Bemsivir®
(Remdesivir)

100mg IV Injection

Description

Remdesivir is a prodrug that metabolizes into its active form GS-441524. An adenosine nucleotide analog, GS-441524 interferes with the action of viral RNA-dependent RNA polymerase and evades proofreading by viral exoribonuclease (ExoN), causing a decrease in viral RNA production. It was unknown whether it terminates RNA chains or causes mutations in them.

Indication and Usage

Emergency use Authorization (EUA) of Remdesivir for the treatment of suspected or laboratory confirmed Corona Virus Disease 2019 (COVID-19) in adult and children hospitalized with severe disease. Severe disease is defined as patients with an oxygen saturation (SpO2) ≤ 94% on room air or requiring supplemental oxygen or requiring mechanical ventilation or requiring extracorporeal membrane oxygenation (ECMO). Specifically, Remdesivir is only authorized for hospitalized adult and pediatric patients for whom use of an intravenous agent is clinically appropriate.

Dosage and Administration

Treatment Initiation and Dosing Regimens:

• Empiric treatment of hospitalized patients with suspected COVID-19 can be considered pending laboratory confirmation of SARS-CoV-2 infection.

• A treatment course of 10 days is recommended for adults and pediatric patients requiring invasive mechanical ventilation and/or extracorporeal membrane oxygenation.

• A treatment course of 5 days is recommended for adults and pediatric patients not requiring invasive mechanical ventilation and/or ECMO. If a patient does not demonstrate clinical improvement, treatment may be extended for up to 5 additional days (i.e., up to a total of 10 days).

• Remdesivir can be used at any time after onset of symptoms in hospitalized patients.

• All patients must have an estimated glomerular filtration rate (eGFR) determined before dosing.

• Hepatic laboratory testing should be performed in all patients prior to starting remdesivir and daily while receiving remdesivir.

Adult Patients:

• For adults requiring invasive mechanical ventilation and/or ECMO, the dosage of remdesivir is a single loading dose of 200 mg infused intravenously over 30 to 120 minutes on Day 1 followed by once-daily maintenance doses of 100 mg infused intravenously over 30 to 120 minutes for 9 days (days 2 through 10).

• For adults not requiring invasive mechanical ventilation and/or ECMO, the dosage of remdesivir is a single loading dose of 200 mg infused intravenously over 30 to 120 minutes on Day 1 followed by once-daily maintenance doses of 100 mg infused intravenously over 30 to 120 minutes for 4 days (days 2 through 5). If a patient does not demonstrate clinical improvement, treatment may be extended for up to 5 additional days (i.e., up to a total of 10 days).

Pediatric Patients:

• For pediatric patients with body weight ≥40 kg requiring invasive mechanical ventilation and/or ECMO, the adult dosage regimen of one loading dose of remdesivir 200 mg IV (infused over 30 to 120 minutes) on Day 1 followed by remdesivir 100 mg IV (infused over 30 to 120 minutes) once daily for 9 days (days 2 through 10) will be administered.

• For pediatric patients with body weight ≥40 kg not requiring invasive mechanical ventilation and/or ECMO, the adult dosage regimen of one loading dose of remdesivir 200 mg IV (infused over 30 to 120 minutes) on Day 1 followed by remdesivir 100 mg IV (infused over 30 to 120 minutes) once daily for 4 days (days 2 through 5) will be administered. If a patient does not demonstrate clinical improvement, treatment may be extended for up to 5 additional days (i.e., up to a total of 10 days).

• Use of the adult dose in these pediatric patients is expected to maintain exposures of both remdesivir and the nucleoside analog GS-441524 generally within the expected adult steady-state exposure range following administration of the adult therapeutic dosage regimen in healthy volunteers.

• For pediatric patients with body weight between 3.5 kg and <40 kg, use remdesivir for injection, 100 mg, lyophilized powder only. Administer a body weight-based dosing regimen of one loading dose of remdesivir 5 mg/kg IV (infused over 30 to 120 min) on Day 1 followed by remdesivir 2.5 mg/kg IV (infused over 30 to 120 min) once daily for 9 days (for pediatric patients requiring invasive mechanical ventilation and/or ECMO, days 2 through 10) or for 4 days (for pediatric patients not requiring invasive mechanical ventilation and/or ECMO, days 2 through 5). If a patient does not demonstrate clinical improvement, treatment may be extended for up to 5 additional days (i.e., up to a total of 10 days). Use of this weight-based dosing regimen is expected to maintain remdesivir exposure that is comparable to that observed in adults while limiting the exposure of the nucleoside analog GS-441524 in very young children.

Method of Reconstitution

• Reconstitute with 19 ml of water for injection (100 mg). After reconstitution, each vial contains a 5 mg/ml Remdesivir concentrated solution with sufficient volume to allow withdrawal of 20 ml (100 mg Remdesivir).

• Dilute the reconstituted powder (i.e. concentrated solution) in intravenous fluids up to 250 ml prior to intravenous administration.

• Diluents that may be used: 0.9 % (9 mg/ml) sodium chloride in water (saline) or 5 % (50 mg/ml) glucose (dextrose) in water.

• The diluted solutions should be used immediately.

Side Effects

In the Ebola trial, researchers noted side effects of Remdesivir that included: Increased liver enzyme levels that may indicate possible liver damage. Typical antiviral drug side effects include nausea and vomiting.

Contraindications

• Hypersensitivity to the active substance(s) or to any of the excipients

• Evidence of multi-organ failure

• The use of more than one pressor for septic shock (the use of 1 pressor at low/medium doses for inotropic support due to the use of sedation and paralytics while on the ventilator is allowed)

• ALT > 5 x upper limit of normal (ULN) by local laboratory measure

• Renal failure (eGRF < 30 ml/min) or dialysis or continuous veno-venous hemofiltration

Warnings and Precautions

In clinical studies, transient elevations in ALT and AST have been observed with single doses of Remdesivir up to 225 mg and multiple

once-daily doses of Remdesivir 150 mg for up to 14 days, with mild, reversible PT prolongation in some subjects but without any clinically relevant change in INR or other evidence of hepatic effects. The mechanism of these elevations is currently unknown. In nonclinical animal studies, toxicity findings were consistent with dose-dependent and reversible kidney injury and dysfunction. In clinical studies, no evidence of nephrotoxicity has been observed with single doses of Remdesivir up to 225 mg or multiple once-daily doses of Remdesivir 150 mg for up to 14 days.

Drug Interactions

Remdesivir itself is not believed to affect other medications, however, other medications may affect Remdesivir. Some medications will boost the Remdesivir level in the bloodstream, and some will reduce it. Some antibiotics that may do this include: Clarithromycin and Rifampicin.

Use in Specific Populations

Pregnancy and Lactation: It is unknown if Remdesivir will affect a fetus or impact a pregnancy. In rats and monkeys, Remdesivir affected kidney development in fetuses. It is unknown if Remdesivir passes into breast milk. Consult your doctor before breastfeeding.

Paediatric Population: The safety and efficacy of Remdesivir in children below 12 years have not yet been established. No data available.

Overdose

There is no known antidote for Remdesivir. In the case of overdose, the subject should receive standard treatment for overdose and supportive therapy based on the subject's signs and symptoms.

Pharmaceutical Precautions

- Infusion should not be used if container is leaking, solution is cloudy or it contains un-dissolved particle(s).
- To be sold on prescription of a registered medical practitioner only.
- Store below 30°C.
- Keep out of sight and reach of children.
- Protect from sunlight, moisture and heat.
- The reconstituted solution in vial is stable below 30°C upto 4 hour.
- The reconstituted solution in vial is stable at 2°C - 8°C upto 24 hour.
- Do not freeze or refrigerate.

Commercial Pack

Bemsivir® 100 mg Lyophilized Powder: Each box containing one vial of Remdesivir INN 100 mg powder for infusion and one ampoule of 20 ml Water for Injection BP.

BEXIMCO PHARMA

Manufactured by
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