PRIOR AUTHORIZATION POLICY

POLICY: Antivirals – Ribavirin (Inhaled Products) Prior Authorization Policy
- Virazole® (ribavirin inhalation solution – Bausch, generic)

REVIEW DATE: 06/07/2023

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Ribavirin is a synthetic nucleoside with antiviral activity.[1] Ribavirin inhalation solution (referred to as aerosolized ribavirin in this policy) is indicated for the treatment of hospitalized infants and young children with severe lower respiratory tract infections due to **respiratory syncytial virus** (RSV). Treatment early in the course of severe lower respiratory tract infection may be necessary to achieve efficacy.

Disease Overview

RSV causes seasonal annual epidemics worldwide with year-round disease seen in some tropical locations. By 2 years of age, most children have experienced a primary infection; re-infection can occur throughout life.[3] Subsequent infections are usually less severe than a primary infection, particularly among otherwise healthy older children and adults. Recurrent RSV infection manifests as mild upper respiratory tract illness and seldom involves the lower respiratory tract.[2]

Aerosolized ribavirin has also been used off-label in adults for RSV and for other respiratory viral infections, most commonly in immunocompromised patients.[3,4]

Guidelines

The American Academy of Pediatrics (2021) states that no available treatment shortens the course of bronchiolitis or hastens the resolution of RSV symptoms.[2]

Management of young children hospitalized with bronchiolitis is supportive. Because of limited evidence for a clinically relevant benefit, potential toxic effects, and high cost, routine use of aerosolized ribavirin is not recommended.

Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice (2019) recommend aerosolized ribavirin in lung transplant recipients with upper or lower respiratory tract infection.[3] Treatment with aerosolized or oral ribavirin for non-solid organ recipients with lower respiratory tract disease can be considered. Aerosolized ribavirin is also a therapeutic option in lung transplant recipients with parainfluenza virus and human metapneumovirus.

The National Comprehensive Cancer Network guidelines for the prevention and treatment of cancer-related infections (version 3.2022 – October 28, 2022) recommend consideration of aerosolized ibavirin for the treatment of lower respiratory tract RSV disease (category 3).[4] Comments related to the recommendation are to limit to patients undergoing stem cell transplant or with leukemia and, that despite limited information in immunocompromised adults with RSV, use should be considered given the potential morbidity and mortality associated with RSV infection.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of aerosolized ribavirin. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with aerosolized ribavirin as well as the monitoring required for adverse events and long-term efficacy, approval requires aerosolized ribavirin to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Virazole® (ribavirin inhalation solution (Bausch, generic)
is(are) covered as medically necessary when the following criteria is(are) met for fda-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Respiratory Syncytial Virus (RSV), Treatment.** Approve for 1 month if the patient meets the following criteria (A, B, and C):
   - **A)** Patient is < 2 years of age; AND
   - **B)** Patient is hospitalized; AND
   - **C)** The medication is prescribed by or in consultation with a critical care or pulmonary specialist.

Other Uses with Supportive Evidence

2. **Respiratory Virus Treatment, Excluding COVID-19.** Approve for 1 month if the patient meets the following criteria (A, B, and C):
   A) Patient is hospitalized; AND
   B) Patient meets ONE of the following criteria (i, ii, or iii):
      i. Patient is a solid organ transplant recipient; OR
      ii. Patient has had a hematopoietic stem cell transplant; OR
      iii. Patient has cancer AND
   C) The medication is prescribed by or in consultation with a critical care specialist, transplant physician, oncologist, infectious diseases physician, or pulmonologist.

CONDITIONS NOT COVERED

Virazole® (ribavirin inhalation solution (Bausch, generic) is(are) considered experimental, investigational or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **COVID-19 (Coronavirus Disease 2019).** Data are preliminary, additional study is needed.[5,6] A Phase I, open-label, non-US (Greece, Brazil, and Mexico), non-randomized, two-arm study was conducted to evaluate the safety and efficacy of aerosolized ribavirin (as Virazole) in hospitalized adults with significant respiratory distress due to COVID-19 (n = 51).[5] Patients received aerosolized ribavirin (100mg/mL for 30min or 50mg/mL for 60min) twice daily for up to 6 days. Improvement of one or more level in clinical status severity was observed in 31.4% (n = 16/51) and 78.4% (n = 40/51) of patients at end-of-treatment and day 30, respectively. Of 21 patients who required a ventilator, 16 (76.2%) were able to discontinue ventilator use. One case series reported on five hospitalized adults with COVID-19 who received aerosolized ribavirin (100 mg/mL twice daily for 6 days) solution as part of a compassionate use program in Italy (patients were also managed in accordance with Italian treatment guidelines for COVID).[6] All patients fully recovered. Ribavirin is not addressed as a recommended treatment modality in guidelines from the Infectious Diseases Society of America or the National Institutes of Health.[7,8]

REFERENCES

1. Virazole® inhalation solution [prescribing information]. Bridgewater, NJ: Baush Health; May 2019.
2. Respiratory Syncytial Virus. In: Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH (Eds). Red Book: 2021-2024 Report of the Committee of Infectious Diseases. 32nd Edition, Itasca, IL: American Academy of Pediatrics; 2021.
3. Manuel O and Estabroook M; on behalf of the American Society of Transplantation Infectious Diseases Community Practice. RNA respiratory viral infections in solid organ transplant recipients: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clinical Transplantation.* 2019;33:e13511.
4. The NCCN Prevention and Treatment of Cancer-Related Infections Clinical Practice Guidelines in Oncology (version 3.2022 – October 28, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 5, 2023.

5. Poulakou G, Barakat M, Israel RJ and Bacci MR; on behalf of the Virazole Collaborator Group for COVID-19 Respiratory Distress. Ribavirin aerosol in hospitalized adults with respiratory distress and COVID-19: An open-label trial. *Clin Transl Sci.* 2023;16(1):165-174.
6. Messina E, Danise A, Ferrari G, et al. Ribavirin aerosol in the treatment of SARS-CoV-2: a case series. *Infect Dis Ther*. 2021;10:2791-2804.
7. Bhimraj A, Morgan RL, Hirsch Shumaker A, et al. Infectious Diseases Society of America Guidelines on the treatment and management of patients with COVID-19. Available at: https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/. Updated May 15, 2023. Accessed on June 5, 2023.
8. COVID-19 treatment guidelines panel. Coronavirus disease 2019 (COVID-19) treatment guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines.nih.gov/. Updated April 20, 2023. Accessed on June 5, 2023.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	06/22/2022
Annual Revision	No criteria changes.	06/07/2023

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