

PRIOR AUTHORIZATION POLICY

- POLICY:** Hepatitis C – Ribavirin Prior Authorization Policy
- ribavirin tablets (generic)
 - ribavirin capsules (generic)
 - Rebetol® (ribavirin oral solution – Schering Plough; obsolete 07/31/2019)
 - Ribasphere® (ribavirin tablets and capsules – Kadmon, generic; obsolete 01/31/2020 [capsules], 01/01/2019 [tablets])

REVIEW DATE: 09/15/2021

OVERVIEW

Ribavirin is an antiviral agent with direct antiviral activity in tissue culture against many RNA viruses.¹⁻³ Ribavirin increases the mutation frequency in the genomes of several viruses and ribavirin triphosphate inhibits hepatitis C virus (HCV) polymerase in a biochemical reaction.

The products contained in this Prior Authorization policy are indicated for use **in combination with pegylated interferons or interferon for the treatment of chronic HCV** in adults and children with compensated disease. Ribavirin remains a component of some regimens for the management of HCV.⁵ The specific indications vary slightly among the oral ribavirin products:

- Ribavirin capsules are indicated in combination with PegIntron® (peginterferon alfa-2b injection) or Intron A® (interferon alfa-2b injection) for the treatment of chronic HCV in patients ≥ 3 years of age with compensated liver disease.^{1,14}
- Ribavirin tablets in combination with Pegasys® (peginterferon alfa-2a) are indicated for the treatment of patients ≥ 5 years of age with chronic HCV with compensated liver disease who have not previously been treated with interferon alfa.¹⁵ Ribasphere is indicated in adults in combination with Pegasys for the treatment of compensated chronic HCV in patients previously untreated with interferon alfa.³

Ribavirin has been used off-label to treat other systemic viral infections including herpes simplex virus, respiratory syncytial virus^{2,6,7}, human metapneumovirus infection⁸⁻⁹, adenovirus⁸, influenza, severe acute respiratory syndrome, coronavirus, La Crosse encephalitis, Nipah encephalitis, Lassa fever^{10,13}, hemorrhagic fever with renal syndrome¹⁰, Crimean-Congo hemorrhagic fever^{10,11}, Bolivian hemorrhagic fever¹⁰, and hantavirus pulmonary infection^{10,12} plus a variety of other systemic viral infections.⁵

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of ribavirin. The intent of this Prior Authorization program is to ensure ribavirin is not used in the absence of an alfa interferon or a direct-acting antiviral for the treatment of hepatitis C virus (HCV). All approvals are provided for 1 year unless otherwise noted below. Because of the specialized skills required for evaluation and diagnosis of patients being treated with ribavirin, as well as the monitoring required for adverse events and efficacy, approval requires ribavirin (for hepatitis C indications) to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: The use of a pegylated interferon or non-pegylated interferon or a direct-acting antiviral for hepatitis C virus (HCV) in the past 130 days. This is used as a surrogate marker for HCV. If the criteria

for prior use of a pegylated interferon or non-pegylated interferon or direct-acting antiviral for HCV are not met at the point-of-service, coverage will be determined by Prior Authorization criteria.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of ribavirin is recommended in those who meet the following criteria:

FDA-Approved Indications

1. Hepatitis C Virus (HCV). Approve for 1 year if the patient meets the following criteria (A and B)

A) Patient meets ONE of the following criteria (i or ii):

i. The medication is prescribed in combination with interferon alfa or peginterferon alfa; OR

Note: Examples of interferon alfa or peginterferon alfa are Intron A (interferon alfa 2-b injection), Pegasys (pegylated interferon alfa-2a injection), PegIntron (pegylated interferon alfa-2b injection).

ii. The medication is prescribed in combination with a direct-acting antiviral for hepatitis C virus (HCV); AND

Note: Examples of direct-acting antivirals for HCV are Epclusa (velpatasvir/sofosbuvir tablets), Sovaldi (sofosbuvir tablets/oral pellets), Harvoni (ledipasvir/sofosbuvir tablets/oral pellets), Viekira Pak (paritaprevir/ombitasvir/ritonavir tablets + dasabuvir, co-packaged), Zepatier (elbasvir/grazoprevir tablets).

B) The medication is prescribed by or in consultation with a gastroenterologist, hepatologist, liver transplant physician, or infectious diseases physician.

Other Uses with Supportive Evidence

2. Other Systemic Viral Infections. Approve for 1 year.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of ribavirin is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Rebetol® capsules and oral solution [prescribing information]. Whitehouse Station, NJ: Merck & Co., Inc.; January 2020.
 2. Mori T, Nakamura Y, Kato, et al. Oral ribavirin therapy for lower respiratory tract infection of respiratory syncytial virus complicating bronchiolitis obliterans after allogeneic hematopoietic stem cell transplantation. *Int J Hematol.* 2011;93:132-134.
 3. Ribasphere® [prescribing information]. Warendale, PA: Kadmon Pharmaceuticals; September 2017.
 4. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. Testing, managing, and treating hepatitis C. Updated. Available at: <http://www.hcvguidelines.org>. Accessed on August 10, 2021.
 5. Razonable RR. Antiviral drugs for viruses other than human immunodeficiency virus. *Mayo Clin Proc.* 2011;86(10):1009-1026.
 6. Shah JN and Chemaly RF. Management of RSV infection in adult recipients of hematopoietic stem cell transplantation. 2011;117:2755-2763.
 7. Khanna N, Widmer AF, Decker M, et al. Respiratory syncytial virus infection in patients with hematological disease: Single-center study and review of the literature. *Clin Infect Dis.* 2008;46:402-412.
 8. Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant.* 2009;15:1143-1238.
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9. Shahda S, Carlos WG, Kiel PJ, Khan BA, and Hage CA. The human metapneumovirus: a case series and review of the literature. *Transpl Infect Dis*. 2011;13(3):324-328.
 10. Ippolit G, Feldmann H, Lanini S, et al. Viral hemorrhagic fevers: advancing the level of treatment. *BMC Med*. 2012;10:31.
 11. Ergonul O, Keske S, Celdir MG, et al. Systematic review and meta-analysis of postexposure prophylaxis for Crimean-Congo Hemorrhagic Fever Virus among healthcare workers. *Emerg Infect Dis*. 2018;24(9):1642-1648.
 12. The Centers for Disease Control and Prevention. Hantavirus. Last Updated: January 18, 2021. Available at: <https://www.cdc.gov/hantavirus/hfrs/index.html>. Accessed on August 10, 2021.
 13. Bausch DG, Hadi CM, Khan SH, Lertora JJL. Review of the literature and proposed guidelines for the use of oral ribavirin as postexposure prophylaxis for lassa fever. *Clin Infect Dis*. 2010;51(12):1435-1441.
 14. Ribavirin capsules [prescribing information]. East Windsor, NJ: Aurobindo Pharma USA, Inc; February 2020.
 15. Ribavirin tablets [prescribing information]. East Windsor, NJ: Aurobindo Pharma USA, Inc; November 2020.
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