Drug of the Season

Drug : **Remdesivir**

Class : **Antiviral**

Dosing Form : 100mg, 200mg

Strength : Injection

DCGI Approval : 22.06.2020

USFDA Approval : 1st May 2020, the FDA issued emergency use authorization (EUA)

Indication: Remdesivir is indicated for adults and pediatric patients (12 years of age or 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.

Dosing Information:

Adult Dosing:

Intravenous route

COVID-19, Hospitalized patients

a) Patients NOT Requiring Invasive Mechanical Ventilation and/or Extracorporeal Membrane Oxygenation (ECMO)
   1) Loading dosage: 200 mg IV loading dose on day 1.
   2) Maintenance dosage: 100 mg IV once daily on days 2 through 5; may extend for an additional 5 days if clinical improvement is not demonstrated.

b) Patients Requiring Invasive Mechanical Ventilation and/or Extracorporeal Membrane Oxygenation (ECMO)
   1) Loading dosage: 200 mg IV loading dose on day 1.
   2) Maintenance dosage: 100 mg IV once daily on days 2 through 10.

Pediatric Dosing:

Intravenous route

COVID-19, Hospitalized patients

a) 12 Years or Older and 40 kg or Greater.
   1) Patients NOT Requiring Invasive Mechanical Ventilation and/or Extracorporeal Membrane Oxygenation (ECMO).
      a) Loading dosage: 200 mg IV loading dose on day 1.
      b) Maintenance dosage: 100 mg IV once daily on days 2 through 5; may extend for an additional 5 days if clinical improvement is not demonstrated.
   2) Patients Requiring Invasive Mechanical Ventilation and/or Extracorporeal Membrane Oxygenation (ECMO).
      a) Loading dosage: 200 mg IV loading dose on day 1.
      b) Maintenance dosage: 100 mg IV once daily on days 2 through 10.

Pharmacokinetics

Drug Concentration Levels

a) Peak Concentration: IV, single-dose, 3 to 225 mg: Linear pharmacokinetic profile.

b) Area Under the Curve: IV, single-dose, 3 to 225 mg: Linear pharmacokinetic profile.

ADME

Metabolism

- Multiple cell types: Extensive
- Remdesivir triphosphate (GS-443902; major): Active
- Substrate of CYP2C8, CYP2D6, CYP3A4
- Substrate of OAPT1B1 and P-gp transporters; impact likely limited with parenteral.
- administration
- Inhibitor of CYP3A4, OATP1B1, OATP1B3, BSEP, MRP4, and NTCP; impact likely limited by rapid clearance.

Excretion

- Renal excretion: 74%, changed and unchanged
- Fecal excretion: 18%

Contraindications: Known hypersensitivity to remdesivir or any component of the product.

Cautions

- **Concomitant use:** Not recommended in combination with chloroquine phosphate or hydroxychloroquine sulfate as it may result in reduced antiviral activity of remdesivir.
- **Hepatic:** Transaminase elevations have been reported, including serious cases; monitoring recommended and discontinuation may be necessary.
- **Immunologic:** Hypersensitivity reactions including infusion-related and anaphylactic reactions have been reported during and following administration; monitoring recommended and dose adjustment and discontinuation of therapy may be necessary.
- **Renal:** Use not recommended in patients with an estimated GFR less than 30 mL/min.

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.

Adverse Effects

Common

- **Gastrointestinal:** Nausea
- **Other:** Fever

Serious

- **Cardiovascular:** Cardiac arrest
- **Hepatic:** Hepatotoxicity, Increased liver aminotransferase level, abnormal liver function tests
- **Immunologic:** Anaphylaxis, Hypersensitivity reaction
- **Renal:** Acute injury of kidney
- **Respiratory:** Respiratory failure
- **Other:** Infusion reaction

Drug-Drug Interactions

Category	Drug/s (Examples)	Interaction Effect	Management
Antimalarial*	Chloroquine	May result in risk of reduced antiviral activity of remdesivir.	Contraindicated for concurrent use.
Antimalarial*	Hydroxychloroquine	May result in risk of reduced antiviral activity of remdesivir.	Contraindicated for concurrent use.

Severity: *The interaction may be life-threatening and/or require medical intervention to minimize or prevent serious adverse effects.

Effects in Pregnancy

Severity	Management
Moderate	Fetal risk cannot be ruled out. Available evidence is inconclusive or is inadequate for determining fetal risk when Remdesivir is used in pregnant women or women of childbearing potential. Weigh the potential benefits of drug treatment against potential risks before prescribing Remdesivir during pregnancy.

Effect in Lactation

Severity	Management
Major	Infant risk cannot be ruled out. Available evidence and/or expert consensus is inconclusive or is inadequate for determining infant risk when Remdesivir is used during breast-feeding. Weigh the potential benefits of treatment against potential risks before prescribing Remdesivir during breast-feeding.

Medication Counselling: Advice to watch for side effects like infusion-related reactions and hepatic adverse reactions.

References:

1. http://www.micromedexsolutions.com/

2. http://www.cdsco.nic.in/