Instructions for Preparation and Administration of Remdesivir (GS-5734™) for Injection, 100 mg

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1. PURPOSE AND SCOPE

The purpose of this document is to provide instructions related to the storage, handling, preparation, and administration of remdesivir (GS-5734™) for injection, 100 mg. Remdesivir (GS-5734™) for injection is supplied as a lyophilized formulation for reconstitution with sterile water for injection and dilution into 0.9% saline. Following reconstitution and dilution, administration is via intravenous infusion.

2. SAFETY INSTRUCTIONS

2.1. General Safety Considerations

- Remdesivir can be prepared in a standard pharmacy setting and does not require a clean room or fume hood.
- Standard personal protective equipment should be used when handling and preparing remdesivir for administration (e.g., lab coat and disposable gloves).
- Established and applicable procedures and policies for hazardous waste disposal should be followed for disposal of materials that have come in contact with remdesivir.
- Follow the instructions as given in the current version of the Material Safety Data Sheet and the additional considerations listed below.

2.2. Breakage of Glass Vials containing Remdesivir

- Suitable personal protective equipment (*e.g.*, lab coat and disposable, chemical resistant gloves) should be worn during cleanup.
- Do not attempt to pick up broken glass as it can pierce gloves and result in skin injury. A suitable brush or pair or forceps or tweezers should be used for cleanup of broken glass.
- Collect any remdesivir lyophilized formulation with a suitable brush and dispose per established and applicable procedures and policies for hazardous waste disposal.
- Properly dispose of all equipment (e.g., brush) utilized for cleanup per established and applicable procedures and policies for hazardous waste disposal.
- Clean the affected area twice with water followed by one cleaning with a suitable detergent solution.
- Dispose all wet, contaminated paper towels per established and applicable procedures and policies for hazardous waste disposal.

2.3. Spillage of Solutions Containing Remdesivir

- Standard personal protective equipment (e.g., lab coat and disposable gloves) should be worn during cleanup.
- Remove any visible spillage with clean, dry paper towels.
- Clean the affected area twice with water followed by one cleaning with a suitable detergent solution.
- Dispose all wet, contaminated paper towels per established and applicable procedures and policies for hazardous waste disposal.

2.4. Unused Remdesivir Drug Product or Diluted Drug Product for Infusion

Remdesivir (GS-5734™) for injection does not contain any preservative and is intended for single-use. Any remaining reconstituted remdesivir (GS-5734™) for injection and/or diluted remdesivir solution for infusion will be disposed per local applicable hazardous waste disposal policies and procedures.

3. GENERAL INFORMATION

3.1. Description

Remdesivir (GS-5734™) for injection, 100 mg, is a preservative-free, white to off-white or yellow, lyophilized solid containing 100 mg of remdesivir that is to be reconstituted with 19 mL of sterile water for injection and diluted into 0.9% saline prior to administration by intravenous (IV) infusion. Following reconstitution, each vial contains a 5 mg/mL remdesivir concentrated solution with sufficient volume to allow withdrawal of 20 mL (100 mg of remdesivir). Remdesivir (GS-5734™) for injection, 100 mg, is supplied as a sterile product in a single-use, 30 mL, Type 1 clear glass vial.

In addition to the active ingredient, remdesivir (GS-5734™) for injection contains the following inactive ingredients: sulfobutylether-β-cyclodextrin sodium salt (SBECD), water for injection, hydrochloric acid, and sodium hydroxide. Hydrochloric acid and sodium hydroxide are used to adjust the formulation to a pH of 3.0 to 4.0.

3.2. Storage Instructions

3.2.1. Storage of Remdesivir (GS-5734™) for Injection

Remdesivir (GS-5734™) for injection should be stored below 30 °C prior to use. Remdesivir (GS-5734™) for injection is recommended to be reconstituted and diluted within the same day as administration. Remdesivir (GS-5734™) for injection does not contain any preservative and is intended for single-use. Any unused remdesivir material should be discarded.

3.2.2. Storage of Reconstituted Solution Containing Remdesivir (GS-5734™) for Injection and Remdesivir Solution for Infusion

The total storage time of reconstituted solution containing remdesivir (GS-5734™) for injection and any prepared remdesivir solution for infusion should not exceed 4 hours at room temperature (20 °C to 25 °C) or 24 hours at refrigerated temperature (2 °C to 8 °C). Any unused remdesivir material should be discarded.

4. MATERIALS

4.1. Materials Provided by the Sponsor

Remdesivir (GS-5734™) for injection, 100 mg, is supplied as a sterile, single-use, preservative-free, white to off-white or yellow, lyophilized solid containing 100 mg of remdesivir that is to be reconstituted with 19 mL of sterile water for injection. The reconstituted solution containing remdesivir (GS-5734™) for injection should be further diluted into 0.9% saline prior to IV infusion (remdesivir solution for infusion).

Following reconstitution, each vial contains sufficient volume to withdraw 20 mL of 5 mg/mL reconstituted solution containing remdesivir (GS-5734™) for injection (100 mg of remdesivir). Reconstituted solution containing remdesivir (GS-5734™) for injection is hypertonic and must be diluted in 0.9 % saline prior to administration according to instructions in Section 5.

4.2. Materials to be Provided by the Clinical Site

Materials (0.9% saline infusion bags, infusion lines, injection syringes and sterile water for injection) specified in writing by the sponsor should be used for administration of remdesivir, or equivalent. The infusion pump and infusion sets should be prepared according to instructions supplied by the manufacturers.

A list of materials and equipment shown to be compatible with remdesivir (GS-5734™) for injection is provided in Section 6. Sterile needles of suitable size (e.g., 21G x 1”) are required for reconstitution and subsequent withdrawal and dilution of the reconstituted solution containing remdesivir (GS-5734™) for injection.

5. PREPARATION INSTRUCTIONS

5.1. Refer to Individual Single Patient Protocol for Specific Dosing Instruction

Per the Single Patient Protocol, the recommended adult dosing and duration of remdesivir (GS-5734™) for injection is 200 mg on the first day followed by 9 days of 100 mg once-daily to be administered via IV infusion in a total volume of up to 250 mL of 0.9% saline over 30 minutes. The infusion time may be extended up to 60 minutes in situations where 30 minutes is not operationally feasible.

Refer to the Individual Single Patient Protocol for pediatric dosing recommendations as the recommended adult dosing is not appropriate for pediatric patients.

Remdesivir (GS-5734™) for injection requires reconstitution with sterile water for injection and further dilution into 0.9% saline prior to IV administration. Table 1 includes the volume requirements for preparing the 200 mg and 100 mg remdesivir doses into 100 or 250 mL saline infusion bags. Please note that two vials of remdesivir (GS-5734™) for injection will need to be reconstituted to prepare the loading dose of 200 mg. Table 2 and Table 3 include the volume requirements for preparing pediatric weight-based dosing regimens at 5 mg/kg and 2.5 mg/kg respectively. Smaller saline infusion bags (e.g. 50 or 100 mL) should be used for pediatric dosing. For additional dosing information please refer to the Individual Single Patient Protocol.

Table 1: Recommended 200 mg and 100 mg Dose Preparation for Remdesivir Solution for Infusion

Dose (mg)	Infusion bag volume to be used (mL)	Volume of saline to be withdrawn and discarded from 0.9% saline infusion bag (mL)	Required volume of reconstituted remdesivir (GS-5734™) for injection (mL)	Suitable Syringe Size (mL)
200 (2 vials)	250	40	2 x 20	20
	100	40	2 x 20	20
100 (1 vial)	250	20	20	20
	100	20	20	20

Table 2: Recommended Loading Dose Preparation for Pediatric Body Weight < 40 kg

Body Weight (kg)	Pediatric Loading Dose for Body Weight < 40kg 5 mg/kg (mg)	Infusion bag volume to be used (mL)	Volume of saline to be withdrawn and discarded from 0.9% saline infusion bag (mL)	Required volume of reconstituted remdesivir (GS-5734™) (mL)	Suitable Syringe Size (mL)
2	10	50	2	2	3
3	15		3	3	3
4	20		4	4	5
5	25		5	5	5
7.5	37.5	100	7.5	7.5	10
10	50		10	10	10
15	75		15	15	20
20	100		20	20	20
25	125		25	25	30
30	150		30	30	30
35	175		35	35	30

Table 3: Recommended Maintenance Dose Preparation for Pediatric Body Weight < 40 kg

Body Weight (kg)	Pediatric Maintenance Dose for Body Weight < 40kg 2.5 mg/kg (mg)	Infusion bag volume to be used (mL)	Volume of saline to be withdrawn and discarded from 0.9% saline infusion bag (mL)	Required volume of reconstituted remdesivir (GS-5734™) (mL)	Suitable Syringe Size (mL)
2	5	50	1	1	1
3	7.5		1.5	1.5	3
4	10		2	2	3
5	12.5		2.5	2.5	3
7.5	18.8	100	3.8	3.8	5
10	25		5	5	10
15	37.5		7.5	7.5	10
20	50		10	10	10
25	63		13	13	20
30	75		15	15	20
35	88		18	18	20

5.2. General Instructions for Preparation of Remdesivir Solution for Infusion

- Aseptic technique should be used where appropriate during handling, preparation, and administration.
- Ensure that the work area is clean and clear of obstructions.
- Ensure that all necessary equipment and materials are available.
- Two vials of remdesivir (GS-5734™) for injection will be used for the initial loading dose. Remdesivir solution for infusion should be prepared on the same day as administration.
- One vial of remdesivir (GS-5734™) for injection will be used per patient per treatment day for each day following the initial loading dose. Remdesivir solution for infusion should be prepared on the same day as administration.
- The total storage time of reconstituted solution containing remdesivir (GS-5734™) for injection and any prepared remdesivir solution for infusion should not exceed 4 hours at room temperature (20 °C to 25 °C) or 24 hours at refrigerated temperature (2 °C to 8 °C) from the time of reconstitution.
- Excess reconstituted solution containing remdesivir (GS-5734™) for injection and any prepared remdesivir solution for infusion that is not used for administration should be discarded.

5.3. Instructions for Reconstitution of Remdesivir (GS-5734™) for Injection

1. Remove vials of remdesivir (GS-5734™) for injection from storage.
2. Aseptically reconstitute remdesivir (GS-5734™) for injection, 100 mg, by addition of 19 mL of sterile water for injection using a suitably sized syringe and needle (e.g. 20 mL syringe fitted with 21G x 1.0" needle). Immediately shake the vial for 30 seconds. Discard the vial if the vacuum in the vial does not pull the sterile water for injection into the vial.
3. Allow the contents of the vial to settle for 2 to 3 minutes. Each reconstituted vial of remdesivir solution for infusion contains a minimum volume of 20 mL of reconstituted solution containing remdesivir (GS-5734™) for injection. A clear solution should result.

   Note: 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. This procedure can be repeated as necessary until the contents of the vial are completely dissolved.

4. Carefully inspect each vial to ensure that the container closure is free from defects and the solution is essentially free of any particulate matter.

5.4. Instructions for Dilution of Reconstituted Remdesivir (GS-5734™) for Injection with 0.9% Saline

1. Using Table 1, Table 2, or Table 3 above, determine the volume of 0.9% saline to withdraw and discard from the infusion bag.

2. Remove and discard the required volume of 0.9% saline from the infusion bag using an appropriately sized syringe and needle.

3. Withdraw the required volume of reconstituted solution containing remdesivir (GS-5734™) for injection into an appropriately sized syringe as defined in Table 1, Table 2, or Table 3. As each vial of reconstituted solution containing remdesivir (GS-5734™) for injection will contain overfill, it is common for residual solution to remain in the vial after withdrawing the required amount. Only withdraw the exact volume of reconstituted solution containing remdesivir (GS-5734™) for injection defined in Table 1, Table 2, or Table 3 for each dose. Discard any unused reconstituted solution containing remdesivir (GS-5734™) for injection.

4. Inject the appropriate volume of reconstituted solution containing remdesivir (GS-5734™) for injection slowly into the 0.9% saline infusion bag and invert the bag 20 times to obtain a uniform mixture.

5. Appropriately label the infusion bag containing remdesivir solution for infusion with the following: protocol number, subject ID, subject initials, dose and dosing date.

5.5. Storage of Remdesivir Solution for Infusion

After reconstitution and/or dilution with 0.9% saline, the total storage time before administration (including any time before or after dilution) should not exceed 4 hours at room temperature (20°C to 25°C) or 24 hours at refrigerated temperature (2°C to 8°C).

5.6. Administration

Only the materials (infusion bags, infusion lines, and injection syringes) specified in writing by the sponsor should be used for administration of remdesivir, or those which are equivalent. The infusion pump and infusion sets should be prepared and primed according to instructions supplied by the manufacturers. Solution from the prepared infusion bag may be used for priming if the infusion set is designed to minimize solution waste during the priming step. If priming to waste, normal saline should be used as it is important to deliver the full volume of the prepared study drug (or placebo) during administration. A list of materials shown to be compatible with remdesivir (GS-5734™) for injection is provided in Section 6.

Following reconstitution and dilution, remdesivir solution for infusion in 0.9% saline should be administered as an IV infusion over 30 minutes. The infusion time may be extended up to 60 minutes in situations where 30 minutes is not operationally feasible. Please refer to Table 4 for flow rates that should be used to deliver remdesivir within the recommended time.

Table 4. Recommended Rates of Infusion for Remdesivir Solution for Infusion

Infusion bag Volume (mL)	Infusion Time (min)	Rate of Infusion (mL/min)
250	30	8.33
	60	4.17
100	30	3.33
	60	1.67
50	30	1.67
	45	1.11
	60	0.83

When the administration of remdesivir solution is complete, flush the IV line with at least 30 mL of 0.9% saline at the same infusion rate to ensure that all the remdesivir solution has been administered.

6. MATERIALS SHOWN TO BE COMPATIBLE WITH REMDESIVIR (GS-5734™) FOR INJECTION*

Material	Manufacturer	Part Number
Infusion pump: Must be capable of infusion rates listed in Table 4		
Plum A+	Hospira/Abbott	12680-04-04
Infusion sets: Length and gauge suitable for infusion rates in Table 4		
Lifeshield Primary Plumset CLAVE Port, Clave Y-Site, 103", Non-DEHP	Hospira	12538-28
Smallbore Extension Set, PVC non-DEHP	B. Braun Medical	471960 / ET06S
EXT SET, LIFESHIELD MACROBORE INJ SITE LF, Extension Set LifeShield® 16.5 Inch 5.2 mL DEHP-Free	Hospira	1268928
Solution Set Continu-Flo®, 105" PVC-DEHP with filter	Baxter	2C6572
Administration Set, 102" PVC non-DEHP with filter	Baxter	2H6480
Administration Set SafeDay™, 104" PVC non-DEHP with filter	B.Braun Medical	352904
Infusion fluid/bag: 50mL, 100mL, or 250mL		
0.9% Sodium Chloride Injection USP, 250 mL Viaflex container	Baxter Healthcare	2B1322
0.9% Sodium Chloride Injection USP, 50 mL Viaflex container		2B1306, 2B1301, 2B1308
0.9% Sodium Chloride Injection USP, 250 mL	Hospira	798302
0.9% Sodium Chloride Injection USP, 250 mL	B. Braun Medical	L8002
0.9% Sodium Chloride, DEHP, PVC, 250mL	Hospira	NDC 0409-7983-02
0.9% Sodium Chloride, Non-DEHP, Non-PVC, 250mL	B Braun Medical	NDC 0264-7800-20

Material	Manufacturer	Part Number
Syringes:		
1 mL Sterile Syringe, Luer-Lok™ Tip	BD	309628
3 mL Sterile Syringe, Luer-Lok™ Tip		309657
5 mL Sterile Syringe, Luer-Lok™ Tip		309646
10 mL Sterile Syringe, Luer-Lok™ Tip		309604
20 mL Sterile Syringe, Luer-Lok™ Tip		302830
30 mL Sterile Syringe, Luer-Lok™ Tip		302832
1 mL Norm-Ject® Luer Syringe	Henke Sass Wolf GmbH	4010.200V0
20 mL Norm-Ject® Luer Syringe		4200.X00V0

*It is acceptable to use alternative pumps and infusion sets that are not the prescribed in this Pharmacy Manual if determined to be equivalent in performance and material

For questions and inquiries regarding this pharmacy manual, please email RDV.PM.Inquiry@gilead.com