

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

Reference Number: CP.PHAR.141

Effective Date: 11.16.16

Last Review Date: 11.21

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Ribavirin (Copegus[®], Moderiba[®], Rebetol[®], Ribasphere[®], and 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 (peginterferon alfa-2a) in patients 5 years of age and older with compensated liver disease not previously treated with interferon alpha, and in adult CHC patients coinfecting 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.

It is the policy of health plans affiliated with Centene Corporation[®] 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 must meet prior authorization criteria for Epclusa[®], Harvoni[®], Mavyret[™], Sovaldi[®], Zepatier[®], Viekira Pak[®], or Vosevi[®] for combination use;
4. For Brand ribavirin product request, medical justification supports inability to use generic ribavirin formulation (e.g., contraindications to excipients);
5. Member meets one of the following (a or b):

- a. For Copegus, Moderiba, Ribasphere: age \geq 5 years;
- b. For Rebetol: age \geq 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 the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Centene Corporation or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. For Brand ribavirin product request, medical justification supports inability to use generic ribavirin formulation (e.g., contraindications to excipients);
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 Centene Corporation and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid 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

- Copegus, Moderiba, Rebetol, and Ribasphere are contraindicated in:
 - Women who are pregnant
 - Men whose female partners are pregnant
 - Patients with hemoglobinopathies (e.g., thalassemia major, sickle-cell anemia)
 - Coadministration with didanosine
 - Patients with autoimmune hepatitis (when in combination with Pegasys)
 - When used in combination with Pegasys: Copegus, Moderiba, and Ribasphere are additionally contraindicated in patients with hepatic decompensation (Child-Pugh B or C) in cirrhotic CHC patients.
- Rebetol only:
 - Patients with known hypersensitivity reactions such as Stevens-Johnson syndrome, toxic epidermal necrolysis, and erythema multiforme to ribavirin or any component of the product
 - Creatinine clearance less than 50 mL/min
- 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

Indication	Dosing Regimen	Maximum Dose															
CHC	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.	1,400 mg/day															
	<table border="1"> <thead> <tr> <th>Body Weight kg (lbs)</th> <th>Rebetol Daily Dose</th> <th>Rebetol Number of Capsules</th> </tr> </thead> <tbody> <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>1000 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> </tbody> </table>		Body Weight kg (lbs)	Rebetol Daily Dose	Rebetol Number of Capsules	< 66 (< 144)	800 mg/day	2 x 200-mg capsules A.M. 2 x 200-mg capsules P.M.	66-80 (145-177)	1000 mg/day	2 x 200-mg capsules A.M. 3 x 200-mg capsules P.M.	81-105 (178-231)	1,200 mg/day	3 x 200-mg capsules A.M. 3 x 200-mg capsules P.M.	> 105 (231)	1,400 mg/day	3 x 200-mg capsules A.M. 4 x 200-mg capsules P.M.
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VI. Product Availability

Drug	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. 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.

5. 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Minor changes to verbiage and grammar. References updated.	07.07.17	11.17
4Q 2018 annual review: added HIM and Medicaid lines of business; added Moderiba and Ribasphere to the CP.CPA.252 policy; added Daklinza combination use to the policy; simplified policy to state “member must meet prior authorization criteria for” HCV agents as existing criteria were repetitive of approval criteria for an HCV agent; added age limit; references reviewed and updated.	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 for HIM line of business off-label use revised from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	08.05.21	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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering

benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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