IVIREM

Lyophilized Powder for Infusion 100mg

(Remdesivir)

آئی ویریم

(ریمڈیسویر) لائیوفلائیزڈ پاؤڈر برائے انفیوژن ۱۰۰ ایم جی/ویل

SINGLE DOSE VIAL FOR I.V. USE ONLY

صرف وریدی استعمال کے لئے

COMPOSITION: Each Lyophilized vial contains:
Remdesivir ... 100mg. (As per Innovator's Specs.)

DESCRIPTION: Remdesivir is a single stereoisomer monophosphoramidate prodrug of a nucleoside analog that is being developed for the treatment of Coronavirus (CoV) disease. Remdesivir for compassionate use is provided in lyophilized powder dosage form. The powder for concentrate for solution for infusion containing 100mg Remdesivir is to be reconstituted with sterile water for injection and diluted into IV Infusion fluids prior to IV administration.

PHARMACODYNAMICS: Remdesivir is an adenosine nucleotide prodrug that distributes into cells where it is metabolized to form the pharmacologically active Remdesivir triphosphate. Remdesivir triphosphate acts as an analog of adenosine triphosphate (ATP) and competes with the natural ATP substrate for incorporation into nascent RNA chains by the SARS-CoV-2 RNA-dependent RNA polymerase, which results in delayed chain termination during replication of the viral RNA. Remdesivir triphosphate is a weak inhibitor of mammalian DNA and RNA polymerases with low potential for mitochondrial toxicity.

PHARMACOKINETICS: The pharmacokinetics (PK) of Remdesivir have been evaluated in adults in several Phase 1 trials. Following single-dose, 2-hour IV administration of Remdesivir solution formulation at doses ranging from 3 to 225 mg, Remdesivir exhibited a linear PK profile. Following single-dose, 2-hour IV administration of Remdesivir at doses of 75 and 150 mg, both the lyophilized and solution formulations provided comparable PK parameters (AUC_{inf}, AUC_{last}, and C_{max}), indicating similar formulation performance.

SPECIFIC POPULATIONS: Pharmacokinetic differences based on sex, race, and age have not been evaluated. The pharmacokinetics of Remdesivir in pediatric patients has not been evaluated/established.

Renal Impairment: Because the excipient SBECD is renally cleared and accumulates in patients with decreased renal function, administration of drugs formulated with SBECD (such as Remdesivir) is not recommended in adult and pediatric patients (>28 days old) with eGFR less than 30ml per minute or in full-term neonates (≥7 days and ≤28 days old) with serum creatinine clearance ≥1mg/dL unless the potential benefit outweighs the potential risk.

INDICATIONS: Emergency use Authorization (EUA) of IVIREM (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 oxygen saturation (SpO2) ≤ 94% on room air or requiring supplemental oxygen or requiring mechanical ventilation or requiring extracorporeal membrane oxygenation (ECMO). Specially, IVIREM (Remdesivir) is only authorized for hospitalized adult and pediatric patients for whom use of an intravenous agent is clinically appropriate..

DOSAGE AND ADMINISTRATION:

GENERAL INFORMATION:
- The optimal dosing and duration of treatment is unknown. The suggested dose and duration may be updated as data from clinical trials becomes available.
- Adult and pediatric patients (>28 days old) must have an eGFR determined and full-term neonates (≥7 days to ≤28 days old) must have serum creatinine determined before dosing of Remdesivir.
- Hepatic laboratory testing should be performed in all patients prior to starting Remdesivir and daily while receiving Remdesivir.
- Remdesivir should be administered via intravenous (IV) infusion only. Do not administer as an intramuscular (IM) injection

METHOD OF PREPARATION:
- For each vial, aseptically reconstitute Remdesivir lyophilized powder by addition of 19ml of Sterile Water for Injection using a suitably sized syringe and needle.
- Discard the vial if a vacuum does not pull the Sterile Water for Injection into the vial.
- Care should be taken during admixture to prevent inadvertent microbial contamination. Immediately shake the vial for 30 seconds. Allow the contents of the vial to settle for 2 to 3 minutes.
- A clear solution should result. If the contents of the vial are not completely dissolved, shake the vial again for 30 seconds and allow the contents to settle for 2 to 3 minutes.
- Repeat this procedure as necessary until the contents of the vial are completely dissolved. Following reconstitution, each vial contains 100mg/20ml (5mg/ml) of Remdesivir solution.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Inspect the vial to ensure the container closure is free from defects and the solution is free of particulate matter.
- After reconstitution, the total storage time before administration should not exceed 4 hours at room temperature or 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]).

DILUTION: Withdraw the required volume of saline from the bag, according to table below and using an appropriately sized syringe and needle. Discard the saline that was withdrawn from the bag. Now transfer the required volume of reconstituted Remdesivir for injection, according to below table and using an appropriately sized syringe to the selected infusion bag. Discard any unused portion remaining in the Remdesivir vial. Gently invert the bag 20 times to mix the solution in the bag. Do not shake. The prepared diluted solution is stable for 4 hours at room temperature (20°C to 25°C [68°F to 77°F]) or 24 hours in the refrigerator at 2°C to 8°C (36°F to 46°F).

Remdesivir Dose	0.9% saline infusion bag volume to be used	Volume of saline to be withdrawn and discarded from 0.9% saline infusion bag	Required volume of reconstituted Remdesivir for injection
200mg (2 vials)	250ml	40ml	2 x 20ml
	100ml	40ml	2 x 20ml
100mg (1 vial)	250ml	20ml	20ml
	100ml	20ml	20ml

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ADMINISTRATION: Administer the diluted solution with the infusion rate described in table below. After infusion is complete, flush with at least 30ml of 0.9% saline.

Infusion Bag Volume	Infusion Time	Rate of Infusion
250ml	30 minutes	8.33ml/min
	60 minutes	4.17ml/min
	120 minutes	2.08ml/min
100ml	30 minutes	3.33ml/min
	60 minutes	1.67ml/min
	120 minutes	0.83ml/min

Adult Patients: • The recommended dosage in adults requiring invasive mechanical ventilation and/or ECMO is a single loading dose of Remdesivir 200mg on Day 1 followed by once-daily maintenance doses of Remdesivir 100mg for 9 days.
• The recommended dosage in adults not requiring invasive mechanical ventilation and/or ECMO is a single dose of Remdesivir 200mg on Day 1 followed by once-daily maintenance doses of Remdesivir 100mg for 4 days. 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 is to be administered via intravenous infusion in a total volume of up to 250ml 0.9% saline over 30 to 120 minutes.
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 200mg IV (infused over 30 to 120 minutes) on Day 1 followed by Remdesivir 100mg IV (infused over 30 to 120 minutes) once daily for 9 days will be ad ministered.
• **For pediatric patients with body weight ≥40kg not requiring invasive mechanical ventilation and/or ECMO,** the adult dosage regimen of one loading dose of Remdesivir 200mg IV (infused over 30 to 120 minutes) on Day 1 followed by Remdesivir 100mg 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).
• **For pediatric patients with body weight between 3.5kg and <40kg,** use Remdesivir for injection, 100mg, lyophilized powder only. Administer a body weight-based dosing regimen of one loading dose of Remdesivir 5mg/kg IV (infused over 30 to 120 min) on Day 1 followed by Remdesivir 2.5mg/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). Pediatric patients (>28 days old) must have an eGFR determined and full-term neonates (≥7 days to ≤28 days old) must have serum creatinine determined before dosing.

CONTRAINDICATIONS: Remdesivir is contraindicated in patients with known hypersensitivity to any ingredient of Remdesivir. Given the benefit-risk ratio in patients with acute COVID-19 infection, no dose modification is recommended at the present time. Remdesvir is contraindicated in patients with severe hepatic impairment and multi-organ failure. Given the benefit-risk ratio in patients with acute COVID-19 infection, no dose modification is recommended at the present time in patients with mild and moderate renal impairment. Remdesivir is contraindicated in patients with severe renal impairment.

ADVERSE EFFECTS: There are limited clinical data available for Remdesivir. Serious and unexpected adverse events may occur that have not been previously reported with Remdesivir use. Infusion-related reactions have been observed during, and/or have been temporally associated with, administration of Remdesivir. Signs and symptoms may include hypotension, nausea, vomiting, diaphoresis, and shivering. If signs and symptoms of a clinically significant infusion reaction occur, immediately discontinue administration of Remdesivir and initiate appropriate treatment. The use of Remdesivir is contraindicated in patients with known hypersensitivity to Remdesivir. An adverse reaction associated with Remdesivir in clinical trials in healthy adult subjects was increased liver transaminases. Additional adverse reactions associated with the drug, some of which may be serious, may become apparent with more widespread use.

OVERDOSAGE: There is no human experience of acute overdosage with Remdesivir. Treatment of overdose with Remdesivir should consist of general supportive measures including monitoring of vital signs and observation of the clinical status of the patient. There is no specific antidote for overdose with Remdesivir.

WARNING & PRECAUTION: Hepatic laboratory testing should be performed in all patients prior to starting Remdesivir and daily while receiving Remdesivir. There are limited clinical data available for Remdesivir. Serious and unexpected adverse events may occur that have not been previously reported with Remdesivir use. Some of the adverse reactions have been described above.

DRUG INTERACTIONS: Drug interaction trials of Remdesivir and other concomitant medications have not been conducted in humans.

FERTILITY, PREGNANCY AND LACTATION: Pregnancy: Remdesivir should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus.
Breast-feeding: There is no information regarding the presence of Remdesivir in human milk, the effects on the breastfed infant, or the effects on milk production.
Fertility: There are no clinical studies on fertility with Remdesvir

INSTRUCTIONS: Store below 30°C. Protect from heat, light and moisture. Keep out of the reach of children.

PRESENTATION: IVIREM Lyophilized Powder for Infusion 100mg (Remdesivir) is supplied in glass vial along with two ampoules of 10ml sterile water for injection.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایات: ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، روشنی اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔

PHARMA
Manufactured by:
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