Clinical Policy: Ribavirin (Copegus, Moderiba, Rebetol, Ribasphere)

Reference Number: ERX.SPA.271
Effective Date: 12.01.18
Last Review Date: 11.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Ribavirin (Copegus®, Moderiba®, Rebetol®, Ribasphere®, Ribasphere® RibaPak®) is a nucleoside analogue.

FDA Approved Indication(s)
Copegus, Moderiba, and Ribasphere are indicated for the treatment of chronic hepatitis C (CHC) virus infection in combination with Pegasys in patients 5 years of age and older with compensated liver disease not previously treated with interferon alpha, and in adult CHC patients coinfected with HIV.

Rebetol is indicated for the treatment of CHC in combination with interferon alfa-2b (pegylated and nonpegylated) for the treatment of CHC in patients 3 years of age or older with compensated liver disease.

Limitation(s) of use: Patients with the following characteristics are less likely to benefit from re-treatment after failing a course of therapy: previous nonresponse, previous pegylated interferon treatment, significant bridging fibrosis or cirrhosis, and genotype 1 infection.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Copegus, Moderiba, Rebetol, and Ribasphere are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Hepatitis C Infection (must meet all)**:**

1. Diagnosis of chronic hepatitis C virus (HCV) infection as evidenced by detectable serum HCV RNA levels by quantitative assay in the last 6 months;
2. Prescribed by or in consultation with a gastroenterologist, hepatologist, infectious disease specialist, or provider who has expertise in treating HCV based on a certified training program (*see Appendix E*);
3. Member meets prior authorization criteria for Epclusa®, Harvoni®, Mavyret™, Sovaldi®, Zepatier®, Viekira Pak®, or Vosevi® for combination use;
4. Member must use a generic ribavirin formulation, unless contraindicated to excipients or clinically significant adverse effects are experienced;
5. Member meets one of the following (a or b):
   a. For Copegus, Moderiba, Ribasphere: Age ≥ 5 years;
   b. For Rebetol: Age ≥ 3 years;
6. Dose does not exceed:
   a. Copegus, Moderiba, Ribasphere: 1,200 mg per day;
   b. Rebetol: 1,400 mg per day.

Approval duration: Coincides with duration for Epclusa, Harvoni, Mavyret, Sovaldi, Zepatier, Viekira Pak, or Vosevi authorization

B. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Chronic Hepatitis C Infection (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Member must use a generic ribavirin formulation, unless contraindicated to excipients or clinically significant adverse effects are experienced;
4. If request is for a dose increase, new dose does not exceed:
   a. Copegus, Moderiba, Ribasphere: 1,200 mg per day;
   b. Rebetol: 1,400 mg per day.

Approval duration: Coincides with duration for Epclusa, Harvoni, Mavyret, Sovaldi, Zepatier, Viekira Pak, or Vosevi authorization

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CHC: chronic hepatitis C
FDA: Food and Drug Administration
HCV: hepatitis C virus
HIV: human immunodeficiency virus

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Copegus, Moderiba, Rebetol, and Ribasphere:
    - Women who are pregnant
    - Men whose female partners are pregnant
    - Hemoglobinopathies (e.g., thalassemia major, sickle-cell anemia)
    - Coadministration with didanosine
    - Autoimmune hepatitis (when in combination with Pegasys)
    - Copegus, Moderiba, and Rebetol: hepatic decompensation (Child-Pugh B or C) in cirrhotic CHC patients (when in combination with Pegasys)
  - Rebetol only:
    - Creatinine clearance < 50 mL/min
    - Known hypersensitivity reactions such as Stevens-Johnson syndrome, toxic, epidermal necrolysis, and erythema multiforme to ribavirin or any component of the product
- Boxed warning(s):
  - Copegus, Moderiba, and Ribasphere: risk of serious disorders and ribavirin-associated effects
  - Rebetol: embryo-fetal toxicity, hemolytic anemia, and monotherapy not recommended

Appendix D: General Information

- Copegus, Moderiba, Rebetol and Ribasphere brands are no longer commercially being manufactured.

Appendix E: Healthcare Provider HCV Training

- Acceptable HCV training programs and/or online courses include, but are not limited to the following:
  - Hepatitis C online course (https://www.hepatitisc.uw.edu/): University of Washington is funded by the Division of Viral Hepatitis to develop a comprehensive, online self-study course for medical providers on diagnosis, monitoring, and management of hepatitis C virus infection. Free CME and CNE credit available.
  - Fundamentals of Liver Disease (https://liverlearning.aasld.org/fundamentals-of-liverdisease): The AASLD, in collaboration with ECHO, the American College of Physicians (ACP), CDC, and the Department of Veterans Affairs, has developed Fundamentals of Liver Disease, a free, online CME course to improve providers' knowledge and clinical skills in hepatology.
  - Clinical Care Options: http://www.clinicaloptions.com/hepatitis.aspx
  - CDC training resources: https://www.cdc.gov/hepatitis/resources/professionals/trainingresources.htm

V. Dosage and Administration

<table>
<tr><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>CHC</td><td>The daily dose of administered orally in two divided doses. The dose should be individualized to the patient depending on baseline disease characteristics (e.g., genotype), response to therapy, and tolerability of the regimen.
<table>
<tr><th>Body Weight kg (lbs)</th><th>Rebetol Daily Dose</th><th>Rebetol Number of Capsules</th></tr>
<tr><td>< 66 (< 144)</td><td>800 mg/day</td><td>2 x 200-mg capsules A.M.
2 x 200-mg capsules P.M.</td></tr>
<tr><td>66-80 (145-177)</td><td>1,000 mg/day</td><td>2 x 200-mg capsules A.M.
3 x 200-mg capsules P.M.</td></tr>
<tr><td>81-105 (178-231)</td><td>1,200 mg/day</td><td>3 x 200-mg capsules A.M.
3 x 200-mg capsules P.M.</td></tr>
<tr><td>> 105 (231)</td><td>1,400 mg/day</td><td>3 x 200-mg capsules A.M.
4 x 200-mg capsules P.M.</td></tr>
</table></td><td>1,400 mg/day</td></tr>
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VI. Product Availability

Drug Name	Availability
Ribavirin (Copegus)	Tablet: 200 mg (brand version no longer being manufactured)
Ribavirin (Moderiba)	Tablet: 200 mg (brand version no longer being manufactured) Dose pack, tablet: 400 mg, 600 mg (brand version no longer being manufactured)
Ribavirin (Rebetol)	Capsule: 200 mg (brand version no longer being manufactured) Oral solution: 40 mg/mL (brand version no longer being manufactured)
Ribavirin (Ribasphere, Ribasphere RibaPak)	Tablets: 200 mg, 400 mg, 600 mg (brand version no longer being manufactured) RibaPak compliance pack, tablets: 800 mg/day, 1000 mg/day, 1,200 mg/day (brand version no longer being manufactured)

VII. References

1. Rebetol Prescribing Information. Whitehouse Station, NJ; Merck and Co; January 2020. Available at: https://www.merck.com/product/. Accessed August 5, 2021.
2. Copegus Prescribing Information. South San Francisco, CA: Genentech USA Inc, August 2015. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/021511s029lbl.pdf. Accessed August 5, 2021.
3. Moderiba Prescribing Information. North Chicago, IL: AbbVie Inc.; December 2017. Available at: https://www.rxabbvie.com/pdf/moderiba_PI.pdf. Accessed August 5, 2021.
4. Ribasphere Prescribing Information. Warrendale, PA: Kadmon Pharmaceuticals, LLC; September 2017. Available at: http://www.kadmon.com/files/ribasphere-tablets-pi.pdf. Accessed August 5, 2021.
5. American Association for the Study of Liver Diseases/ Infectious Disease Society of America (AASLD-IDSA). HCV guidance: recommendations for testing, managing, and treating hepatitis C. Last updated March 12, 2021. Available at: https://www.hcvguidelines.org/. Accessed August 5, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	07.31.18	11.18
4Q 2019 annual review: no significant changes; references reviewed and updated.	08.05.19	11.19
4Q 2020 annual review: added Mavyret and Vosevi, removed Olysio & Technivie from combination use criterion as they are no longer commercially available; expanded prescriber requirement to include a “provider who has expertise in treating HCV based on a certified training program”; Appendix E (Healthcare Provider HCV Training) added; references reviewed and updated.	08.09.20	11.20
4Q 2021 annual review: no significant changes; added redirection to generic formulation; removed Daklinza criteria references as Daklinza has been discontinued; references reviewed and updated.	09.07.21	11.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.