Atrium Health Wake Forest Baptist Guideline for Use of Ribavirin in the Treatment of Respiratory Syncytial Virus (RSV) Infection

General Information

Aerosolized ribavirin has been shown in limited clinical studies to have modest benefit in the treatment of RSV pneumonia in bone marrow transplant (BMT) patients. There are only observational reports of its use in solid organ transplant or other immunocompromised patients, and except in lung transplant patients there is not enough data to assess its efficacy. Likewise, only observational reports describe successful use of oral ribavirin for RSV disease.

Aerosolized ribavirin is difficult to administer and is teratogenic in experimental animals. It has to be administered in a controlled environment using special equipment by trained respiratory therapists. When the drug is administered, pregnant or possibly pregnant women should not be allowed in the room, and visitors should not be in the room except for rare exceptions. For detailed information about administration of aerosolized ribavirin, please refer to the WFBH policy titled "Delivery of Inhaled Ribavirin".

Infectious Diseases consultation (adult or pediatric) is strongly suggested if ribavirin therapy is being considered. Aerosolized ribavirin is on the list of drugs whose use is restricted by WFBH, thus preapproval by the Adult Infectious Diseases Consult service (if ID consultation is obtained), the CAUSE PAGER, or Pediatric Infectious Diseases is required. Oral ribavirin requires preapproval for use in pediatric patients but not for adults.

Candidate Patients

Members of the WFBH CAUSE team, the Department of Pediatrics, and Adult Infectious Diseases developed the following criteria for use of ***aerosolized*** ribavirin at WFBH.

- Identification of RSV in a respiratory specimen (nasopharyngeal or BAL) by either Respiratory Virus Panel (RVP) or RSV antigen or Biofire® FilmArray Pneumonia Panel
- Evidence of *lower* respiratory tract disease (pneumonia)
- Infection is considered potentially life-threatening, e.g. patients receiving care in an intensive care unit and/or requiring mechanical ventilation due to respiratory failure.
- Recipient of BMT as described in the table below:

Adult patients (18 years or older)	Pediatric patients (≥ 60 days post-menstrual age)
• Undergoing or status post BMT	• Less than or equal to 6 months after allogeneic BMT
	• Greater than 6 months after allogeneic BMT AND receiving immunosuppressive treatment

	• Less than or equal to 3 months post-autologous BMT

Use of *aerosolized* ribavirin for other severely immunocompromised patients is generally not recommended, though it may be considered, with appropriate consultation, in some circumstances including but not limited to: solid organ transplant patients on significant immunosuppressive medication and patients with hematologic malignancy undergoing myelosuppressive chemotherapy.

Oral ribavirin represents a practical alternative to *aerosolized* ribavirin and may be suitable for the following patient types:

- BMT patients with RSV pneumonia that is not considered life-threatening
- Non-BMT patients with RSV pneumonia who are severely immunocompromised (as described above)
- Severely immunocompromised patients with *upper* respiratory tract disease who are at high risk of progression to *lower* respiratory tract disease

Patients with exacerbation of COPD or other underlying lung disease caused by RSV are not candidates for ribavirin.

Patients with respiratory infection caused by viruses other than RSV, e.g. Coronavirus or Parainfluenza virus, are not candidates for ribavirin.

Ribavirin Dosing and Duration

See Appendix 1 and 2 for recommended doses of ribavirin for adult and pediatric patients, respectively.

Recommended duration of ribavirin therapy:*

Aerosolized	3-7 days depending on clinical response
Oral	5 days

*extending ribavirin treatment beyond the recommended duration may be considered for patients with life-threatening pneumonia who do not respond by 7 days of therapy

Adjunctive Immune Globulin

Intravenous immune globulin has been used with ribavirin in observational reports and should be considered for BMT patients with life-threatening RSV pneumonia.

IVIG is the preferred immune globulin product for adult patients. The recommended dose of IVIG is 500mg/kg IV every other day x 3 doses

Palivizumab is the preferred immune globulin product for pediatric patients. The recommended dose of palivizumab is 15mg/kg IV x 1 dose.

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Appendix 1, Recommended Ribavirin Dosing for **Adults** with RSV Infection

Creatinine clearance (mL/min)	**Oral** Ribavirin Dose (all doses PO)						
	50-57kg	58-67kg	68-77kg	78-87kg	88-97kg	98-107kg	108-117kg
>80	Q8h+ 200/400/400	400mg Q8h	Q8h+ 400/400/600	Q8h+ 400/600/600	600mg Q8h	Q8h+ 600/600/800	Q8h+ 600/800/800
50-80	400mg Q12h	Q12h+ 400/600	400mg Q8h	400mg Q8h	Q8h+ 400/400/600	600mg Q8h	600mg Q8h
30-50	Daily dosing 400mg alternating 200mg	Daily dosing 400mg alternating 200mg	400mg Q24h	400mg Q24h	Daily dosing 600mg alternating 400mg	600mg Q24h	600mg Q24h
10-30	200mg Q24h*	200mg Q24h*	Daily dosing 400mg alternating 200mg	Daily dosing 400mg alternating 200mg	Daily dosing 400mg alternating 200mg	400mg Q24h	400mg Q24h
<10 or iHD	200mg Q24h*	200mg Q24h*	Daily dosing 400mg alternating 200mg	Daily dosing 400mg alternating 200mg	Daily dosing 400mg alternating 200mg	400mg Q24h	400mg Q24h

+ The number of mg per dose corresponding to this frequency are listed. For example, "Q8h 400/600/600" is appropriately ordered 400mg at 0600, 600mg at 1400, and 600mg at 2200.

* Consider loading/first dose of 400mg

Aerosolized ribavirin dose: 6,000mg administered over 6-9 hours once daily. For administration instructions, refer to WFBH policy titled "Delivery of Inhaled Ribavirin".

References

- Antimicrob Agents Chemother 2013;57:6097-6105.
- Ann Pharmacother 2012;46:558-66.

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Appendix 2, Recommended Ribavirin Dosing for **Pediatric Patients** with RSV Infection

Oral ribavirin dose: 20mg/kg/day PO divided into three equal doses. Upward titration of the ribavirin dose is an option for patients who do not respond as expected after 48 hours of therapy. The dose may be increased by 10mg/kg/day up to a maximum dose of 50mg/kg/day divided into three equal doses. *Note: Lack of improvement in respiratory status after dose escalation of oral ribavirin is not sufficient reason to change to aerosolized ribavirin. Infectious Diseases consultation is recommended.*

Aerosolized ribavirin dose: 6,000mg administered over 6-9 hours once daily. For administration instructions, refer to WFBH policy titled “Delivery of Inhaled Ribavirin”.