RXADVANCE
2 Park Central Drive
Southborough, MA 01772

| | |
|---|---|
| **Clinical Policy Title:** | artesunate |
| **Policy Number:** | RxA.637 |
| **Drug(s) Applied:** | artesunate |
| **Original Policy Date:** | 07/09/2020 |
| **Last Review Date:** | 09/14/2020 |
| **Line of Business Policy Applies to:** | All lines of business |

## Background

Artesunate for Injection is an antimalarial indicated for the initial treatment of severe malaria in adult and pediatric patients. Treatment of severe malaria with Artesunate for Injection should always be followed by a complete treatment course of an appropriate oral antimalarial regimen.

Limitation(s) of Use:
Artesunate for Injection does not treat the hypnozoite liver stage forms of Plasmodium and will therefore not prevent relapses of malaria due to Plasmodium vivax or Plasmodium ovale. Concomitant therapy with an antimalarial agent such as an 8-aminoquinoline drug is necessary for the treatment of severe malaria due to P. vivax or P. ovale.

## Dosing Information

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| Artesunate | severe malaria | 2.4 mg/kg administered intravenously at 0 hours, 12 hours, and 24 hours and thereafter administered once daily until the patient is able to tolerate oral antimalarial therapy | 2.4 mg/kg |

## Dosage Forms

- For Injection: 110 mg of artesunate as a powder in a single-dose vial for constitution with the supplied sterile diluent.

## Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

**I. Initial Approval Criteria**

**A. Severe malaria** (must meet all)

1. Diagnosis of malaria confirmed by microscopy or members with strong clinical suspicion of malaria for whom a timely, reliable microscopic diagnosis is not available;
2. Member needs parenteral treatment due one or more of the following reasons (must meet a or b):

a. Severe malaria based on at least one of the following:
    i. High parasite density (≥5%)
    ii. Impaired consciousness
    iii. Seizures
    iv. Circulatory collapse/shock
    v. Pulmonary edema or acute respiratory distress syndrome (ARDS)
    vi. Acidosis
    vii. Acute kidney injury
    viii. Abnormal bleeding or disseminated intravascular coagulation (DIC)
    ix. Jaundice (must be accompanied by at least one other sign)
    x. Severe anemia (Hb <7 g/dL)
b. Member has inability to take oral medications despite attempt after an oral antiemetic;
3. If severe malaria is due to P vivax or P ovale, member is given concomitant therapy with an antimalarial agent such as an 8-aminoquinoline drug, according to the prescriber;
4. Dose does not exceed 2.4mg per kg;

**Approval Duration:** 7 days (one-time authorization)

## II. Continued Therapy Approval

### A. Severe malaria

1. Re-authorization is not allowed. Members must meet initial approval criteria. Review initial approval criteria for relapses or new cases of severe malaria.

**Approval Duration**: N/A

## III. Appendices

**APPENDIX A: Abbreviation/Acronym Key**

ARDS: acute respiratory distress syndrome
DIC: disseminated intravascular coagulation

**APPENDIX B: Therapeutic Alternatives**

| Drug name | Dosing Regimen | Dose Limit/Maximum Dose |
|---|---|---|
| Coartem™( artemether-lumefantrine) | Coartem tablets should be administered over 3-days for a total of 6 doses: an initial dose, second dose after 8 hours and then twice daily (morning and evening) for the following two days.<br>• The adult dosage for patients with bodyweight of 35 kg and above is 4 tablets per dose for a total of 6 doses<br>• The number of tablets per dose for children is determined by bodyweight:<br>  ○ 5 to <15 kg – 1 tablet<br>  ○ 15 to <25 kg – 2 tablets<br>  ○ 25 to <35 kg – 3 tablets<br>  ○ 35 kg and over – 4 tablets | See regimen |

| | | |
|---|---|---|
| atovaquone-proguanil (Malarone™) | • Adults: Four adult strength tablets as a single daily dose for 3 days.<br>• Pediatrics: Dosage based on body weight (see package insert) | See dosing regimen |
| quinine sulfate (Qualaquin) | • Adults (≥ 16 years of age): 648 mg (two capsules) every 8 hours for 7 days<br>• Patients with severe chronic renal impairment: one loading dose of 648 mg (two capsules) followed 12 hours later by 324 mg (one capsule) every 12 hours for 7 days | See dosing regimen |
| Mefloquine (Lariam) | • For treatment of mild to moderate malaria in adults caused by P. vivax or mefloquine susceptible strains of P. falciparum: Five tablets (1250 mg) mefloquine hydrochloride to be given as a single oral dose.<br>• For patients with acute P.vivax malaria, 1250 mg orally as a single dose; subsequent treatment with an 8-aminoquinolone derivative agent (eg, primaquine) is suggested to avoid relapse after initial treatment of acute infection | See dosing regimen |

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*

**APPENDIX C: Contraindications/Boxed Warnings**

- Contraindication(s):
  - Hypersensitivity (eg, anaphylaxis) to artesunate or any component of the formulation.

- Boxed Warning(s):
  - None

**APPENDIX D: General Information**

- According to CDC guidelines, IV artesunate is suggested as the drug of choice for the treatment of severe malaria, regardless of Plasmodium species; initiate treatment as soon as possible. Intravenous artesunate is available as part of an expanded-use investigational new drug protocol, and may be obtained through CDC by contacting the malaria hotline; while waiting for IV artesunate, consider interim treatment with an oral antimalarial agent. The preferred antimalarial for interim oral treatment is artemether-lumefantrine (Coartem™) because of its fast onset of action. Other oral options include atovaquone-proguanil (Malarone™), quinine, and mefloquine. Intravenous or oral clindamycin and tetracyclines, such as doxycycline, are not adequate for interim treatment. When IV artesunate arrives, immediately discontinue the oral medication and start parenteral treatment. Each dose of IV artesunate is 2.4 mg/kg. A dose of IV artesunate should be given at 0, 12, and 24 hours.

**References**

1. Artesunate IV Prescribing Information. Amivas LLC. May, 2020. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213036s000lbl.pdf Accessed July 1, 2020.
2. Malarone Prescribing Information. Research Triangle Park, NC. GlaxoSmithKline. Feb 2019. Available at https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Malarone/pdf/MALARONE.PDF. Accessed on July 9, 2020.

3. Coartem Prescribing Information. East Hanover, NJ. Novartis Pharmaceuticals Corporation. April 2009. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/022268lbl.pdf Accessed on July 9, 2020.
4. Mefloquine Hydrochloride. Prescribing Information. Columbus, OH. Roxane Laboratories, Inc. June 2013. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/076523s007lbl.pdf. Accessed on July 9, 2020.
5. Treatment of Malaria: Guidelines for Clinicians (United States). Centers for Disease Control and Prevention. Available at https://www.cdc.gov/malaria/diagnosis_treatment/clinicians1.html#severe. Accessed on July 9, 2020

| Review/Revision History | Review/Revision Date | P&T Approval Date |
|---|---|---|
| Policy established. | 07/09/2020 | 09/14/2020 |