

PRIOR AUTHORIZATION POLICY

POLICY: Hepatitis C – Ribavirin

- Copegus[®] (ribavirin tablets – Roche, generics)
- Moderiba[™] (ribavirin tablets and dose packs – AbbVie)
- Rebetol[®] (ribavirin capsules – Schering Plough, generics)
- Rebetol[®] (ribavirin oral solution – Schering Plough)
- Ribasphere[®] (ribavirin tablets – Kadmon, generics)

TAC APPROVAL DATE: 09/26/2018

OVERVIEW

Ribavirin is an antiviral agent with direct antiviral activity in tissue culture against many RNA viruses.¹⁻⁴ 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. The specific indications vary slightly among the oral ribavirin products: Rebetol oral solution and 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 Copegus in combination with Pegasys[®] (peginterferon alfa-2a) is 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.² Ribasphere is indicated in adults in combination with Pegasys for the treatment of compensated chronic HCV in patients previously untreated with interferon alfa.³ Moderiba is indicated with Pegasys for the treatment of patients ≥ 5 years of age with chronic HCV who have compensated liver disease and have not been previously treated with interferon alfa. Ribavirin remains a component of many recommended therapies for the treatment of chronic HCV and recurrent hepatitis C post-liver transplantation by the American Association for the Study of Liver Diseases (AASLD)/Infectious Diseases Society of America (IDSA) in their guidance for the management of hepatitis C.⁵

Other Systemic Viral Infections

Ribavirin has been used off-label to treat other systemic viral infections including herpes simplex virus (HSV), respiratory syncytial virus (RSV)^{7,8,15}, human metapneumovirus infection (hMPV)⁹⁻¹⁰, adenovirus⁹, influenza, severe acute respiratory syndrome, coronavirus, La Crosse encephalitis, Nipah encephalitis, Lassa fever¹¹, hemorrhagic fever with renal syndrome¹¹, Crimean-Congo hemorrhagic fever (CCHF)^{11,12}, Bolivian hemorrhagic fever¹¹, and hantavirus pulmonary infection^{11,13} plus a variety of other systemic viral infections.⁶

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 (DAA) for the treatment of HCV. Because of the specialized skills required for evaluation and diagnosis of patients with hepatitis C, 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. All approvals are provided for 1 year unless otherwise noted below.

Automation: The use of a pegylated interferon or non-pegylated interferon or a direct-acting antiviral (DAA) for HCV in the past 130 days. This is used as a surrogate marker for hepatitis C. If the criteria for prior use of a pegylated interferon or non-pegylated interferon or DAA 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 ribavirin for 1 year in patients who meet the following criteria (A and B):
 - A) The patient meets one of the following criteria (i or ii):
 - i. Ribavirin is prescribed in combination with interferon alfa or peginterferon alfa (Intron A® [interferon alfa 2-b injection], Pegasys [pegylated interferon alfa-2a], PegIntron [pegylated interferon alfa-2b]); OR
 - ii. Ribavirin is prescribed in combination with a direct-acting antiviral (DAA) for hepatitis C virus [HCV] (e.g., Daklinza [daclatasvir tablets], Epclusa [velpatasvir/sofosbuvir tablets], Sovaldi [sofosbuvir tablets], Harvoni [ledipasvir/sofosbuvir tablets], Olysio [simeprevir capsules], Technivie [paritaprevir/ombitasvir/ritonavir tablets], Viekira Pak [paritaprevir/ombitasvir/ritonavir tablets + dasabuvir, co-packaged], Viekira XR™ [paritaprevir/ombitasvir/ritonavir/dasabuvir tablets], Zepatier™ [elbasvir/grazoprevir tablets]); AND
 - B) Ribavirin 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 ribavirin for 1 year.

Although data are limited, ribavirin has been used off-label to for the treatment and prevention of many rare systemic viral infections.⁶⁻¹⁵ Ribavirin has been used off-label to treat HSV, RSV, hMPV, influenza, severe acute respiratory syndrome coronavirus, La Crosse encephalitis, Nipah encephalitis, Lassa fever, hemorrhagic fever with renal syndrome, CCHF, Bolivian hemorrhagic fever, and hantavirus pulmonary infection plus a variety of other systemic viral infections.⁶

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Ribavirin has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

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.; October 2017.
2. Copegus® tablets [prescribing information]. South San Francisco, CA: Genentech USA, Inc; August 2015.
3. Ribasphere® [prescribing information]. Warendale, PA: Kadmon Pharmaceuticals; September 2017.
4. Moderiba™ [prescribing information]. North Chicago, IL: AbbVie, Inc; December 2017.
5. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. Testing, managing, and treating hepatitis C. Updated May 24, 2018. Available at: <http://www.hcvguidelines.org>. Accessed on September 7, 2018.
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8. 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.
9. 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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16. Lucey MR, Terrault N, Ojo L, et al. Long-term management of the successful adult liver transplant: 2012 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. *Liver Trans.* 2013;19(1):3-26.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	No criteria changes. Automation changed to screen for HCV DAA use.	09/30/2015
Annual revision	Updated automation to 130 look-back period.	09/21/2016
	Removed Roferon A from list of examples with which ribavirin can be prescribed. Added Epclusa, Daklinza, Zepatier and Viekira XR to the list of direct-acting antivirals (DAAs) ribavirin can be prescribed in combination with.	09/21/2016
Annual revision	No criteria changes	09/20/2017
Annual revision	Hepatitis C Virus (HCV): Removed Infergen from list of examples with which ribavirin can be prescribed (obsolete > 3 years).	09/26/2018

TAC – Therapeutic Assessment Committee; PAS – Prior Authorization Services; AASLD – American Association for the Study of Liver Diseases; IDSA – Infectious Diseases Society of America; DEU – Drug Evaluation Unit; * For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>; HCV – Hepatitis C virus; DAA – Direct-acting antiviral.