# Artesunate Injection Kit

## A. Specific requirements

Artesunate Injection Kit consists of a vial of **Artesunate** Injection; an ampoule of 5% Sodium Bicarbonate Injection; an ampoule of Sodium Chloride Solution and Disposable Syringe along with Disposable needle. The individual items contained in the product shall be currently registered in the country of manufacture and shall meet all requirements of the licensing authority of the country of manufacture. The individual items contained in the product shall also be currently registered in India and shall meet all the requirements of the licensing authority in India.

## Artesunate Injection:

**Description:**

**Artesunate** Injection contains a sterile powder containing Artesunate.
Each vial shall contain -
Artesunate IP 60 mg
Artesunate Injection complies with WHO working document QAS/10.365/FINAL May 2011 (Adopted text for addition to The International Pharmacopoeia) The powder for injection and the reconstituted injection comply with the monograph for “Parenteral Preparations” included in the latest edition of International Pharmacopoeia.

The injection is constituted by dissolving the contents of the sealed container in the requisite amount of Sterile Water for Injections, immediately before use.

The quality of Artesunate injection should conform to the requirements of IP or other Pharmacopoeia of equivalent accuracy in case of international transactions.

**Labelling:**

The label on each vial shall conform to the requirements of I.P and shall appear in the language of English/Hindi. All labelling should be in weatherproof ink and shall withstand immersion in water and remain intact. In addition to the requirements given in IP, all labels shall state the quantity of Artesunate contained in the sealed container, the name of the manufacturer, manufacturing license number, address of manufacturer, lot number, and expiry date. The label shall conform to the requirements of Rule 96 of Drugs & Cosmetic Act.

**Packing:**

**Primary Package:**
5 ml Vial (IP type 1 clear)(Containing Artesunate Powder for injection) closed with 20 mm Bromobutyl Rubber Plug and Sealed with flip off seal and plastic overcap.

## Sodium Bicarbonate Injection:

**Description:**

A clear, colourless solution.
Each ampoule shall contain 1 ml of Sodium Bicarbonate Injection (5%W/v).

The quality of Sodium Bicarbonate and Sterile Water for Injection should conform to the requirements of IP. If not mentioned in IP then other Pharmacopoeia of equivalent accuracy in case of international transactions may be followed.

**Labelling:**

The label on each ampoule shall conform to the requirements of I.P and shall appear in the language of English/Hindi.

All labelling should be in weatherproof ink and shall withstand immersion in water and remain intact. In addition to the requirements given in IP, all labels shall state the name of the manufacturer, manufacturing license number, address of manufacturer, lot number, and expiry date.

**Packing:**
**Primary Package:**

IP Type 1 clear plain glass ampoules. Each ampoule shall contain 1 ml of Sodium Bicarbonate injection (5%w/v). The ampoule should be sufficiently transparent to permit visual inspection of the contents.

## Sodium Chloride Injection:

**Description:**

A clear, colourless solution.
Each ampoule shall contain 5 ml of Sodium Chloride Injection (0.9%W/v).

The quality of Sodium Chloride and Sterile Water for Injection should conform to the requirements of IP. If not mentioned in IP then other Pharmacopoeia of equivalent accuracy in case of international transactions may be followed.

**Labelling:**
The label on each ampoule shall conform to the requirements of I.P and shall appear in the language of English/Hindi.

All labelling should be in weatherproof ink and shall withstand immersion in water and remain intact. In addition to the requirements given in IP, all labels shall state the name of the manufacturer, manufacturing license number, address of manufacturer, lot number, and expiry date.

**Packing:**

**Primary Package:**

IP Type 1 clear plain glass/FFS ampoule. Each ampoule shall contain 5 ml of Sodium Chloride injection (0.9%w/v). The ampoule should be sufficiently transparent to permit visual inspection of the contents.

**Secondary Package for Atresunate Injection + Sodium bicarbonate Injection + Sodium Chloride Injection:**

One vial of Artesunate Injection, one ampoule of Sodium bicarbonate Injection and one ampoule of Sodium Chloride Injection are packed in PVC blisters sealed, thermo-formated trays having high rigidity and sufficient impact strength to provide break resistance packaging.

The tray along with **Instructions for reconstitution and administration of Artesunate Injection** should be packed in a box for easy handling, transport and distribution. It shall be fabricated from Millboard/ grey board/ cardboard with a minimum of bursting strength of 300gsm.

**Labelling for secondary packaging:**

A label must be affixed either on the top and/or front surface of the secondary package. It should indicate number of boxes of Artesunate injection + Sodium Bicarbonate Injection + Sodium Chloride Injection. Separately the name of the manufacturer, batch number, date of manufacture, date of expiry of Artesunate Injection, Sodium Bicarbonate Injection and Sodium Chloride Injection should be given. The master batch number of the Kit along with Date of Expiry should be given. The label should also give Storage requirements. The label shall conform to the requirements of Rule 96 of Drugs & Cosmetic Act.

**Quality Assurance:**

**Compliance:**

The Supplier shall guarantee that the products as packed for shipment (a) comply with all provisions of the specification and related documents; (b) meet the recognized standards for safety, efficacy and quality; (c) are fit for the purposes made known to the Seller (d) are free from defects in workmanship and in materials and (e) the product has been manufactured as per WHO GMP requirements.

**Evidence:**

The Supplier shall provide objective evidence, acceptable to the Purchaser, of the satisfaction of the requirements of this document for which no specific inspection has been mentioned.

The Supplier shall provide a copy of the manufacturing record and procedures to the Purchaser for each lot intended for shipment.

The Supplier shall provide a copy of the Certificate of Analysis for each lot intended for shipment**.**

The Supplier shall provide to the Purchaser a copy of the approval on demand of each source material, constituent material and component for each lot intended for shipment.

The test data for raw materials including water for injection, glass container, in-process, finished product and packaging material testing must be on record for each lot shipped and must be made available to Purchaser's representatives when requested.

Details of samples lifted for testing (such as Millboard/Greyboard boxes, batch no. etc;) should be pasted on the packing of 5 Ply Shipper and records to this effect to be made available to the purchaser

## Disposable Syringe and Disposable Needle:

### Description (Disposable Syringe):

Disposable Syringes are Sterile Hypodermic Syringes for Single Use and are fabricated from **virgin** plastic. They shall conform to the standards given in IS 10258:2002. These are medical device intended for immediate use for administration of injectable preparations. They are supplied sterile and pyrogen – free and not to be re-sterilised or reused. The plastics and elastomer materials (**polypropylene and polyethylene**) of which the barrel and piston are made comply with the relevant specifications issued by BIS. The Syringes comply with the following standards regarding Dimensions including dead volume.

| **Capacity of the Syringe**<br><br>**ml** | **Tolerance eq. or ex. to cap.** | **Tolerance < half of cap.** | **Max. Dead Vol.**<br><br>**ml** | **Length of long Graduation Mark, mm** | **Overall length of scale, mm** | **Scale Interval**<br><br>**ml** | **Increment. Between Graduation lines ml** |
|---|---|---|---|---|---|---|---|
| 05 | +_4% of expelled vol | +_1.5% nominal Cap, +1% of expelled Vol. | 0.075 | 8 | 36 | 0.50 | 1 |

Polydimethylsiloxane (Silicone Oil) is applied to the internal walls of the barrel to assist in the smooth operation of the syringe but no excess be ensured capable of contaminating the contents at the time of use.

### Description (Disposable Needles):

Sterile Hypodermic Needles for Single Use comprise of a length of hypodermic grade stainless steel tube connected to a hub that is designed to mate with a syringe or an IV set. They shall conform to the standards given in IS 10654:2002. The other end of the tube is sharpened at the tip as per IS requirements. The tube is covered with a shield made from polypropylene. The hub fabricated from poly propylene is colour coded as per the requirements of ISO 6009. The union of the hub and needle tube is carried out with epoxy adhesive. This medical device in conjunction with Syringe is intended for

immediate use for administration of injectable preparations. They are supplied sterile and pyrogen – free and not to be re-sterilised or reused.

The Hypodermic needles shall comply with the following standards regarding Dimensions:

| **Needle Gauge** | **Colour of the hub** | **Nominal Length of the tube mm** | **Tolerance In length mm** | **Nominal outside diameter Of needle mm** | **Diameter of stylet for normal walled tubing mm** |
|---|---|---|---|---|---|
| 23 | Blue | 25 | + 1, -2 | 0.6 | 0.25 |

**Labelling:**

The label on each strip shall conform to the requirements of I.P and shall appear in the language of English/Hindi.

All labelling should be in weatherproof ink and shall withstand immersion in water and remain intact. In addition to the requirements given in Drugs & Cosmetic Act 1940 and rules there under, following information should be available:

- A description of the syringe including the capacity/ A description of the Needle including the Gauge and the nominal length
- The word ‘Sterile’
- That the syringe/needle is for single use only
- A solvent incompatibility
- The batch number
- Name and address of the manufacturer
- Date of Manufacture and Date of Expiry
- Warning that the syringe is not to be used if the packaging is damaged or sterility protector is loose
- CE marking
- ISO symbol for “do not re-use”

**Labelling for secondary packaging:**

**Secondary Package:**

A label must be affixed either on the top and/or front surface of the secondary package. It should indicate:

- A description of the syringe including the capacity and the type of nozzle/ A description of the needle including the gauze and the nominal length
- Quantity of primary packages
- The word ‘Sterile’
- That the syringe is for single use only
- The batch number
- The date (month and year) of sterilization
- Name and address of the manufacturer
- Date of Manufacture and Date of Expiry
- Information for handling, storage and transportation

**Quality Assurance:**

**Compliance:**

The Supplier shall guarantee that the products as packed for shipment (a) comply with all provisions of the specification and related documents; (b) meet the recognized standards for safety, efficacy and quality; (c) are fit for the purposes made known to the Seller (d) are free from defects in workmanship and in materials and (e) the product has been manufactured as per cGMP included in Schedule M - III. (f) the product is WHO pre-qualified and (g) the product should conform to ISO 13485.

**Evidence:**

The Supplier shall provide objective evidence, acceptable to the Purchaser, of the satisfaction of the requirements of this document for which no specific inspection has been mentioned.

The Supplier shall provide a copy of the manufacturing record and procedures to the Purchaser for each lot intended for shipment.

The Supplier shall provide a documentary evidence that the sterilization of the syringes has been carried out by validated sterilization procedures (with appropriate controls and recording devices) in case it has been carried out in their premises. If the facilities of other institution is used for sterilization, the approval of the licensing authority and documentary evidence for validated sterilization procedure should be made available.

The supplier shall provide a documentary evidence that the inks, glues and adhesives for the marking on the package and on the assembly of the syringe and its package (Wherever necessary) do not migrate across the walls.

The supplier shall provide documentary evidence in regards to bio-comapatibility of the device as per the requirements given in “Biological Evaluation of Medical Devices” IS 12572.

The supplier shall provide a certificate of analysis of Polydimethylsiloxane (used for lubrication) conforming to the requirements of IP.

The supplier shall provide a copy of CE certificate.

The Supplier shall provide a copy of the Certificate of Analysis for each lot intended for shipment

**Packing:**

**Primary Package:**

Each syringe and needle shall be packed and sealed separately in a primary container. The material of each container should not have detrimental effects on the contents. The material and design should be such as to ensure:

a) The maintenance of sterility under dry, clean and adequately ventilated storage conditions;

b) The minimum risk of contamination of the contents during opening of the container and removal of the contents;
c) Adequate protection of the contents during normal handling, transit and storage;
d) That once opened, the container cannot be easily resealed, and it should be obvious that the container has been opened.

Paper-PVC Blister:

- PVC Film: Transparent, clear, food grade, blister forming PVC film, film gauge- 200microns, PE coating: 25 microns.
- Hard tempered Blister paper, VMCH coated, Thickness: 0.025mm

**Secondary Package:**

The primary package should be packed in boxes for easy handling, transport and distribution. The box may contain --- primary packages. It shall be fabricated from Millboard/ grey board/ cardboard with a minimum of bursting strength of 400gsm.

## B. Inspection:

The Purchaser may inspect and sample, or cause to be sampled, the product at the Supplier's factory and/or warehouse at a mutually agreeable time prior to the shipment of the product.

## C. Testing::

The Purchaser may cause independent laboratory testing to be performed as deemed necessary to assure that the goods conform to the prescribed requirements. The said laboratory testing shall be of the Purchaser's choice if suitably equipped and qualified to conduct quality assurance tests on the product.

## D. Labelling on Shipper Package:

The external surface of insulated packages should be either white or in the natural color of corrugated carton.

The labels on tertiary packaging must be attached to at least two sides.

The label should include the name of the product, the number of secondary package (boxes) of Artesunate Injection + Sodium Bicarbonate Injection + Sodium Chloride Injection and Disposable Syringes plus Disposable Needles, the name of the manufacturer, Mater batch number and date of expiry.

The label shall include bar code and be tear proof to be pasted on smooth surface to enable it to be read by bar code reader.

## E. Packing for Shipper Package:

The secondary packages of Artesunate Injection + Sodium Bicarbonate Injection + Sodium Chloride Injection and that of Syringes + needles shall be packed in weather resistant triple walled insulated corrugated 5-ply cartons, each ply having strength of minimum 150gsm. It should be fabricated from virgin quality 'A' grade material. Burst factor of individual ply should be not less than 22. GSM of the shipper should be not less than 13 $Kg/cm^2$ . Overall dimensions of the carton should be such that the product does not get damaged during transportation and storage.

## F. Shelf Life of Artesunate Injection Kit:

**36** months, At least $5/6^{th}$ of the shelf life must remain at the time of shipment. The supplier will provide manufacturer's stability test data substantiating the claimed shelf life in the offered package

The expiry date of the Artesunate Injection Kit shall be the same as that of Artesunate Injection being the constituent of product with the shortest shelf life.

## G. Numbering of shipper packaging:

All boxes should be numbered consecutively. Shipping documents should be included in the box labelled number 1 (consignee wise),

## H. Qualification of the Manufacturer:

The Bidder shall furnish a certificate from the competent Regulatory Authority that the manufacturer of the pharmaceutical product is licensed to manufacture these products. The manufacturing facility must conform to WHO-GMP standards. In case of medical devices the manufacturing facility must conform to the standards given in ISO 13485 and Schedule M-III of Drugs & Cosmetic Act.

## I. Recalls:

If products must be recalled because of problems with product quality or adverse reactions to the drug, the Supplier will be obliged to notify the purchaser providing full details about the reason leading to the recall and shall take steps to replace the product in question at its own cost with a fresh batch of acceptable quality, or withdraw and give a full refund if the product has been taken off the market due to safety problems.

## J. Model Inserts:

An insert containing information in regards to adverse drug reactions and precautions (to be observed while taking the drug) of all the drugs included in the product should form part of each secondary pack.

## K. Colour Coding:

The labels on secondary packing, and shipper package shall be identified by WHITE background.

## L. Bar Coding:

Bar code shall be used to track down the product. It shall be printed on the label of Shipper containing

1) Product identification(GTIN 14) using application identifier (01)
2) Expiry Date in YYMMDD format & using application identifier (17)
3) Master batch number using application identifier (10)

*Complete details on GS1 standards along with technical guidelines can be downloaded from www.gs 1india.org or www.gs1.org*

## M. Documentation

Supplier shall provide to Purchaser a copy of the batch record, including all quality assurance documentation for the product being supplied.

**Advance notice of arrival and advance shipping documentation:**

Copies of the documentation for the goods to be shipped must be sent at least seven days in advance of arrival of the shipment. In the case of an individual contract for a specific destination that requires a longer period of advance notice, a longer period should apply. The consignee(s) shall be intimated well in advance by registered letter/e-mail/ telephone, so that the products are collected from the airport immediately after arrival.

The documentation must include the following:

- Pre-advice defined by the Purchaser
- Airway bill (AWB);
- Supplier's invoice;
- Packing list;
- Lot release certificate (LRC) as per the requirements issued by the national regulatory authority (NRA) of the country of manufacture for each lot and
- Any other document, certificate or instruction specified in the individual order.

The documents shall be sent by e-mail and fax by the freight forwarder or the manufacturer to the consignee, the Purchaser, and any other parties specified in the individual contract.

The pre-advice must contain the following information:

- Purchase order reference;
- Consignee requisition reference;
- Number of packages and gross weight (in kilograms).
- Value of shipment (in Indian Rupees and US $);
- AWB and flight number(s);
- Date and time for place of departure, transit (if applicable), and arrival;

- Instructions for collection;
- Any other information specified in the individual contract must also be included for the consignee.

The following information shall be stated on the airway bill:

- Consignee's name, address, telephone number (including mobile no.) and e-mail ID.
- Purchase order reference;
- Consignee's requisition reference;

• Instructions to: "Telephone consignee upon arrival *(repeat telephone number);*

## N. Dispatch:

Shipments should be scheduled to arrive outside weekends and/or public holidays in the country and airline bookings should be made well ahead of the date of departure.