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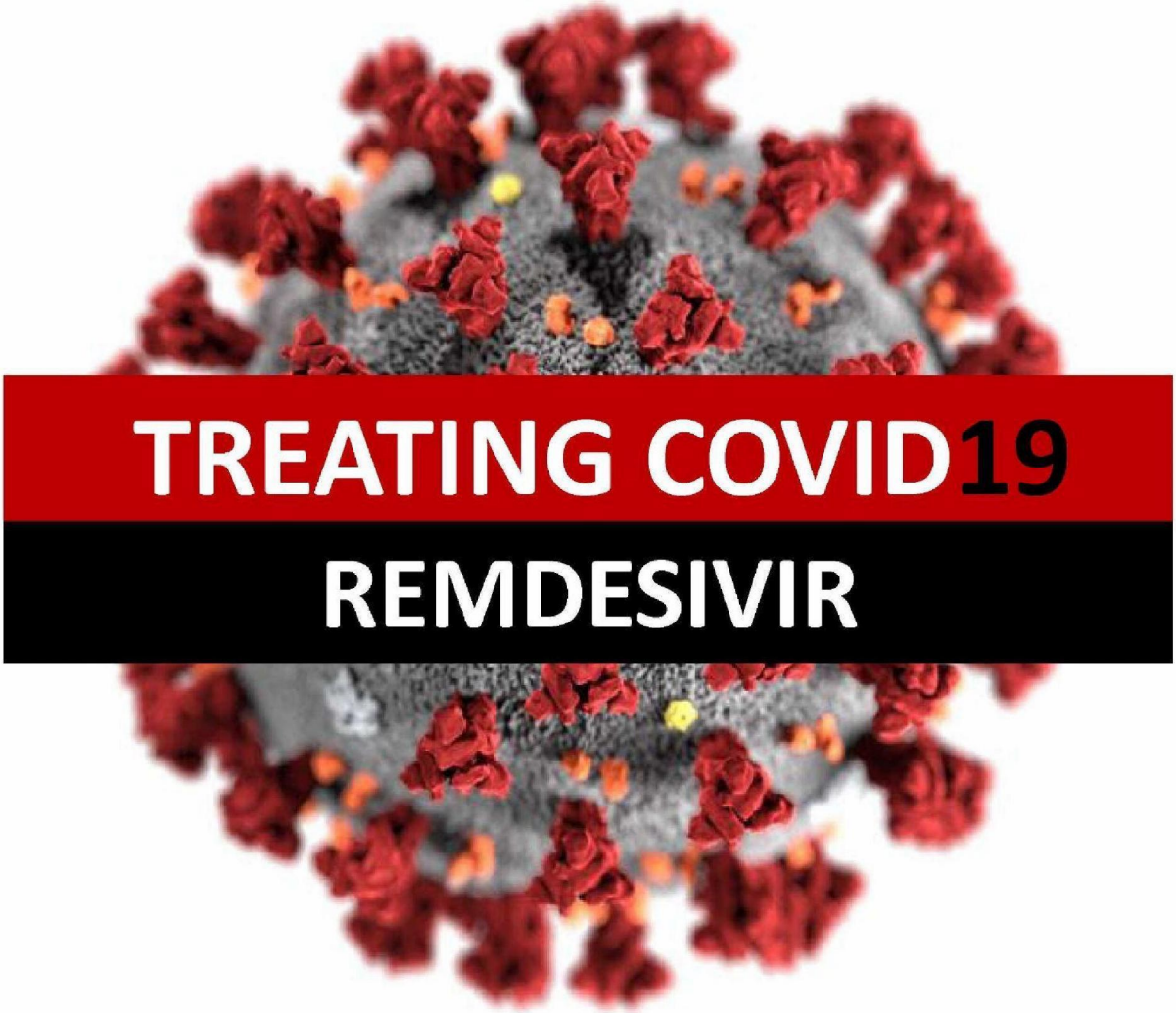

TREATING COVID19

REMDESIVIR

SUSTAINABLE DEVELOPMENT GOALS ADVOCATES

FOR DETAILS CONTACT:

Skyquest Technology Group

5.1.2e @protonmail.com

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Remdesivir
for Injection

100 mg

COMPOSITION
Each vial contains :
Remdesivir ..... 100 mg.
Sulfobutyl ether beta-cyclodextrin
Sodium ..... q.s.
HCl /NaOH have been added for pH adjustment

DESCRIPTION
Remdesivir (formerly GS-5734) is a prodrug of a modified adenine nucleoside analog GS-441524. Remdesivir undergoes efficient metabolic conversion in cells and tissues to active nucleoside triphosphate metabolite that inhibits viral RNA polymerases, but not host RNA or DNA polymerases. Remdesivir exhibits a potential for clinical efficacy against viruses and other filovirus infections based on the following:
1) Potent in vitro activity in multiple relevant cell types against multiple virus isolates, including the virus variants isolated during the 2014-16 outbreak in West Africa.
2) Potent and consistent in vitro antiviral activity against diverse species of the virus family, including Zaire, Sudan, and Bundibugyo viruses, as well as Marburg virus.
3) Preclinical pharmacokinetic profile in non-human primates and other relevant animal species indicating high and persistent levels of pharmacologically active nucleoside triphosphate metabolite in peripheral blood mononuclear cells (PBMCs); this measurement is used as a surrogate for drug levels in cells relevant for virus infection, supporting once daily administration.
4) Preclinical safety profile supporting safe clinical administration at doses potentially active against virus infections.
5) Clinical safety profile from > 100 human subjects dosed with intravenous remdesivir supports the clinical dosing regimen recommended for the treatment of virus. Single and repeated doses of remdesivir were safely administered in Phase 1 studies in healthy human subjects, prevail IV study in male virus disease survivors, as well as during compassionate use for the treatment and post exposure prophylaxis of virus infection.
6) Potent therapeutic efficacy in virus-infected rhesus monkeys, the most relevant in vivo preclinical model of viruses, at drug exposures that were well tolerated and can be safely achieved in humans. The in vivo therapeutic efficacy has been demonstrated in non-human primates against multiple virus variants including Kikwit/1995 and Makona/2014 as well as against Marburg virus Angola/2005 infections.
7) Tissue distribution studies in non-human primates indicate effective penetration and distribution of remdesivir into immune privileged sites (genital tract, eye, and to some extent brain) that may represent a persistent reservoir of viruses. Relatively high levels of remdesivir metabolites were also detected in human semen following single and repeated administration of remdesivir, suggesting potential for antiviral effect in human genital tract.
8) Sufficient supply of remdesivir drug product is available in a stable lyophilized formulation that does not require cold chain for transport and storage.

INDICATIONS
Consistent antiviral activity against all tested filoviruses (Zaire, Sudan, Bundibugyo, and Marburg). Similar antiviral activity was observed also against pathogenic viruses (MERS and SARS CoV) and paramyxoviruses (Nipah and Hendra).
Primary indication currently in clinical development is for the treatment of laboratory-confirmed viral infection. In addition, preclinical data support expansion into treatment of Marburg virus and other filovirus infections as well as into filovirus post exposure prophylaxis.
All patients including children of any age and pregnant women with laboratory confirmed viral infection.

DOSAGE AND ADMINISTRATION
The remdesivir dosing regimen for adult and adolescent (≥ 40 kg) patients with acute viral infection is as follows: Remdesivir Injection 150 mg diluted with sodium chloride 0.9% Injection 100ml should be infuse once daily slowly over 30 min. The treatment should be followed up to 10 days maintenance dose by taking care of the side effect and patient's condition. The recommended Remdesivir dosing duration is a total of 10 days, but dosing may be continued for an additional 4 days at 100 mg IV once daily if virus remains detectable in plasma at day 10 of treatment.
For pediatric patients with body weight < 40 kg, a body weight-based dosing regimen of one loading dose of remdesivir 5 mg/kg IV (infused over 30 min) daily for 10 days. Remdesivir 2.5 mg/kg IV (infused over 30 min) be used as maintenance dose. but dosing may be continued for an additional 4 days at 50 mg IV once daily if virus remains detectable in plasma at day 10 of treatment
There are no clinical safety or pharmacokinetic (PK) data available for remdesivir in patients with renal and/or hepatic impairment. Given the benefit: risk ratio in patients with acute viral infection, no dose modification is recommended at the present time for patients with renal and/or hepatic impairment.

PHARMACOKINETICS
The PK of the exact proposed dosing regimen has not been evaluated, but sufficient clinical data exists to support this regimen.
Following single-dose, 2-hour IV infusion of remdesivir solution formulation at doses ranging from 3 to 150 mg, remdesivir exhibited a dose-linear PK. Repeated once-daily 1-hour infusions of 150 mg remdesivir solution formulation demonstrated time-linear PK through 14 days. Following single-dose, 2-hour IV administration of remdesivir solution formulation at doses of 75 and 150 mg, remdesivir exhibited similar PK profiles as the lyophilized formulation.
Even though remdesivir 75 mg administered IV over 30 minutes provided similar parent exposure as the same dose administered over 2 hours, PBMC exposure of GS-443902 was higher than remdesivir 150 mg administered IV over 2 hours. This data supports the administration over the shorter time interval of 30 minutes as a more effective dosing method for maximizing the intracellular levels of the active metabolite GS-443902.
A prolonged intracellular half-life of more than 35 hours was observed for GS-443902 in PBMCs, supporting the once-daily dosing of remdesivir.
Furthermore, an accumulation ratio of 2.7 to 3.5-fold for intracellular metabolites suggests that a 200 mg remdesivir loading dose will better facilitate the achievement of subsequent steady-state PBMC levels of GS-443902 following repeat 100 mg daily maintenance dosing of remdesivir, which might be critical in the treatment of acutely infected patients.

Rationale for Dose Selection:
The proposed dosing regimen for patients with viral infection was selected to provide similar systemic remdesivir exposure to that observed in filovirus infected rhesus and cynomolgus monkeys successfully treated with remdesivir. Efficacy studies in virus infected rhesus and Marburg virus-infected cynomolgus monkeys treated with a single 10 mg/kg loading dose followed by 11 days of a once-daily 5 mg/kg maintenance dose of remdesivir provided 100% and 83% survival, respectively, against the lethal effects of filovirus when initiated on Day 4 and 5 post infection, respectively. The recommended dosing regimen reflects the current estimation of the effective dose. The efficacy of this dosing regimen in virus infected patients has not been determined in a controlled randomized clinical study. The final human dosing regimen might be further modified based on the outcome of future clinical trials as well as animal models of viral diseases.
The 200 mg loading dose and 100 mg maintenance dose for up to 13 days is lower than that previously administered to and well-tolerated by one patient with active virus meningitis who received 2 days of remdesivir 150 mg IV once daily followed by 12 days of remdesivir 225mg IV once daily. In addition, 150 mg IV once daily dosing for up to 14 days was generally well tolerated in healthy volunteers supporting the use of 100 mg daily doses of remdesivir for up to 14 days in viral-infected patients.

Route of administration:
Intravenous infusion for 30 minutes. No special training or equipment is required for the drug administration.
If possible, daily monitoring or renal (creatinine and BUN) and liver (ALT, AST) functions should be performed.

Preparation:
Remdesivir lyophilized formulation for injection is a preservative-free, white to off-white or yellow lyophilized solid containing 100 mg remdesivir that is to be reconstituted with 29 mL of Sterile Sodium Chloride Solution 0.9% and diluted into intravenous infusion fluids prior to intravenous administration.
Preparation of Remdesivir for IV administration will require Sterile Sodium Chloride Solution 0.9% (to reconstitute the product) and 0.9% sodium chloride USP (normal saline for infusion). (100 mL preferred).

CONTRAINDICATIONS
There are no known incompatibilities or contraindications for co-administration of remdesivir with ZMapp or other antibodies. No inhibition of VSV replication by remdesivir was observed in vitro.

PRESENTATION
It is supplied as a sterile product in a single use, 50 mL Type I clear glass vial. Each vial is sealed with a rubber stopper and aluminum over seal with a plastic flip off cap.

STORAGE
Store at a temperature not exceeding 30°C. Protect from light.
Keep out of the reach of children.

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Analytical Testing Record of Finished Product **INJECTABLE**
(As per Schedule U & G.M.P)
Certificate of Analysis

REMDESIVIR FOR INJECTION 100MG

	Test Report No. : KPA/FP/112/8960/001/2654	Pharmacopoeia Reference IHS	
Batch No. : TN-1246	Mfg. Date : June 2020	Exp. Date : May 2022	Party Code: P02727
Date of receipt of Finish Sample : 02/06/2020	Sample Size : 20 VIALS	Batch Size : 5200 VIALS	
Date of receipt of Sterility Sample : 02/06/2020	Analyst : 5.1.2e	Pharmacopoeia Applied IHS	

Analytical Data

Packing Presentation: Transparent type-I, glass vials with paper label and sealed red color flip off

Tests	Specifications	Observations
Description	It should be white to off white colored lyophilized cake.	Off white colored lyophilized cake.
Identification. By. HPLC	The retention time of the major peak in the chromatogram of the Assay preparation corresponds to that in the chromatogram of the Standard preparation.	Identified
Color and clarity of solution	Clear solution after reconstitution.	After reconstitution clear solution.
Water Contents	Not more than 1.0%.	0.17%
Uniformity of Dosage units	L1= Maximum allowable acceptance value for first 10 units is not more than 15, L2= Maximum allowable acceptance value for 30 units is not more than 25.	2.9
Particulate Matter >= 10 µm	Not more than 6000 particles	176
>= 25 µm	Not more than 600 particles	9
Sterility test	To be sterile	It is sterile.

Assay	Limit	Claim	Result	%age	Protocol Applied
Each vial contains: Remdesivir	90% -110%	100 mg	98.5 mg	98.5%	In House Specification

Conclusion : The above product complies with above specifications and meets the standard quality.

5.1.2e

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100 mg
(Lyophilized)
for Injection
Remdesivir

Remdesivir
for Injection
(Lyophilized)
FOR IV USE ONLY
Single dose vial
100 mg
Antiviral Drug

Each vial contains:
Remdesivir ..... 100 mg.
Sulfobutyl ether beta-cyclodextrin Sodium ..... q.s.
HCl / NaOH have been added for pH adjustment
Dosage: As directed by the Physician.
Storage: Store at a temperature not exceeding 30°C. Protect from light.
Direction for use:
Dissolve the contents of the vial in 29 ml Sterile Sodium Chloride Solution 0.9%.
Further dissolve in Sterile Sodium Chloride Solution 0.9% for IV infusion, slowly infuse the solution in 30 minutes, preferred total volume 100 ml. The dose should be approx 1 mg/ml after dissolution.
Use immediately after dissolving the contents.
If any foreign Particle is visible after dissolving the contents, Please do not use the solution.

Remdesivir
for Injection
(Lyophilized)
FOR IV USE ONLY
Single dose vial
100 mg
Antiviral Drug

Caution: It is dangerous to take without medical supervision.

Keep out of the reach of children.

Mfg. Lic. No.: 1804-B

1 89 04187 28105 9

Amritsar - India

47x18 mm
unvarnished area
Do not print this colour

Expiry Date is 24 months from the Mfg. Date. For eg. 02/2020 to 01/2022

Check List for Labeling														
Work Order No. :	Version	Pharmacop.	Spell.	Compo.	Batch, Mfg. Exp.	Expiry as per Schedule 'P'	M.R.P.	Mfg. Lic.No./ Nutral Code	Packing	Category	Mfg. Name	Reg.No.	Check Order for strength, Volume & Packing	STORAGE
	English													
Matching all parameters between Box and Label														
Matching the parameter with label of leader brand														

Previous specimen artwork : NEW	Designed by : Ramesh Kumar	Order Quantity	Party Name	Packing
Checked by : / Production Incharge / QC Incharge	Approved by : Q.A.	Authorized by: M.D.	Party Approval	Card Board used for carton : □ G/B □ W/B □ I.T.C. □ Pearl	Each vial packed in a printed carton with leaflet.

Certification & Inspection

Certificate of Compliance

Certificate Number: UQ-20200624013

This is to certify that

SKYQUEST TECHNOLOGY CONSULTING PRIVATE LIMITED

at

C-50 SAMATVA BUNGLOWS, BEFORE CLUB O7, SHELLA, SOUTH BOPAL, AHEMDABAD-380058

Has successfully implemented the Quality management System and been found working satisfactorily as per the norms of **"Good Manufacturing Practice"** as laid down by " **World Health Organisation** "which has been in conformance to the requirements of

WHO-GMP

MANUFACTURER AND DISTRIBUTOR FOR PPE, COVER ALL, N-95 MASK, 3- PLY MASK, GLOVES, CORONA SPRAY, SANITISER, GOGGLES FROM WOVEN/NON-WOVEN AND PLASTIC MATERIALS AND OTHER PROTECTIVE GEARS AND DIAGNOSTIC EQUIPMENT

MANUFACTURER AND DISTRIBUTOR FOR PHARMACEUTICAL DRUGS AND FINE CHEMICALS

This certificate is issued under the following conditions:

1. It applies only to the quality system maintained in the manufacture of above referenced Models Products.
2. The certificate remains valid until the manufacturing conditions or the quality systems are changed and is subject to continuous surveillance according to the WHO-GMP Guidelines
3. The certificate validity is conditioned by positive results or surveillance audits.

Validity of this certificate can be verified at www.ukcertifications.org.uk/verify

Date of Certification	24th June 2020
1st Surveillance Audit Due	23rd June 2021
2nd Surveillance Audit Due	23rd June 2022
Certificate Expiry (subject to the company maintaining its system to the required standard)	23rd June 2023

5.1.2e

Authorised Signatory

UK Certification & Inspection Ltd.

GOOD MANUFACTURING PRACTICE WHO - GMP CERTIFIED QUALITY PRODUCT

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Company No. 11847851