For the use of a Registered Medical Practitioner or Hospital or Laboratory only

REMDESIVIR FOR INJECTION 100mg (LYOPHILIZED)

CBDESVIR

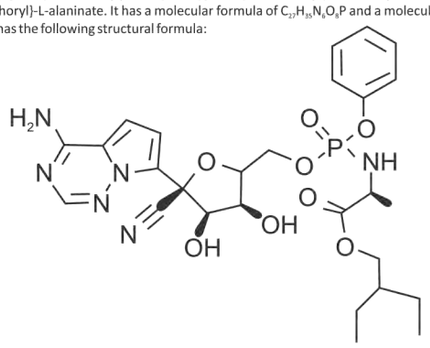
Rx Only

COMPOSITION

Each vial contains:
Remdesivir 100mg
Excipients ..... q.s.

DESCRIPTION

Remdesivir is a nucleoside ribonucleic acid (RNA) polymerase inhibitor. The chemical name for Remdesivir is 2-ethylbutyl N-{(S)-[2-C-(4- aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-2,5-anhydro-d-altrononitril-6-Oyl]phenoxyphosphoryl}-L-alaninate. It has a molecular formula of $C_{27}H_{35}N_6O_8P$ and a molecular weight of 602.6 g/mol. Remdesivir has the following structural formula:



Physical Appearance:

Lyophilized Powder: Remdesivir for injection, 100 mg, is a sterile, preservative-free lyophilized powder that is to be reconstituted with 19 mL of Sterile Water for Injection and further diluted into 0.9% sodium chloride infusion bag prior to administration by intravenous infusion. Remdesivir for injection, 100 mg, is supplied in a single-dose clear glass vial. The appearance of the lyophilized powder is white to off-white to yellow.

Injection Solution: Remdesivir for injection, 100 mg/20 mL (5 mg/mL), is a sterile, preservative-free, clear, colourless to yellow, aqueous-based concentrated solution that is to be diluted into 0.9% sodium chloride infusion bag prior to administration by intravenous infusion. Remdesivir injection, 100 mg/20 mL (5 mg/mL), is supplied in a single-dose clear glass vial.

CLINICAL PHARMACOLOGY

Mechanism of Action: Remdesivir is an adenosine nucleotide prodrug that distributes into cells where it is metabolized to form the pharmacologically active nucleoside triphosphate metabolite. Metabolism of Remdesivir to Remdesivir triphosphate has been demonstrated in multiple cell types. 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 has been evaluated in adults in several Phase 1 trials.

The pharmacokinetics of Remdesivir and metabolites has not been in evaluated in patients with COVID-19. 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.

Remdesivir 75 mg lyophilized formulation administered IV over 30 minutes provided similar peripheral blood mononuclear cell (PBMC) exposure of the active triphosphate metabolite GS-443902 as Remdesivir 150 mg lyophilized formulation administered IV over 2 hours.

Following a single 150 mg intravenous dose of [14C]-Remdesivir, mean total recovery of the dose was >92%, consisting of approximately 74% and 18% recovered in urine and feces, respectively. The majority of Remdesivir dose recovered in urine was metabolite GS-441524 (49%), while 10% was recovered as Remdesivir.

Specific Populations

Sex, Race and Age: Pharmacokinetic differences based on sex, race, and age have not been evaluated.

Pediatric Patients: The pharmacokinetics of Remdesivir in pediatric patients has not been evaluated. PBPK modeling of pharmacokinetic data from healthy adults was used to derive pediatric doses. PBPK modeling incorporated in vitro data for Remdesivir and other similar compounds along with age-dependent changes in physiology (e.g., organ volume/function, blood flow), metabolism, distribution, and elimination of Remdesivir. Pediatric doses are expected to result in comparable steady-state exposures of Remdesivir and metabolites as observed in healthy adults following administration of the recommended dosage regimen.

WARNINGS AND PRECAUTIONS

There are limited clinical data available for Remdesivir. Serious and unexpected adverse events may occur that have not been previously reported with Remdesivir use.

Hypersensitivity: Including Infusion-Related and Anaphylactic Reactions Hypersensitivity reactions including infusion-related and anaphylactic reactions have been observed during and following administration of Remdesivir. Signs and symptoms may include hypotension, tachycardia, bradycardia, dyspnea, wheezing, angioedema, rash, nausea, vomiting, diaphoresis, and shivering. Slower infusion rates, with a maximum infusion time of up to 120 minutes, can be considered to potentially prevent these signs and symptoms. If signs and symptoms of a clinically significant hypersensitivity reaction occur, immediately discontinue administration of Remdesivir and initiate appropriate treatment. The use of Remdesivir is contraindicated in patients with known hypersensitivity to Remdesivir.

Increased Risk of Transaminase Elevations: Transaminase elevations have been observed in healthy volunteers who received 200 mg of Remdesivir followed by 100 mg doses for 5-10 days. Transaminase elevations have also been reported in patients with COVID-19 who received Remdesivir in clinical trials. As transaminase elevations have been reported as a component of COVID-19, including in patients receiving placebo in clinical trials of Remdesivir, discerning the contribution of Remdesivir to transaminase elevations in this patient population is challenging. Hepatic laboratory testing should be performed in all patients prior to starting Remdesivir and daily while receiving Remdesivir.

Remdesivir should not be initiated in patients with ALT greater than or equal to 5 times the upper limit of normal at baseline.

Remdesivir should be discontinued in patients who develop: ALT greater than or equal to 5 times the upper limit of normal during treatment with Remdesivir. Remdesivir may be restarted when ALT is less than 5 times the upper limit of normal. OR ALT elevation accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR.

Risk of Reduced Antiviral Activity: When co-administered with Chloroquine or Hydroxychloroquine co-administration of Remdesivir and Chloroquine phosphate or Hydroxychloroquinesulfate is not recommended based on in vitro data demonstrating an antagonistic effect of Chloroquine on the intracellular metabolic activation and antiviral activity of Remdesivir.

ADVERSE REACTIONS

The prescribing health care provider and/or the provider's designee are/is responsible for the mandatory reporting of all medication errors and the following selected adverse events occurring during Remdesiviruse and considered to be potentially attributable to Remdesivir.

Deaths

Serious Adverse Events: Serious Adverse Events are defined as:

Death;

A life-threatening adverse event;

Inpatient hospitalization or prolongation of existing hospitalization;

A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;

A congenital anomaly/birth defect;

A medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

DRUG INTERACTIONS

Drug-drug interaction trials of Remdesivirand other concomitant medications have not been conducted in humans. Due to antagonism observed in vitro, concomitant use of Remdesivir with chloroquine phosphate or hydroxychloroquinesulfate is not recommended. In vitro, Remdesivir is a substrate for drug metabolizing enzymes CYP2C8, CYP2D6, and CYP3A4, and is a substrate for Organic Anion Transporting Polypeptides 1B1 (OATP1B1) and P-glycoprotein (P-gp) transporters. In vitro, Remdesivir is an inhibitor of CYP3A4, OATP1B1, OATP1B3, BSEP, MRP4, and NTCP. The clinical relevance of these in vitro assessments has not been established.

MICROBIOLOGY/RESISTANCE INFORMATION

Antiviral Activity: Remdesivir exhibited cell culture antiviral activity against a clinical isolate of SARS-CoV-2 in primary human airway epithelial (HAE) cells with a 50% effective concentration (EC50) of 9.9 nM after 48 hours of treatment. The EC50 value of Remdesivir against SARS-CoV-2 in Vero cells was 137 nM at 24 hours and 750 nM at 48 hours post-treatment. The antiviral activity of Remdesivir was antagonized by chloroquine phosphate in a dose-dependent manner when the two drugs were co-incubated at clinically relevant concentrations in HEp-2 cells infected with respiratory syncytial virus (RSV). Higher Remdesivir EC50 values were observed with increasing concentrations of chloroquine phosphate. Increasing concentrations of chloroquine phosphate reduced formation of Remdesivir triphosphate in normal human bronchial epithelial cells.

Resistance: No clinical data are available on the development of SARS-CoV-2 resistance to Remdesivir. The cell culture development of SARS-CoV-2 resistance to Remdesivir has not been assessed to date. Cell culture resistance profiling of Remdesivir using the rodent CoV murine hepatitis virus identified 2 substitutions (F476L and V553L) in the viral RNAdependent RNA polymerase at residues conserved across CoVs that conferred a 5.6-fold reduced susceptibility to Remdesivir. The mutant viruses showed reduced viral fitness in cell culture and introduction of the corresponding substitutions (F480L and V557L) into SARS-CoV resulted in 6-fold reduced susceptibility to Remdesivir in cell culture and attenuated SARS-CoV pathogenesis in a mouse model.

NONCLINICAL TOXICOLOGY

Carcinogenesis Given the short-term administration of Remdesivir for the treatment of COVID-19, long-term animal studies to evaluate the carcinogenic potential of Remdesivir are not required. Mutagenesis Remdesivir was not genotoxic in a battery of assays, including bacterial mutagenicity, chromosome aberration using human peripheral blood lymphocytes, and in vivo rat micronucleus assays. Impairment of Fertility Nonclinical toxicity studies in rats demonstrated no adverse effect on male fertility at exposures of the predominant circulating metabolite (GS-441524) approximately 2 times the exposure in humans at the RHD. Reproductive toxicity, including decreases in corpora lutea, numbers of implantation sites, and viable embryos, was seen when Remdesivir was administered intravenous daily at a systemically toxic dose (10 mg/kg) in female rats 14 days prior to mating and during conception; exposures of the predominant circulating metabolite (GS-441524) were 1.3 times the exposure in humans at the RHD. Animal Toxicology and/or Pharmacology Intravenous administration (slow bolus) of Remdesivir to male rhesus monkeys at dosage levels of 5, 10, and 20 mg/kg/day for 7 days resulted, at all dose levels, in increased mean urea nitrogen and increased mean creatinine, renal tubular atrophy, and basophilia and casts. Intravenous administration (slow bolus) of Remdesivir to rats at dosage levels of ≥3 mg/kg/day for up to 4 weeks resulted in findings indicative of kidney injury and/or dysfunction.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary: No adequate and well-controlled studies of Remdesivir use in pregnant women have been conducted. Remdesivir should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus. In nonclinical reproductive toxicity studies, Remdesivir demonstrated no adverse effect on embryofetal development when administered to pregnant animals at systemic exposures (AUC) of the predominant circulating metabolite of Remdesivir (GS-441524) that were 4 times (rats and rabbits) the exposure in humans at the recommended human dose (RHD) (see Data).

Animal Data:Remdesivir was administered via intravenous injection to pregnant rats and rabbits (up to 20 mg/kg/day) on Gestation Days 6 through 17, and 7 through 20, respectively, and also to rats from Gestation Day 6 to Lactation/Post-partum Day 20. No adverse effects on embryo-fetal (rats and rabbits) or pre/postnatal (rats) development were observed in rats and rabbits at nontoxic doses in pregnant animals. During organogenesis, exposures to the predominant circulating metabolite (GS-441524) were 4 (rats and rabbits) times higher than the exposure in humans at the RHD. In a pre/postnatal development study, exposures to the predominant circulating metabolite of Remdesivir (GS-441524) were similar to the human exposures at the RHD.

Nursing Mothers Risk Summary: There is no information regarding the presence of Remdesivir in human milk, the effects on the breastfed infant, or the effects on milk production. In animal studies, Remdesivir and metabolites have been detected in the nursing pups of mothers given Remdesivir, likely due to the presence of Remdesivir in milk. 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. Animal Data Remdesivir and its metabolites were detected in the plasma of nursing rat pups, likely due to the presence of Remdesivir and/or its metabolites in milk, following daily intravenous administration of Remdesivir to pregnant mothers from Gestation Day 6 to Lactation Day 20. Exposures in nursing pups were approximately 1% that of maternal exposure on lactation day 10.

Pediatric Use: The safety, effectiveness, or pharmacokinetics of Remdesivir for treatment of COVID-19 has not been assessed in pediatric patients. Physiologically-based pharmacokinetics (PBPK) modeling of pharmacokinetic data from healthy adults was used to derive pediatric doses. Pediatric doses are expected to result in comparable steady-state exposures of Remdesivir and metabolites as observed in healthy adults following administration of the recommended dosage regimen. For pediatric patients with weighing 3.5 kg to less than 40 kg, use Remdesivir (Remdesivir) for injection, 100 mg, and lyophilized powder only. Pediatric patients (older than 28 days) must have eGFR determined and full-term neonates (at least 7 days to less than or equal to 28 days) must have serum creatinine determined before dosing and daily while receiving Remdesivir. Pediatric patients should be monitored for renal function and consideration given for stopping therapy in the setting of substantial decline.

Geriatric Use: The pharmacokinetics of Remdesivir have not been evaluated in patients >65 years of age. In general, appropriate caution should be exercised in the administration of Remdesivir and monitoring of elderly patients, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Renal Impairment: Patients with eGFR greater than or equal to 30 mL/min have received Remdesivir for treatment of COVID-19 with no dose adjustment. The safety and efficacy of Remdesivir have not been assessed in patients with severe renal impairment or ESRD. The pharmacokinetics of Remdesivirhas not been evaluated in patients with renal impairment. Remdesivir is not recommended in adults and pediatric patients (at least 28 days old) with eGFR less than 30 mL/min or in full-term neonates (at least 7 days and less than or equal to 28 days old) with serum creatinine greater than or equal to 1 mg/dL unless the potential benefit outweighs the potential risk. Adult and pediatric patients (greater than 28 days old) must have eGFR determined and full-term neonates (at least 7 days to less than or equal to 28 days old) must have serum creatinine determined before dosing and daily while receiving Remdesivir. 11.6 Hepatic Impairment The pharmacokinetics of Remdesivirhave not been evaluated in patients with hepatic impairment. It is not known if dosage adjustment is needed in patients with hepatic impairment, and Remdesivir should only be used in patients with hepatic impairment if the potential benefit outweighs the potential risk. Hepatic laboratory testing should be performed in all patients prior to starting Remdesivir and daily while receiving Remdesivir.

OVERDOSAGE

There is no human experience of acute overdosage with Remdesivir. Treatment of overdose with Remdesivirshould 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.

DOSAGE AND ADMINISTRATION

Important Testing Prior to and During Treatment and Route of Administration

Adult and pediatric patients (greater than 28 days old) must have an eGFR determined and full-term neonates (at least 7 days to less than or equal to 28 days old) must have serum creatinine determined before dosing of Remdesivir and daily while receiving Remdesivir.

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

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

Recommended Dosage in Adult Patients

The recommended dosage in adults is a single loading dose of Remdesivir 200 mg on Day 1 followed by once-daily maintenance doses of Remdesivir 100 mg from Day 2 via IV infusion.

For patients requiring invasive mechanical ventilation and/or ECMO, total treatment duration is 10 days.

For patients not requiring invasive mechanical ventilation and/or ECMO, total treatment duration is 5 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).

Administer Remdesivir via IV infusion in a total volume of up to 250 mL 0.9% sodium chloride over 30 to 120 minutes.

Recommended Dosage in Pediatric Patients

For pediatric patients weighing 3.5 kg to less than 40 kg, the dose should be calculated using the mg/kg dose according to the patient's weight.

For pediatric patients weighing 3.5 kg to less than 40 kg, use Remdesivirfor injection, 100 mg, and lyophilized powder only.

Refer to Table 1 below for recommended dosage form and dosage in pediatric patients according to weight.

Table 1: Recommended Dosage Form and Dosage in Pediatric

BODY WEIGHT	RECOMMENDED DOSAGE FORM	LOADING DOSE (ON DAY 1)	MAINTENANCE DOSE (FROM DAY 2)
3.5kg to less than 40kg	Remdesivir Lyophilized Powder for Injection ONLY	5mg/kg	2.5mg/kg
40kg and higher	Remdesivir Lyophilized Powder for Injection OR Remdesivir Injection	200mg	100mg

- For pediatric patients requiring invasive mechanical ventilation and/or ECMO, total treatment duration is 10 days.
- For pediatric patients not requiring invasive mechanical ventilation and/or ECMO, total treatment duration Is 5 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).

Pregnancy

Remdesivirshould be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus. **Renal Impairment**

Adult and pediatric patients (greater than 28 days old) must have an eGFR determined and full-term neonates (at least 7 days to less than or equal to 28 days old) must have serum creatinine determined before dosing and daily while receiving Remdesivir. To calculate eGFR, providers/laboratories can use the methodology of their preference.

Hepatic Impairment: It is not known if dosage adjustment is needed in patients with hepatic impairment, and Remdesivir should only be used in patients with hepatic impairment if the potential benefit outweighs the potential risk. Hepatic laboratory testing should be performed in all patients prior to starting Remdesivir and daily while receiving Remdesivir.

Dose Preparation and Administration

Adults and Pediatric Patients Weighing 40 kg and Higher Adults and pediatric patients weighing 40 kg and higher can use Remdesivir for injection, 100 mg, lyophilized powder and Remdesivir injection, 100 mg/20 mL (5 mg/mL), solution.

Remdesivir (Remdesivir) for Injection, 100 mg, Lyophilized Powder

Reconstitution Instructions

Remove the required number of single-dose vial(s) from storage. For each vial:

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 [36°F to 46°F]).

Dilution Instructions:

Care should be taken during admixture to prevent inadvertent microbial contamination. It is always recommended to administer IV medication immediately after preparation when possible.

The reconstituted Remdesivir lyophilized powder for injection, containing 100 mg/20 mL Remdesivir solution, should be further diluted in 100 mL or 250 mL 0.9% sodium chloride infusion bags.

Using Table 2, determine the volume of 0.9% sodium chloride to withdraw from the infusion bag.

Table 2: Recommended Dilution Instructions Using Reconstituted Remdesivirfor Injection Lyophilized Powder in Adults and Pediatric Patients Weighing 40 kg and Higher

REMDESIVIR DOSE	0.9% SODIUM CHLORIDE INFUSION BAG VOLUME TO BE USED	VOLUME TO BE WITHDRAWN AND DISCARDED FROM 0.9% SODIUM CHLORIDE INFUSION BAG	REQUIRED VOLUME OF RECONSTITUTED REMDESIVIR FOR INJECTION
200mg (2 vials)	250mL	40mL	40mL (2 × 20 ml)
	100mL	40mL	40mL (2 × 20 ml)
100mg (1 vial)	250mL	20ml	20ml
	100mL	20ml	20ml

- Withdraw and discard the required volume of 0.9% sodium chloride from the bag per Table 2 using an appropriately sized syringe and needle.
- Withdraw the required volume of reconstituted Remdesivir for injection from the Remdesivir vial using an appropriately sized syringe per Table 2. Discard any unused portion remaining in the Remdesivir vial.
- 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. 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).

Administration Instructions:

The prepared diluted solution should not be administered simultaneously with any other IV medication. The compatibility of Remdesivir injection with IV solutions and medications other than 0.9% sodium chloride is not known. Administer the diluted solution with the infusion rate described in Table 3.

Table 3: Recommended Rate of Infusion — Diluted Remdesivir (Remdesivir) for Injection Lyophilized Powder in Adults and Pediatric Patients Weighing 40 kg and Higher

INFUSION BAG VOLUME	INFUSION TIME	RATE OF INFUSION
250mL	30 min	8.33mL/ min
	60 min	4.17mL/ min
	120 min	2.08mL/ min
100mL	30 min	3.33mL/ min
	60 min	1.67mL/ min
	120 min	0.83mL/ min

Remdesivir Injection, 100 mg/20 mL (5 mg/mL), Solution

Dilution Instructions

Care should be taken during admixture to prevent inadvertent microbial contamination. It is always recommended to administer IV medication immediately after preparation when possible.

- Remove the required number of single-dose vial(s) from storage. Each vial contains 100 mg of Remdesivir. For each vial:
- Equilibrate to room temperature (20°C to 25°C [68°F to 77°F]). Sealed vials can be stored up to 12 hours at room temperature prior to dilution.
- Inspect the vial to ensure the container closure is free from defects and the solution is free of particulate matter.
- Using Table 4, determine the volume of 0.9% sodium chloride to withdraw from the infusion bag.

Table 4: Recommended Dilution Instructions— Remdesivir (Remdesivir) Solution in Adults and Pediatric Patients Weighing 40 kg and Higher

REMDESIVIR DOSE	0.9% SODIUM CHLORIDE INFUSION BAG VOLUME TO BE USED	VOLUME TO BE WITHDRAWN & DISCARDED FROM 0.9% SODIUM CHLORIDE INFUSION BAG	REQUIRED VOLUME OF REMDESIVIR INJECTION SOLUTION
200mg (2 vials) 100mg (1 vial)	250mL	40mL 20mL	40mL (2 × 20 ml) 20mL

- Withdraw and discard the required volume of 0.9% sodium chloride from the bag per Table 4 using an appropriately sized syringe and needle.
- Withdraw the required volume of Remdesivir injection solution from the Remdesivir vial using an appropriately sized syringe per Table 4.
- Pull the syringe plunger rod back to fill the syringe with approximately 10 mL of air.
- Inject the air into the Remdesivir injection vial above the level of the solution.
- Invert the vial and withdraw the required volume of Remdesivir injection solution into the syringe. The last 5 mL of solution requires more force to withdraw.
- Discard any unused solution remaining in the Remdesivir vial.
- Transfer the required volume of Remdesivir injection solution to the infusion bag.
- 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).

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 0.9% sodium chloride is not known.

Administer the diluted solution with the infusion rate described in Table 5.

Table 5: Recommended Rate of Infusion—Diluted Remdesivir (Remdesivir) Solution in Adults and Pediatric Patients Weighing 40 kg and Higher

INFUSION BAG VOLUME	INFUSION TIME	RATE OF INFUSION
250mL	30 min	8.33mL/ min
	60 min	4.17mL/ min
	120 min	2.08mL/ min

Dose Preparation and Administration, Pediatric Patients Weighing 3.5 kg to Less Than 40 kg

For pediatric patients weighing 3.5 kg to less than 40 kg, use Remdesivir for injection, 100 mg, lyophilized powder only. Remdesivirfor Injection, 100 mg, Lyophilized Powder

Reconstitution Instructions

Remove the required number of single-dose vial(s) from storage. For each vial:

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 [36°F to 46°F]).

Dilution Instructions

Care should be taken during admixture to prevent inadvertent microbial contamination. It is always recommended to administer IV medication immediately after preparation when possible. Following reconstitution as instructed above, each vial will contain a 100 mg/20 mL (5 mg/mL) Remdesivir concentrated solution. For pediatric patients weighing 3.5 kg to less than 40 kg, the 100 mg/20 mL (5 mg/mL) Remdesivir concentrate should be further diluted to a fixed concentration of 1.25 mg/mL using 0.9% sodium chloride.

The total required infusion volume of the 1.25 mg/mL Remdesivir solution for infusion is calculated from the pediatric weight-based dosing regimens of 5 mg/kg for the Loading Dose and 2.5 mg/kg for each Maintenance Dose.

Small 0.9% sodium chloride infusion bags (e.g., 25, 50, or 100 mL) or an appropriately sized syringe should be used for pediatric dosing. The recommended dose is administered via IV infusion in a total volume dependent on the dose to yield the target Remdesivir concentration of 1.25 mg/mL.

A syringe may be used for delivering volumes less than 50 mL.

Infusion with IV Bag

Prepare an IV bag of 0.9% sodium chloride with volume equal to the total infusion volume minus the volume of reconstituted Remdesivir solution that will be diluted to achieve a 1.25 mg/mL solution.

Withdraw the required volume of reconstituted solution containing Remdesivir for injection into an appropriately sized syringe.

Transfer the required volume of reconstituted Remdesivir for injection to the 0.9% sodium chloride infusion bag.

Gently invert the bag 20 times to mix the solution in the bag. Do not shake.

Infusion with Syringe

Select an appropriately sized syringe equal to or larger than the calculated total infusion volume of 1.25 mg/mL Remdesivir solution needed.

Withdraw the required volume of 100 mg/20 mL (5 mg/mL) reconstituted Remdesivir solution from the vial into the syringe followed by the required volume of 0.9% sodium chloride needed to achieve a 1.25 mg/mL Remdesivir solution.

Mix the syringe by inversion 20 times.

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) (including any time before dilution into intravenous infusion fluids).

Administration Instructions

The prepared diluted solution should not be administered simultaneously with any other medication. The compatibility of Remdesivir (Remdesivir) injection with IV solutions and medications other than 0.9% sodium chloride is not known. Administer the diluted solution with the infusion rate described in Table 6.

Table 6: Recommended Rate of Infusion—Diluted Remdesivirfor Injection Lyophilized Powder for Pediatric Patients Weighing 3.5 kg to Less Than 40

Note: Rate of infusion may be adjusted based on total volume to be infused.

Storage of Prepared Dosages

Lyophilized Powder

After reconstitution, vials can be stored up to 4 hours at room temperature (20°C to 25°C [68°F to 77°F]) prior to administration or 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]). Dilute within the same day as administration.

Injection Solution

Prior to dilution, equilibrate Remdesivir injection to room temperature (20°C to 25°C [68°F to 77°F]). Sealed vials can be stored up to 12 hours at room temperature prior to dilution.

Diluted Infusion Solution

Store diluted Remdesivir solution for infusion up to 4 hours at room temperature (20°C to 25°C [68°F to 77°F]) or 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]).

DOSAGE FORM AND STRENGTH

Remdesivir for injection, 100 mg: Each single-dose vial of Remdesivir for injection 100 mg, contains a sterile, preservative-free white to off-white to yellow lyophilized powder that is to be reconstituted with 19 mL of Sterile Water for Injection and further diluted into 0.9% sodium chloride infusion bag prior to administration by intravenous infusion. Following reconstitution, each vial contains 100 mg/20 mL (5 mg/mL) Remdesivir re-concentrated solution.

HOW SUPPLIED

Lyophilized Powder

Remdesivir for injection, 100 mg, is supplied as a single-dose vial containing a sterile, preservative-free white to off-white to yellow lyophilized powder that is to be reconstituted with 19 mL of Sterile Water for Injection and further diluted into 0.9% sodium chloride infusion bag prior to administration by intravenous infusion. Following reconstitution, each vial contains 100 mg/20 mL (5 mg/mL) Remdesivir re-concentrated solution.

Discard unused portion.

The container closure is not made with natural rubber latex.

STORAGE AND HANDLING

Do not reuse or save unused Remdesivir lyophilized powder, injection solution, or diluted solution for infusion for future use. *Lyophilized Powder*

Store Remdesivir for injection, 100 mg, vials below 30°C (below 86°F) 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 [68°F to 77°F]) prior to administration or 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]). Dilute within the same day as administration.

Diluted Solution for Infusion

Store diluted Remdesivir solution for infusion up to 4 hours at room temperature (20°C to 25°C [68°F to 77°F]) or 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]).

Size : 340 X 200mm