MICHIGAN MEDICINE
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INDICATIONS FOR THE USE OF RIBAVIRIN FOR TREATMENT OF RESPIRATORY VIRAL INFECTIONS IN ADULT AND PEDIATRIC HEMATOLOGY PATIENTS

1. This document addresses indications for use and dosing of ribavirin**.**
   Guidelines for administration of aerosolized ribavirin:
   Adult Guidelines
   Pediatric Guidelines (Use of small particle aerosol generation (SPAG) device)
   Pharmacy Dispensing Procedures
   Inhaled Ribavirin Dispensing Procedures for Inpatient Areas

2. Guidelines for the Treatment of Respiratory Syncytial Virus (RSV) in Lung Transplantation are available on OTIS and are not replicated here.

3. Ribavirin therapy should only be considered for infections due to respiratory syncytial virus (RSV). Ribavirin has not been proven to be efficacious for the treatment of infections caused by parainfluenza virus or human metapneumovirus.

4. Aerosolized ribavirin is contraindicated in patients receiving mechanical ventilation due to concerns regarding compatibility with ventilator components. Ribavirin is pregnancy category X.

5. Confirmed RSV infections in the following groups should generally be provided ribavirin therapy:
   a. Patients with a prior history of Bone marrow transplant (BMT):
      i. All BMT patients with RSV infection and an Immunodeficiency Scoring Index ≥7 (See Appendix Below) should receive a Transplant Infectious Diseases consult.
      ii. All BMT patients with RSV upper respiratory tract infection (URTI) and/or lower respiratory tract infection (LRTI) should receive oral ribavirin EXCEPT autologous transplant recipients after a year post-transplant (case-by-case in that group).
      iii. There is not robust evidence that treatment of RSV infections in adults after BMT with inhaled ribavirin improves patient outcomes compared to use of oral ribavirin. Therefore, use of inhaled ribavirin is generally not recommended.
   b. Acute myeloid leukemia (AML)/Acute lymphoblastic leukemia (ALL) without a prior history of BMT:
      i. Oral ribavirin therapy is recommended for patients with URTI/LRTI in the setting of uncontrolled leukemia for >30 days or with relapsed/refractory disease undergoing re-induction chemotherapy.
   c. Consideration of treatment with inhaled ribavirin requires a transplant infectious diseases consult as well as a multidisciplinary email discussion involving the primary team attending and pharmacist on service, Antimicrobial Stewardship pharmacy, and the Transplant Infectious Diseases attendings to determine appropriateness of therapy.

6. The criteria in above are not absolutely comprehensive. Exceedingly rare cases may present themselves that are not listed but warrant therapy. Such scenarios should be handled on a case-by-case basis in consultation with Infectious Diseases.

7. Duration of therapy: 5-7 days in most cases

8. Dosing of ribavirin
   a. Aerosolized therapy (non-intubated patients): 2 g (over 2 hours) TID
   b. Oral therapy:
      i. CrCl greater than 50 mL/min: 600 mg TID
      ii. CrCl 31-50 mL/min: 400 mg TID
      iii. CrCl 20- 30 mL/min: 200 mg TID
      iv. Less than 20 or requiring hemodialysis: 200 mg Daily

c. Dose escalation may be considered in patients failing therapy
d. Oral ribavirin has been associated with anemia and extravascular hemolysis.
    i. Dose decreases may be considered in patients developing toxicity, as ribavirin concentration has been correlated with toxicity.
    ii. Significant anemia is unlikely with short durations of therapy (≤5 days), however, the risk increases with longer durations of therapy.
    iii. Use in patients with severe pre-existing anemia should be done with caution and with close monitoring.
    iv. All patients receiving oral ribavirin should be monitored for anemia and hemolysis. As the elimination half-life of ribavirin is ~2 weeks, clinicians should be cognizant of the potential for anemia to present after ribavirin has been discontinued.
e. Pediatrics: Consult Pediatric Infectious Diseases for dosing recommendations

APPENDIX: Immunodeficiency Scoring Index

Criterion	**Points**
ANC <500 cells/µL	3
ALC <200 cells/µL	3
Age ≥40 y	2
Myeloablative conditioning regimen used	1
GVHD, acute or chronic	1
Corticosteroids within the past 30 d	1
Recent engraftment (within 30 d) or pre-engraftment	1
Total	__ (Score ≥7 classified as high risk for progression of disease)

References:
1. Ison MG, Hirsch HH. Community-Acquired Respiratory Viruses in Transplant Patients: Diversity, Impact, Unmet Clinical Needs. Clin Microbiol Rev 32:e00042-19.
2. Foolad F, et al. Oral Versus Aerosolized Ribavirin for the Treatment of Respiratory Syncytial Virus Infections in Hematopoietic Cell Transplant Recipients. Clin Infect Dis 2019;68:1641- 1649.

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