MONOGRAPH

Remdesivir Monograph - Paediatric

Scope (Staff):	Medical, Pharmacy, Nursing
Scope (Area):	All Clinical Areas

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

QUICKLINKS

Dosage/Dosage Adjustments | Administration | Compatibility | Monitoring

DRUG CLASS

Antiviral – for severe acute respiratory syndrome – coronavirus-2 (SARS-CoV-2)[1]

INDICATIONS AND RESTRICTIONS

- Remdesivir can be considered for use in exceptional circumstances in the treatment of severe acute respiratory syndrome – coronavirus-2 (SARS-CoV-2) in the following patients:
  - Patients over 28 days old weighing at least 3kg who do not require oxygen and who are at high risk of deterioration within 7 days of symptom onset.[2]
  - Patients over 28 days old weighing at least 3kg with severe COVID-19 who are likely to progress to ventilation and who need treatment with corticosteroids and oxygen, but not requiring non-invasive or invasive ventilation.[2]

IV: Restricted (red) antiviral

ChAMP approval is required prior to prescription.

CONTRAINDICATIONS

- Hypersensitivity to remdesivir or any component of the formulation.[3-6]

PRECAUTIONS

- Remdesivir should be used cautiously in patients with hepatic or renal impairment.
    - Remdesivir is not approved for use in patients with Alanine aminotransferase (ALT) ≥ 5 times the upper limit of normal (ULN) by local laboratory measure.[1, 3, 7]
    - Remdesivir should not be commenced in patients with an eGFR of <30mL/minute.[1, 3, 7]
- Remdesivir contains sulfobutylether-β-cyclodextrin (SBECD) as a solubility enhancer which is renally cleared and accumulates in patients with decreased renal function.[3, 6].

FORMULATIONS

Listed below are products available at PCH, other formulations may be available, check with pharmacy if required:

- Remdesivir 100 mg **lyophilized** powder for injection

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Treatment of hospitalised patients with severe SARS-CoV-2 infection:

Infants and children ≥ 28 days old and ≥ 3kg:

- 5 mg/kg/dose (to a maximum of 200 mg) as a single IV loading dose on day one followed by 2.5 mg/kg/dose (to a maximum of 100 mg) IV once daily for FOUR (4) days.[2, 4, 6]
- Treatment may be extended out to a TEN (10) day course in discussion with Infectious Diseases team if there is no clinical improvement.[2, 5, 6]

Early treatment (within 7 days of symptom onset) of patients with COVID-19 who are at an increased risk of hospitalisation or death:

Infants and children ≥ 28 days old and ≥ 3kg:

- 5 mg/kg/dose (to a maximum of 200 mg) as a single IV loading dose on day one followed by 2.5 mg/kg/dose (to a maximum of 100mg) IV once daily for TWO (2) days.[2, 4, 6]

Renal impairment:

eGFR calculator

- There are currently no recommendations for dose reductions in renal impairment however, remdesivir is not approved for use in patients with eGFR < 30 mL/minute/1.73m^2.[3, 4, 6].

Hepatic impairment:

- There are currently no recommendations for dose reductions in hepatic impairment however, remdesivir is not approved for use in patients with Alanine aminotransferase (ALT) ≥5 times the upper limit of normal (ULN) by local laboratory measure at baseline.[3]
- Remdesivir should be discontinued in patients who develop:

- ALT ≥ 5 times the upper limit of normal during treatment with remdesivir (may be restarted when ALT is < 5 times the upper limit of normal).[3, 7]
- ALT elevation accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or international normalised ratio (INR).[3, 6, 7]

RECONSTITUTION & ADMINISTRATION

- Remdesivir must be administered in a location with suitable access to personnel and equipment to manage suspected infusion related reactions or anaphylaxis during the infusion and for the 60-minute observation period after completion of the infusion.[4]

Reconstitution:

Remdesivir 100mg lyophilized powder for injection

- Reconstitute each 100 mg vial of remdesivir with 19 mL of Sterile Water for Injection to give a concentration of 100 mg/20 mL.[3, 4, 8]
- Discard the vial if a vacuum does not pull the Sterile Water for Injection into the vial.[4]
- Immediately shake the vial for 30 seconds, then allow the contents of the vial to settle for 2 to 3 minutes. A clear solution should result.[4, 8]
- 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.[4, 8]
- Inspect the vial to ensure the container closure is free from defects and the solution is free of particulate matter.[4]

Administration:

For children and adolescents weighing ≥ 40kg:

- A volume of 250 mL is preferred, but a volume of 100 mL may be used for patients with severe fluid restrictions.[3]

Instructions for a 250 mL infusion bag:[3, 4, 8]

Dose	Volume of sodium chloride 0.9% to remove from **250 mL** infusion bag*	Volume of remdesivir solution 100 mg/20 mL to add to bag	Final volume to infuse
200 mg	55 mL	40 mL	250 mL
100 mg	35 mL	20 mL	250 mL

*Each 250 mL infusion bag has an estimated overage of 15 mL

- Gently invert the bag approximately 20 times to mix the solution once diluted. Do not shake.[3, 4]

Instructions for a 100 mL infusion bag: [3, 4, 8]

Dose	Volume of sodium chloride 0.9% to remove from **100 mL** infusion bag^	Volume of remdesivir solution 100 mg/20 mL to add to bag	Final volume to infuse
200 mg	51 mL	40 mL	100 mL
100 mg	31 mL	20 mL	100 mL

^Each 100 mL infusion bag has an estimated overage of 11 mL

- Gently invert the bag approximately 20 times to mix the solution once diluted. Do not shake.[3, 4]

For children weighing < 40kg:

- Dilute with sodium chloride 0.9% immediately after reconstitution to a final concentration of 1.25 mg/mL.[3, 4]
- Gently invert the bag (or syringe) approximately 20 times to mix the solution once diluted. Do not shake.[4]

IV infusion

- Administer by intravenous infusion over 30 to 120 minutes.[3, 4, 8]
- If the patient develops an infusion-related hypersensitivity reaction, depending on the severity of the reaction and if it is deemed clinically appropriate to continue therapy, the rate of infusion may be reduced to a maximum infusion time of 120 minutes to help minimise symptoms.[1, 3, 8]

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids:

- Sodium chloride 0.9%[8]

Compatible at Y-site:

Compatibilities of IV drugs must be checked when two or more drugs are given concurrently.

MONITORING

- Given the limited experience with remdesivir patients should have ongoing monitoring of appropriate clinical and laboratory levels to aid in the early detection of any potential adverse effects.
- Patients must be monitored and observed for possible anaphylactic and infusion related reactions throughout the infusion and for one hour after completion of the infusion.[5, 6]
- Patients should have the following monitored during treatment with remdesivir:
    - Liver function tests at baseline and periodically during course.[5-7]
    - Injection site – due to risk of irritation in the event of extravasation[6, 8]
    - Renal function and electrolytes[4, 6, 7]

- Prothrombin time[4-6]
- Heart rate[6]

- Remdesivir should be discontinued in patients who develop:
  - ALT ≥ 5 times the upper limit of normal during treatment with remdesivir (may be restarted when ALT is < 5 times the upper limit of normal.)[1, 3, 7]
  - ALT elevation accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or international normalised ratio (INR).[1, 3]

ADVERSE EFFECTS

Common: headache, nausea, vomiting, increased liver transaminases, rash, prolonged prothrombin time.[1, 3, 7]

Rare: hypersensitivity or infusion related reactions (including hypo and hypertension, anaphylaxis, tachycardia, bradycardia, chills, sweating, diaphoresis, hypoxia, fever, shivering, dyspnoea, wheezing, angioedema, rash, nausea and vomiting). In cases of infusion related reactions - slower infusion rates may potentially prevent these reactions.[7, 8]

STORAGE

100 mg **lyophilized** powder for injection

- Store below 30ºC.[3, 8]

INTERACTIONS

This medication may interact with other medications; consult PCH approved references (e.g. Clinical Pharmacology), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

Please note: The information contained in this guideline is to assist with the preparation and administration of **remdesivir**. Any variations to the doses recommended should be clarified with the prescriber prior to administration

Related CAHS internal policies, procedures and guidelines

Antimicrobial Stewardship Policy

ChAMP Empiric Guidelines and Monographs

KEMH Neonatal Medication Protocols

References

1. Australian Medicines Handbook. Adelaide, S. Aust.: Australian Medicines Handbook; 2023 [cited 2024 10th January]. Available from: https://amhonline-amh-net-au.pklibresources.health.wa.gov.au/.
2. National COVID-19 Clinical Evidence Taskforce. COVID-19 Clinical Care guidelines Australia2023 [Available from: https://app.magicapp.org/#/guideline/L4Q5An/section/L6q73j.
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4. Clinical Pharmacology powered by ClinicalKey [Internet]. Elsvier. 2024 [cited 2024 February 6th]. Available from: https://www-clinicalkey-com.pklibresources.health.wa.gov.au/pharmacology/.
5. IBM Micromedex [Internet]. Truven Health Analytics. 2023 [cited 2024 January 15th]. Available from: http://www-micromedexsolutions-com.pklibresources.health.wa.gov.au/micromedex2/librarian.
6. Up To Date - Paediatric Drug information [Internet]. Lexicomp. 2023 [cited 2024 February 13]. Available from: https://www-uptodate-com.pklibresources.health.wa.gov.au/contents/table-of-contents/drug-information/pediatric-drug-information.
7. Paediatric Formulary Committee. BNF for Children: 2023. London: BMJ Group Pharmaceutical Press; 2023.
8. Symons K. Wong Ee. Australian injectable drugs handbook. Abbotsford: The Society of Hospital Pharmacists of Australia; 2023.

Useful resources (including related forms)
National COVID-19 Clinical Evidence Taskforce – living guidelines
Patient consent form

This document can be made available in alternative formats on request for a person with a disability.

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