artesunate – New orphan drug approval

- On May 26, 2020, the FDA announced the approval of Amivas' artesunate, for the initial treatment of severe malaria in adult and pediatric patients. Treatment of severe malaria with artesunate should always be followed by a complete treatment course of an appropriate oral antimalarial regimen.
    - Artesunate 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*.
- According to the CDC, approximately 2,000 cases of malaria are diagnosed in the U.S. each year, with 300 of those infected having severe disease.
- Artesunate is rapidly metabolized into an active metabolite dihydroartemisinin (DHA). Both artesunate and DHA are active against the different asexual forms of the *Plasmodium* parasites and clear parasitemia within 48 to 72 hours.
- The efficacy of artesunate for the treatment of malaria was supported by a randomized, active-controlled, open-label study in Asia and a published, randomized, active-controlled, open-label study in Africa. The first study included 1,461 patients hospitalized with severe malaria and treated with artesunate or quinine. The second study included pediatric patients < 15 years of age and treated with artesunate or quinine.
    - In the first study, the in-hospital mortality rate in the artesunate group was significantly lower than the rate in the quinine group (13% vs. 21%, respectively; odds ratio: 0.59; 95% CI: 0.44, 0.79).
    - In the second study, treatment with artesunate compared to quinine, showed a similar advantage with respect to in-hospital mortality as in the first study.
- Warnings and precautions of artesunate include post-treatment hemolysis, hypersensitivity, and embryo-fetal toxicity in animals.
- The most common adverse effects (≥ 2%) with artesunate use were acute renal failure requiring dialysis, hemoglobinuria, and jaundice.
- The recommended dose of artesunate is 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.
    - Artesunate should be administered with an antimalarial agent that is active against the hypnozoite liver stage forms of *Plasmodium*, such as an 8-aminoquinoline drug, to patients with severe malaria due to *P. vivax* or *P. ovale*.
- Amivas' launch plans for artesunate are pending. Artesunate will be available as an 110 mg powder for reconstitution.