VIRAL HAEMORRHAGIC FEVER

General points on treatment

VHFs are caused by viruses of four distinct families: arena viruses (Lassa fever, Argentine haemorrhagic fever); filoviruses (Ebola and Marburg): bunyaviruses (Crimen-Congo, hantavirus); and flaviviruses (dengue) (1). Lassa fever and Crimean-Congo Haemorrhagic Fever are spread from man to man and are the only two VHFs to be considered in the context of this document. The incubation period for VHF ranges from 4 to 21 days and common presenting symptoms are fever, myalgia and prostration followed by shock and generalised mucus membrane bleeding.

Patients receive intensive supportive therapy and the characteristics of the individual case (e.g. lung involvement) should guide the doctor as to the need for treatment of contacts.

Ribavirin, an anti-viral drug, has been effective in treating some individuals with Lassa fever, Crimean-Congo Haemorrhagic Fever and Haemorrhagic Fever with Renal Syndrome (2,3,4,5). Treatment with convalescent-phase plasma has been used with success in some patients with Argentine haemorrhagic fever (1,6.)

Ribavirin, has been shown to be most effective when given early in the course of the illness. Patients should also receive supportive care consisting of maintenance of appropriate fluid and electrolyte balance, oxygenation and blood pressure, as well as treatment of any other complicating infections (1).

This guidance considers treatment of suspected or confirmed clinical cases of Lassa fever and Crimean-Congo Haemorrhagic Fever and post exposure prophylaxis regimens in case of suspected or confirmed exposure to the virus.

The Dose Recommendations given below are compiled primarily from ref. 7 (based on refs 3 and 8) and 4.

RECOMMENDATIONS

In a mass casualty setting parenteral treatment may not be an option and recommendations for oral treatment should be followed. Otherwise oral therapy should be substituted when the patient's condition improves.

Name of active substance **Role in therapy and prophylaxis**	**Section**	**Treatment of suspected or confirmed clinical cases of VHF** Duration of treatment: 10 days	**Post exposure prophylaxis in case of suspected or confirmed exposure to the pathogen** Duration of prophylaxis: 7 days
Ribavirin	**Posology**	**Adults** **Two iv regimens can be used** • Initial dose of 2 g followed by 1 g every 6 hours for 4 days followed by 0.5 g every 8 hours for 6 days **Or** Initial dose of 30 mg/kg followed by 15 mg/k every 6 hours for 4 days, followed by 7.5 mg/kg every 8 hours for 6 days **Oral regimen:** 2 g orally (loading dose) followed by 4g/day in 4 divided doses for 4 days followed 2g/day for 6 days **Children** No recommendations can be given	**Adults** 2 g/day orally in 4 divided doses **Children** No recommendations can be given
	Contra indications	Ribavirin is embryotoxic and teratogenic. However, given the seriousness of the condition the same product as in non-pregnant adults could be considered. Patients must not breastfeed during therapy.	

	Pregnancy and lactation	Given the seriousness of the condition the same product as in non-pregnant adults should be considered. It is recommended, when possible, to replace breastfeeding by artificial lactation

References

1. CDC webpage (http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/vhf.htm. Viral Hemorrhagic Fevers: Fact Sheets December 2001.

2. NJ Snell. Ribavirin-Expert Opin Pharmacother 2001 Aug;2(8):1317-24

3. McCormick JB, King IJ, Webb PA, Scribner CL, Craven RB, Johnson KM, Elliott LH, Belmont-Williams R. Lassa fever. Effective therapy with ribavirin. N Engl J Med. 1986 Jan 2;314(1):20-6.

4. Fisher-Hoch SP, Khan JA, Rehman S, Mirza S, Khurshid M, McCormick JB Crimean Congo-haemorrhagic fever treated with oral ribavirin. Lancet. 1995 Aug 19;346(8973):472-5.

5. Huggins et al Prospective, double blind, concurrent, placebo controlled clinical trial of intravenous ribavirin therapy of haemorrhagic fever with renal syndrome. JID 1991;164:1119-1127.

6. Ruggiero HA, Perez Isquierdo F, Milani HA, Barri A, Val A, Maglio F, Astarloa L, Gonzalez Cambaceres C, Milani HL, Tallone JC. Treatment of Argentine hemorrhagic fever with convalescent's plasma. 4433 cases]
Presse Med. 1986 Dec 20;15(45):2239-42. French.

7. Afssaps homepage. Plan Biotox (www.agmed.sante.gouv.fr/htm/10/indbio.htm).
AFSSAPS. France, 2001

8. Management of Patients With Suspected Viral Hemorrhagic Fever. Morbidity and Mortality Weekly Report (MMWR). Vol 37 no S-3 p 1-16. February 26, 1988