THE ADMINISTRATION OF ARTESUNATE INJECTIONS (Artesun®) PRACTICAL ASPECTS

Malaria Working Group 2015

1. PACKAGING

1 box of Artesun® (Artesunate produced by Guilin - DINJARTS6V-) contains:

- **1 vial of 60 mg of artesunate powder**
- **1 vial of 5% sodium bicarbonate 1 ml**
- **1 vial of 0.9% sodium chloride 5 ml**

Water for injection is not an appropriate diluent.

2. DOSAGE

The dosage of injectable artesunate is different according to the weight:

For patients weighing <20kg the dosage is 3.0 mg/kg. Patients weighing ≥ 20kg receive 2,4mg/kg.

Give artesunate at 0,12 and 24 hours, then once every 24 hrs until the patient can take oral therapy.

A course of parenteral artesunate has to be followed by a 3-days full course of ACT.

3. ADMINISTRATION ROUTES

Artesunate can be given either using the intra-venous (IV) or intramuscular (IM) route. The intra-venous route is preferred over the intramuscular administration.

For both the IV and IM use, a 2-step preparation is needed: reconstitution with sodium bicarbonate and dilution with sodium chloride. *The volume of sodium chloride to be used is different for IV and IM route.*

Once reconstituted, the artesunate solution is not stable and should be administered within 30 minutes. Because of the rapid degradation of the product, do not store the solution for longer than 30 minutes.

4. IV ADMINISTRATION OF ARTESUNATE

1 vial of artesunate contains 60 mg of artesunate and will be prepared with 1 ml of 5% sodium bicarbonate and 5 ml of 0.9% sodium chloride, so that the end solution contains 10 mg/ml artesunate.

Procedure

- *Peel of the top of the artesunate vial and disinfect the rubber, using 10% povidone iodine or an alcohol swab.*
- *Open already both ampoules so that you can keep the syringe with the needle in your hands during the process.*
- *Draw the 5% sodium bicarbonate 1 ml into a syringe and inject into the artesunate vial.*
- *Move your needle back slightly so it is no longer touching the liquid and withdraw all the air from the vial. This is important to ensure adequate space in the vial to inject the saline solution.*
- *Shake until the artesunate powder is completely dissolved, and the solution becomes clear (normally within 1-2 minutes). Do not shake too vigorously to avoid foaming of the solution. If the solution remains cloudy or a precipitate is present, the parenteral preparation should be discarded.*
- *Draw the 0.9% sodium chloride 5 ml into a syringe, and inject into the artesunate vial.*
- *Draw the required volume of artesunate from the vial (according to the pre-calculated dosing schedule).*
- *The solution has to be administered slowly IV over 2-3 minutes.*

The preferred route of intra-venous administration is through the injection port of an infusion set, using preferably 5% dextrose as infusion fluid (0,9% sodium chloride can be used as well). The infusion needs to be stopped before injecting through the Y site.

It's recommended to flush the catheter with dextrose 5% or 0.9% sodium chloride to avoid that some of the artesunate remains in the catheter. Flushing is required as well before administration if the infusion contained a medicine, anything else than normal saline or glucose 5%, to avoid incompatibilities.

Alternative routes are direct IV or using a pediatric infusion set.

Never inject the artesunate in the perfusion bag: the administration is too slow and there's a risk of degradation before everything is administered. Because of the short half-life, elimination from the bloodstream might start even before everything is administered and the blood concentration might be too low.

Note :

- For patients ≥25 kg, more than 1 vial of artesunate is needed.
- Each vial requires separate reconstitution, dilution and administration.

5. IM ADMINISTRATION OF ARTESUNATE

1 vial of artesunate contains 60 mg of artesunate and will be prepared with 1 ml of 5% sodium bicarbonate and 2 ml of 0.9% sodium chloride, so that the end solution contains 20 mg/ml artesunate.

Procedure

- *Peel of the top of the artesunate vial and disinfect the rubber with povidone iodine 10% or an alcohol swab.*
- *Draw the 1 ml of 5% sodium bicarbonate into a syringe and inject into the artesunate vial.*
- *Move your needle back slightly so it is no longer touching the liquid and withdraw all the air from the vial. This is important to ensure adequate space in the vial to inject the saline solution.*
- *Shake until the artesunate powder is completely dissolved, and the solution becomes clear (normally within 1-2 minutes). Do not shake too vigorously to avoid foaming of the solution. If the solution remains cloudy or a precipitate is present, the parenteral preparation should be discarded*
- *Draw the 2 ml of 0.9% sodium chloride into a syringe and inject into the artesunate vial.*
- *Draw the required volume of artesunate from the vial (according to the pre-calculated dosing schedule).*
- *Change the needle to an IM needle and give the artesunate through deep IM injection in the anterior thigh*

Note:

- For patients ≥ 25 kg, more than 1 vial of artesunate is needed.
- Each vial requires separate reconstitution, dilution and administration.

Do not keep both artemether and artesunate in the same structure, to avoid the risk of erroneous IV administration of artemether.

6. PRE-CALCULATED DOSING SCHEDULE

In order to find the optimal balance between accuracy and simplicity, some of the the volumes have been rounded up to the higher level, taking into account the measurable volumes using the different syringes (1-2-5-10 cc). It is proven that injectable artesunate has wide therapeutic margins and an excellent safety profile.

In case of doubt, always use the recommended dosage of 3mg/kg for children less than 20kg and 2.4 mg/kg for patients of 20kg and more.

DOSING SCHEDULE INJECTABLE ARTESUNATE		
PATIENT WEIGHT <20 KG		
3 mg/kg at 0, 12 & 24 hours, then once a day until oral ACT		
	IV	**IM**
PATIENT WEIGHT (KG)	**SOLUTION 10 MG/ML**	**SOLUTION 20 MG/ML**
<3	**1 ml**	**0,5 ml**
3.0-3.9	**1,2 ml**	**0,6 ml**
4.0-4.9	**1,5 ml**	**0,8 ml**
5.0-5.9	**2 ml**	**1 ml**
6.0-7.9	**2,5 ml**	**1,2 ml**
8.0-9.9	**3 ml**	**1,5 ml**
10.0-12.9	**4 ml**	**2 ml**
13.0-14.9	**4,5 ml**	**2,5 ml**
15.0-16.9	**5 ml**	**2,5 ml**
17.0-19.9	**6 ml**	**3 ml**
PATIENT WEIGHT ≥20 KG		
2,4 mg/kg at 0, 12 & 24 hours, then once a day until oral ACT		
	IV	**IM**
PATIENT WEIGHT (KG)	**SOLUTION 10 MG/ML**	**SOLUTION 20 MG/ML**
20.0-24.9	**6 ml**	**3 ml**
25.0-28.9	**7 ml**	**3,5 ml**
29.0-32.9	**8 ml**	**4 ml**
33.0-36.9	**9 ml**	**5 ml**
37.0-40.9	**10 ml**	**5 ml**
41.0-44.9	**11 ml**	**6 ml**
45.0-49.9	**12 ml**	**6 ml**
50.0-54.9	**13 ml**	**7 ml**
55.0-61.9	**15 ml**	**8 ml**
62.0-66.9	**16 ml**	**8 ml**
67.0-70.9	**17 ml**	**9 ml**
71.0-75.9	**18 ml**	**9 ml**
76.0-80.9	**20 ml**	**10 ml**