Guideline/Protocol Title:	UCSF Medical Center Guideline for Management of Adult Respiratory Syncytial Virus (RSV) - 2022
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PURPOSE/SCOPE:	• To provide a standardized approach for treatment of RSV (respiratory syncytial virus) in adult patients

EXECUTIVE SUMMARY

- In adult patients, RSV can be associated with higher rates for progression from upper respiratory tract infection (URTI) to lower respiratory tract infection (LRTI), especially in immunocompromised patients.[3]
- Risk of severe disease and mortality from RSV is greatest among hematopoietic stem cell transplant (HSCT) and lung transplant patients. [8]
- Ribavirin (RBV) can be used for treatment for RSV, though there is limited literature.
- Optimal dosing for RBV has not been formally established and there is heterogeneity in clinical practice
- This guideline is focused on identifying patients who may benefit from RBV with dosing considerations

BACKGROUND / INTRODUCTION

Background:

Respiratory syncytial virus (RSV) is a common cause of seasonal respiratory viral infections and part of the *Pneumoviridae* family [3-5, 7-8]. Typically, this infection is self-limiting, but can progress from an upper respiratory tract infection (URTI) to a lower respiratory tract infection (LRTI) in immunocompromised hosts such as hematopoeitic stem cell transplant (HSCT) patients. This risk can also impact lung transplant recipients and RSV has been associated with the development of bronchiolitis obliterans syndrome [5].

Adult treatment has included ribavirin (RBV) despite a lack of large, prospective, randomized controlled studies [5,7]. With the current literature, aerosolized and oral RBV may reduce the progression from URTI to LRTI [5,7]. However, there is no consensus on standardized RSV treatment and dosing of RBV. Aerosolized RBV has experienced substantial cost increases over the last several years [7]. Thus, oral ribavirin has emerged as a potential alternative and allows for outpatient use. Of note, oral ribavirin is available as a tablet or capsule, but it is no longer available as a commercial suspension product.

RIBAVIRIN THERAPY

Definitions:

- **Asymptomatic infection**
  - Detection of virus without symptoms or signs of infection
- **Lower respiratory tract infection (LRTI)**
  - Exam, CXR, or CT suggestive of pulmonary involvement

    OR
  - Requires supplemental oxygen therapy above baseline needs
- **Upper respiratory tract infection**
  - Symptomatic (e.g. rhinorrhea, sore throat, congestion)

    AND
  - Does not meet criteria for LRTI

Intended Population:

Treat with Ribavirin (RBV) if patient ≥ 18 years of age with documented infection PLUS

Host	URTI	LRTI
Lung transplant	In general, do not treat. Recommend close clinical monitoring, including lung function monitoring. Consider treatment if: • Significant cough or mucus production • Transplantation or augmentation of immunosuppression within 3 months	Treatment for lower respiratory tract symptoms, including: • Decrease in FEV1 by spirometry • Significant cough, mucus, or shortness of breath • CT changes consistent with LRTI
Non-lung SOT	In general, do not treat	Treat
Allo SCT	Treat if meets any of the below: • pre-engraftment • ≤ 1 month post-transplant • ALC < 0.3 • active GVHD • on immunosuppression	Treat unless >2 years out + off immunosuppression + on no maintenance therapy
Auto SCT	Treat if meets any of the below: • pre-engraftment • ≤ 1 month post-transplant • ALC < 0.3	Treat unless >1 year out + on no maintenance/chemo
Heme malignancy	Treat if: • CAR-T within prior 1 year • 3+ lines of therapy • Bispecific, on treatment or within 6 months of stopping • Pancytopenia on treatment	Treat unless no treatment or chemo for >1 year
Other immunocompromise	In general, do not treat	Treat
Immunocompetent	In general, do not treat	In general, do not treat Consider treatment in patients with severe illness requiring rapid escalation to high-flow oxygen or ICU level care

Exclusion

- Pregnant patients
- Hemoglobinopathies
- Hypersensitivity to ribavirin
- Patients who are on didanosine therapy

Dosing

Renal function (Cr Cl – mL/min)	Dosing
≥50 ml/min	40 to 49 kg = 400 mg po q 12h 50-59 kg = 400 mg po q AM PLUS 600 mg po q PM 60-69 kg = 600 mg po q 12h 70-79 kg = 600 mg po q AM PLUS 800 mg po q PM 80-89 kg = 800 mg po q 12h 90 kg or greater = 600 mg po q 8h
30-49 mL/min (CRRT included)	40 kg to 59 kg = 200 mg po q 12h 60 kg or greater = 200 mg po q 8h
10-29 mL/min	200 mg po daily
< 10 mL/min (intermittent hemodialysis—see Cr Cl 30-49 for CRRT)	200 mg po daily (give daily - on days of hemodialysis, give dose afterwards)
< 10 mL/min (no hemodialysis)	200 mg po daily*

*Consider consulting Adult ASP/ID pharmacist

- Use actual or total body weight when dosing this medication
- Usual maximum is 1800 mg/day and comes in 200 mg strength tablets/capsules

Duration

7 days of therapy is recommended.

Warnings/Precautions:

A boxed warning exists for hemolytic anemia. Use caution in patients with severe baseline anemia or conditions where anemia would exacerbate an underlying condition (e.g. unstable ischemic cardiac disease).[1,2]

A boxed warning also exists regarding the teratogenic effects of ribavirin observed in animal studies. Per the prescribing information, significant teratogenic and embryocidal effects have been demonstrated in all animal species exposed to ribavirin. Therefore, ribavirin is contraindicated in patients who are pregnant and in the partners of patients who are pregnant. Extreme care must be taken to avoid pregnancy during therapy and for 6 months after completion of ribavirin treatment in patients of childbearing potential and in partners of those patients. [1,2]

Handling/Disposal

Ensure to wash hands before and after handling this medication. Follow the FDA guidance on proper disposal of this medication - https://www.fda.gov/consumers/consumer-updates/where-and-how-dispose-unused-medicines

Monitoring

- Counsel patients of childbearing potential and/or partners of people of childbearing potential to use effective methods of contraception during treatment and for the 6 months after treatment due to the teratogenic effects of this medication
- Obtain a pregnancy test prior to treatment if of childbearing potential
- Hazardous drug (refer to handling/disposal section)
- Baseline CBC and creatinine if not performed within 3 months

- Use caution in patients with severe baseline anemia
- Hemolytic anemia is less likely with shorter courses of ribavirin, though the elimination half-life is ~2 weeks, meaning that anemia can present even after cessation of treatment.
  - All patients should be clinically monitored for anemia and hemolysis
  - All inpatients should have CBC and creatinine monitored at least twice weekly
  - In outpatients, consider day 3-4 and day 7-9 CBC, particularly if patient has low baseline hemoglobin or impaired renal function

ADDITIONAL THERAPIES

Intravenous immunoglobulin (IVIG)

- Consider IVIG in patients with severe illness requiring rapid escalation to high-flow oxygen or ICU level care or patients with known immunoglobulin deficiencies
  - Dose IVIG 500 mg/kg 3x weekly for up to 7 days if requiring ongoing hospitalization
    - Use Ideal Body Weight (IBW) for dosing if the patient's height is available
    - Use Total Body Weight (TBW) for dosing if height is unavailable
- **Warnings/Precautions:**
  - Volume overload
  - History of anaphylaxis to IVIG or other blood products. Consult with Allergy about strategies for administration.
  - Thromboembolic events have been associated with IVIG infusion
  - Acute Kidney Injury

Steroids

- In general, steroids should not be administered outside of specific situations, such as certain lung transplant patients and patients with underlying COPD

Reference #	Citation
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3	Marcellin JR, et al. Transpl Infect Dis 2014: 16: 242-250.
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Revision History	
Revision Date	**Update(s)**