Fexinidazole – New orphan drug approval

- On July 19, 2021, Sanofi announced the FDA approval of fexinidazole, for the treatment of both the first-stage (hemolymphatic) and second-stage (meningoencephalitic) human African trypanosomiasis (HAT) due to *Trypanosoma brucei gambiense (T. brucei gambiense)* in patients 6 years of age and older and weighing at least 20 kg.

    - Due to the decreased efficacy observed in patients with severe second stage HAT (cerebrospinal fluid white blood cell count > 100 cells/µL) due to *T. brucei gambiense* disease, fexinidazole should only be used in these patients if there are no other available treatment options.

- Sleeping sickness is a parasitic disease transmitted by the bite of an infected tse-tse fly. It affects mostly populations living in remote rural areas of sub-Saharan Africa. Left untreated, sleeping sickness is almost always fatal.

    - According to the CDC, less than 100 cases of sleeping sickness have been reported annually to the World Health Organization. Infection of international travelers is rare, but it occasionally occurs and most cases of sleeping sickness imported into the U.S. have been in travelers who were on safari in East Africa.

- The efficacy of fexinidazole was established in a randomized, comparative open-label trial in 394 adult patients with late second-stage HAT due to *T. brucei gambiense*. Patients were randomized to a 10-day treatment regimen of either fexinidazole or nifurtimox-eflornithine combination therapy (NECT). The outcome at 18 months was considered a success if patients were classified as a cure or probable cure.

    - Success at 18 months was achieved in 91.2% of patients treated with fexinidazole vs. 97.6% of patients treated with NECT (difference of -6.4, 97% CI: -11.6, -0.1).

- Additional supportive evidence for efficacy in early stage HAT due to *T. brucei gambiense*, and in pediatric patients was obtained from two single-arm studies: a single-arm study in 230 adults (trial 2) and a single-arm study (trial 3) in 125 pediatric patients aged 6 to 15 years old and weighing at least 20 kg.

    - Treatment success proportions in all patients with first- or late-stage HAT were 98.7% (95% CI: 96.2, 99.7) at 12 months in trial 2 and 97.6% (95% CI: 93.1, 99.5) at 12 months in trial 3.
    - The results at 18 months were consistent with the results at 12 months.

- Fexinidazole is contraindicated in:

    - Patients with known hypersensitivity to fexinidazole and/or any nitroimidazole class drugs (eg, metronidazole, tinidazole).
    - Patients with hepatic impairment.

- Warnings and precautions for fexinidazole include decreased efficacy in severe HAT caused by *T. brucei gambiense*, QT interval prolongation, neuropsychiatric adverse reactions, neutropenia, potential for hepatotoxicity, risk of disulfiram-like reactions due to concomitant use with alcohol, and risk of psychotic reactions due to concomitant use with disulfiram.

Continued . . .

- The most common adverse reactions (> 10%) with fexinidazole use were headache, vomiting, insomnia, nausea, asthenia, tremor, decreased appetite, dizziness, hypocalcemia, dyspepsia, back pain, upper abdominal pain, and hyperkalemia.

- Fexinidazole is administered orally, once daily for a total of 10 days (loading dose plus maintenance dose) with food each day at about the same time of the day. The recommended dosage for patients 6 years of age and older is according to body weight.

    — Refer to the drug label for complete dosing and administration recommendations.
    — Patients should be closely followed by their healthcare provider during treatment with fexinidazole.

- Sanofi's launch plans for fexinidazole are pending. Fexinidazole will be available as a 600 mg tablet.