# Ribavirin

NOT RECOMMENDED AS AN ESSENTIAL MEDICINE



EMLc | ATC codes: J05AB04

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| **Indication** | Viral haemorrhagic fever, not elsewhere classified ICD11 code: 1D86 |
| **INN** | Ribavirin |
| **Medicine type** | Chemical agent |
| **List type** | Core |
| **Additional notes** | For the treatment of viral haemorrhagic fevers. |
| **Formulations** | **Parenteral > General injections > IV:** 1000 mg per 10 mL phosphate buffer solution ; 800 mg per 10 mL phosphate buffer solution<br>**Oral > Solid:** 200 mg ; 400 mg ; 600 mg |
| **EML status history** | First added in 2007 (TRS 946)<br>Changed in 2007 (TRS 950)<br>Removed in 2025 (TRS 1064) |
| **Sex** | All |
| **Age** | Also recommended for children |
| **Therapeutic alternatives** | The recommendation is for this specific medicine |
| **Patent information** | Patents have expired in most jurisdictions<br>Read more about patents. |
| **Wikipedia** | Ribavirin |
| **DrugBank** | Ribavirin |

## Expert Committee recommendation

The Expert Committee noted that the justification to use ribavirin for viral haemorrhagic fevers is based on one biased quasi-experimental study from the 1980s. However, the efficacy and safety of ribavirin have not been verified in appropriate follow-up randomized trials. Recent systematic reviews concluded that the available evidence was insufficient to recommend the routine use of ribavirin in Crimean–Congo haemorrhagic fever or Lassa fever given the high risk of bias in the included studies. Additional concerns over the lack of effect of ribavirin for viral haemorrhagic fever emerged. A biological rationale is lacking to support the use of ribavirin in this infection given that its mechanism of action is unknown. Further, evidence points to a potentially harmful effect in patients with mild disease. Based on these considerations, and until the efficacy and safety of ribavirin is verified in further research, the Expert Committee recommended the deletion of ribavirin for the treatment of viral haemorrhagic fevers from the EML and EMLc.

## Background

Ribavirin has been included on the EML and EMLc for use in the treatment of viral haemorrhagic fevers since 2007. Ribavirin is also included on the EML for use in combination with direct-acting antiviral agents in the treatment of hepatitis C virus infection.

## Public health relevance

Lassa fever is an acute viral illness caused by the Lassa virus. It is endemic in Benin, Ghana, Guinea, Liberia, Mali, Nigeria and Sierra Leone, and likely also exists in other west African countries. The overall case fatality rate is 1% but may be 15% or higher among hospitalized patients with severe disease. While ribavirin has been used for Lassa fever, there is now considerable uncertainty about its efficacy and safety for this indication. Early intensive supportive care, including fluid management and

treatment of specific symptoms, can improve survival (1). Crimean–Congo haemorrhagic fever virus is a cause of severe viral haemorrhagic fever outbreaks that have a case fatality rate of up to 40%. Crimean–Congo haemorrhagic fever is endemic in Africa, the Balkans, the Middle East and Asian countries south of the 50th parallel north. Ribavirin has been used as an off-label treatment but there is considerable uncertainty about its efficacy, given the lack of clinical evidence, and its optimal dosing regimens (2).

## Benefits

The justification for the use of ribavirin in the treatment of Lassa fever was mainly based on a quasi-experimental study (divided in two phases) conducted in the 1980s that evaluated the efficacy of ribavirin and Lassa virus–convalescent plasma for the treatment of Lassa fever (3). This study concluded that ribavirin was effective in treating Lassa fever patients based on reduced case fatality rates in patients treated with ribavirin. However, the evidence has been found to be associated with a substantial risk of bias due to the use of historic controls, non-randomized allocation of treatment, heterogenous use of Lassa virus laboratory diagnostic assays and small number of patients. In addition, data from this study suggest a potentially harmful effect in patients with aspartate aminotransferase levels lower than 150 IU/mL and in patients with suspected Lassa fever but without laboratory confirmation. The efficacy and safety of ribavirin has not been further established in appropriate randomized controlled trials. A 2018 Cochrane systematic review of five studies (one randomized controlled trial and four non-randomized studies, 612 participants) evaluated the effects of ribavirin in the treatment of Crimean–Congo haemorrhagic fever (4). Due to insufficient data and a high risk of bias in the non-randomized studies, the authors were unable to determine whether ribavirin reduced mortality, length of hospital stay and risk of needing platelet transfusions, or whether ribavirin was associated with an increased risk of adverse effects. A 2022 systematic review of 13 studies published between 1986 and 2020 evaluated the comparative effectiveness of ribavirin versus no ribavirin treatment on mortality outcomes in patients with Lassa fever (5). Although ribavirin was associated with decreased mortality rates in most studies, these studies were found to be at a critical or serious risk of bias, which undermined the reliability of the findings. A 2019 systematic review and meta-analysis of five retrospective cohort studies and one prospective clinical trial evaluated the efficacy of intravenous ribavirin for the treatment of Lassa fever (6). From the pooled analysis of the retrospective studies, ribavirin was associated with reduced odds of death (odds ratio (OR) 0.13, 95% confidence interval (CI) 0.04 to 0.40; very-low-certainty evidence). However, the included studies had a critical risk of bias due to the allocation processes and were thought to overestimate the treatment effect. From the prospective trial, there was very-low-certainty evidence that ribavirin was associated with reduced mortality in patients with elevated aspartate aminotransferase levels (OR 0.41, 95% CI 0.23 to 0.73), but increased mortality in patients without elevated aspartate aminotransferase levels (OR 2.37, 95% CI 1.07 to 5.25). This trial was considered to have a critical risk of bias due to missing data, participant misclassification, and unreliable randomization and treatment allocation procedures.

## Harms

Ribavirin may be harmful to patients with mild forms of Lassa fever (7). Higher doses than recommended have been associated with hypocalcaemia and hypomagnesaemia. A theoretical reproductive risk in humans exists due to teratogenic effects observed in animals.

## Additional evidence

A 2023 systematic review assessed the availability, scope, standardization and quality of clinical management guidelines for viral haemorrhagic fever (8). The review identified 32 guidelines on viral haemorrhagic fevers, focusing on their quality and evidence. Of these guidelines, 25 (78%) were of low quality and lacked supporting evidence. Only eight guidelines (25%) had been produced or updated in the past 3 years. The guidance on supportive care and therapeutics was often sparse and sometimes contradictory. The authors concluded that guidelines based on uncertain evidence are detrimental to patient care and clinical practice. They emphasized the need for investments in trials to identify optimal treatment strategies for viral haemorrhagic fevers and prioritization of affordable and scalable interventions to improve global health outcomes.

## WHO guidelines

WHO guidance for the clinical management of patients with viral haemorrhagic fevers is currently under review.


1. Lassa fever – fact sheet [internet]. Geneva: World Health Organization; 2024 (https://www.who.int/news-room/fact-sheets/detail/lassa-fever).
2. Crimean–Congo haemorrhagic fever – fact sheet [internet]. Geneva: World Health Organization; 2025 (https://www.who.int/news-room/fact-sheets/detail/crimean-congo-haemorrhagic-fever).
3. McCormick JB, King IJ, Webb PA, Scribner CL, Craven RB, Johnson KM et al. Lassa fever. Effective therapy with ribavirin. N Engl J Med. 1986;314(1):20–6 (https://doi.org/10.1056/nejm198601023140104).

4. Johnson S, Henschke N, Maayan N, Mills I, Buckley BS, Kakourou A et al. Ribavirin for treating Crimean Congo haemorrhagic fever. Cochrane Database Syst Rev. 2018;6(6):CD012713 (https://doi.org/10.1002/14651858.CD012713.pub2).
5. Cheng HY, French CE, Salam AP, Dawson S, McAleenan A, McGuinness LA et al. Lack of evidence for ribavirin treatment of Lassa fever in systematic review of published and unpublished studies1. Emerg Infect Dis. 2022;28(8):1559–68 (https://doi.org/10.3201/eid2808.211787).
6. Eberhardt KA, Mischlinger J, Jordan S, Groger M, Günther S, Ramharter M. Ribavirin for the treatment of Lassa fever: a systematic review and meta-analysis. Int J Infect Dis. 2019;87:15–20 (https://doi.org/10.1016/j.ijid.2019.07.015).
7. Task Force Therapeutics Viral Diseases. Clinical effectiveness of ribavirin against Lassa fever and Crimean-Congo haemorrhagic fever. Brussels: Belgian Health Care Knowledge Centre; 2023 (https://kce.fgov.be/sites/default/files/2023-03/ADVICE_Ribavirin%20LF-CCHF_FINAL.pdf).
8. Rigby I, Michelen M, Dagens A, Cheng V, Dahmash D, Harriss E et al. Standard of care for viral haemorrhagic fevers (VHFs): a systematic review of clinical management guidelines for high-priority VHFs. Lancet Infect Dis. 2023;23(7):e240–e52 (https://doi.org/10.1016/s1473-3099(22)00874-x).