Dilavir

Injection

DRUG INTERNATIONAL LTD.

Composition: Each vial contains Remdesivir INN 100mg as lyophilized powder.

Pharmacology: Remdesivir is a prodrug of a modified adenine nucleoside analog. Remdesivir undergoes efficient metabolic conversion in cells and tissues to active nucleoside triphosphate metabolite that inhibits viral RNA polymerases. Remdesivir is highly selective for viral polymerases and is therefore expected to have a low propensity to cause human toxicity. Remdesivir has wide therapeutic index in a human airway epithelial cell model. It also displays a high genetic barrier to resistance in different viruses and has a long intracellular half-life.

Indication : Emergency use Authorization (EUA) of Remdesivir is a SARS-CoV-2 nucleotide analog RNA polymerase inhibitor indicated for adults and pediatric patients (12 years of age and older and weighing at least 40 kg) for the treatment of coronavirus disease 2019 (COVID-19) requiring hospitalization. Remdesivir should only be administered in a hospital or in a healthcare setting capable of providing acute care comparable to inpatient hospital care.

Dosage & Administration:

General Information

• 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 while receiving Remdesivir.

• Remdesivir should be administered via intravenous (IV) infusion only. Do not administer as an intramuscular (IM) injection.

Adult Patients:

• The recommended dosage in adults requiring invasive mechanical ventilation and/or ECMO (Extracorporeal membrane oxygenation) is a single loading dose of Remdesivir 200 mg on Day 1 followed by once-daily maintenance doses of Remdesivir 100 mg for 9 days.

• The recommended dosage in adults not requiring invasive mechanical ventilation and/or ECMO (Extracorporeal membrane oxygenation) is a single dose of Remdesivir 200 mg on Day 1 followed by once-daily maintenance doses of Remdesivir 100 mg 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 250 ml 0.9% saline over 30 to 120 minutes.

Pediatric Patients: The recommended pediatric dose for pediatric patients weighing between 3.5 kg and <40 kg should be calculated using the mg/kg dose according to the patient's weight.

• 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 (Extracorporeal membrane oxygenation), days 2 through 10) or for 4 days (for pediatric patients not requiring invasive mechanical ventilation and/or ECMO (Extracorporeal membrane oxygenation), 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).

• For pediatric patients with body weight ≥40 kg requiring invasive mechanical ventilation and/or ECMO (Extracorporeal membrane oxygenation), 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 will be administered.

• For pediatric patients with body weight ≥40 kg not requiring invasive mechanical ventilation and/or ECMO (Extracorporeal membrane oxygenation), 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).

Reconstitution Instructions:

• Aseptically reconstitute Remdesivir lyophilized powder by addition of 19 ml of Sterile Water for Injection using a suitably sized syringe and needle per vial.

• Discard the vial if a vacuum does not pull the Sterile Water for Injection into the vial.

• 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 100 mg/20 ml (5 mg/ml) of Remdesivir solution.

• Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

• 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).

Dilution Instructions:

• Care should be taken during admixture to prevent inadvertent microbial contamination. By using the table below, please determine the volume of 0.9% saline to withdraw from the infusion bag. It is always recommended to administer IV medication immediately after preparation when possible.

Recommended Dilution Instructions-Remdesivir for Injection Lyophilized Powder in Adults and Pediatric Patients Weighing ≥40kg

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

• Please withdraw and discard the required volume of saline from the bag following instructions in above table, using an appropriately sized syringe and needle. • Please withdraw the required volume of reconstituted Remdesivir for injection from the Remdesivir vial following instructions in above table, using an appropriately sized syringe. • Please discard any unused portion remaining in the Remdesivir vial. • Please transfer the required volume of reconstituted Remdesivir for injection to the selected infusion bag. • Gently invert the bag 20 times to mix the solution in the bag. Please do not shake.

Administration Instructions: The prepared diluted solution should not be administered simultaneously with any other medication. The compatibility of Remdesivir Injection with IV solutions and medications other than saline is not known.

Please administer the diluted solution with the infusion rate described in the below table.

Recommended Rate of Infusion-Diluted Remdesivir for Injection Lyophilized Powder in Adults and Pediatric Patients Weighing ≥ 40kg

Infusion bag volume	Infusion time	Rate of Infusion
250 mL	30 min	8.33 mL/min
	60 min	4.17 mL/min
	120 min	2.08 mL/min
100 mL	30 min	3.33 mL/min
	60 min	1.67 mL/min
	120 min	0.83 mL/min

Or, as directed by the registered physician.

Contraindications: It is contraindicated in patients with known hypersensitivity to any ingredient of this product. Remdesivir is not recommended in patients with eGFR less than 30ml/min.

Precautions: Increased risk of transaminase elevations. Hypersensitivity reactions including infusion-related and anaphylactic reactions have been observed during and following administration of Remdesivir.

Side Effects: An adverse reaction associated with Remdesivir in clinical trials in healthy adult subjects was increased liver transaminases.

Use in Pregnancy And Lactation: There is no adequate and well-controlled studies in pregnant women. Remdesivir should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus. There is no information regarding the presence of Remdesivir in human milk, the effects on the breastfed infant, or the effects on milk production. Because of the potential for viral transmission to SARS-CoV-2-negative infants and adverse reactions from the drug in breastfeeding infants, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Remdesivir and any potential adverse effects on the breastfed child from Remdesivir or from the underlying maternal condition.

Drug Interaction: 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.

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.

Storage: Keep away from light and out of the reach of children. Please do not reuse or save unused Remdesivir lyophilized powder, injection solution, or diluted solution for infusion for future use. This product contains no preservative.

Lyophilized Powder: Please store Remdesivir for injection, 100 mg, vials below 30°C until required for use. Do not use after expiration date.

• After reconstitution, vials can be stored up to 4 hours at room temperature (20°C to 25°C) prior to administration or 24 hours at refrigerated temperature (2°C to 8°C). Please dilute within the same day as administration.

Diluted Solution for Infusion: Please store diluted Remdesivir solution for infusion up to 4 hours at room temperature (20°C to 25°C) or 24 hours at refrigerated temperature (2°C to 8°C).

Packing : Each combipack contains one vial of lyophilized powder of Remdesivir INN 100 mg and two ampoules of 10ml water for injection BP.