2. 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
3. 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.