Ribavirin

Essential medicine status ✓

ATC codes: J05AP01

Indication	Chronic hepatitis C ICD11 code: 1E51.1
INN	Ribavirin
Medicine type	Chemical agent
List type	Core
Additional notes	For the treatment of hepatitis C, in combination with direct acting anti-viral medicines
Formulations	**Parenteral > General injections > IV:** 1000 mg per 10 mL phosphate buffer solution ; 800 mg per 10 mL phosphate buffer solution **Oral > Solid:** 200 mg ; 400 mg ; 600 mg
EML status history	First added in 2013 (TRS 985)
Sex	All
Age	Adolescents and adults
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Ribavirin
DrugBank	Ribavirin

Summary of evidence and Expert Committee recommendations

Globally, approximately 150 million people are infected with hepatitis C and it is estimated that 350 000 people die each year from hepatitis C-related liver disease (1). The goal of therapy is to produce a sustainable virological response (SVR) which can potentially result in the reversal of liver injury and can prevent serious consequences such as cirrhosis, end-stage liver disease, hepatocellular carcinoma and death. When compared with standard interferon-alfa alone, interferon-alfa in combination with ribavirin increased the SVR from 10–20% to 40–60% (2, 3). The long-acting pegylated formulation in combination with ribavirin has further increased SVR rates to 50–60% for genotype 1 and to 80% for genotypes 2 and 3 (4, 5). A recent meta-analysis showed that treatment success rates in low- and middle-income countries were similar to those obtained in high-income countries (6). Head-to-head randomized controlled trials – including the large randomized IDEAL trial (n = 3070) – demonstrated similar SVR rates for peginterferon alfa-2a and alfa-2b (41% versus 39% in IDEAL) in combination with ribavirin (7). While peginterferon alfa-2a or alfa-2b in combination with ribavirin has been the standard of care for chronic hepatitis C, the new direct-acting oral antiviral agents (boceprevir and telapravir) are more effective but more expensive (8, 9). The Expert Committee noted that there are several more direct-acting antivirals in development. Pegylated interferons + ribavirin are associated with a range of adverse events that often require dose reduction and discontinuation. Adverse events that resulted in treatment termination were reported in 39 studies and were present in 4% (95% CI: 3–5) (6). Peginterferon alfa-2a and alfa-2b appear to be similarly tolerated (3). Before treatment patients must be screened, RNA measurements and genotyping (which require high-level laboratory support) must take place, and facilities are required for liver biopsy and for detecting and managing complications. WHO is developing guidelines for the screening, care and treatment of hepatitis C. Other expert bodies such as NICE (10), the European Association for the Study of the Liver (11) and the American Association for the Study of Liver Diseases (12) recommend peginterferon alfa-2a or alfa-2b with ribavirin for treatment of hepatitis C. Ribavirin was already listed in the EML and EMLc for viral haemorrhagic fevers. The Expert Committee agreed on the public health need for these medicines and, because of the high level of expertise and facilities needed and the high cost, decided to list pegylated

interferon alfa-2a and alfa-2b in the complementary list, to be used with ribavirin for treatment of hepatitis C when these products are available. The Expert Committee stressed the need to follow the development of direct oral hepatitis C protease inhibitors and to consider applications for triple therapy or all-oral options for the treatment of hepatitis C. References: 1. Hepatitis C (WHO Fact Sheet, No. 164). Geneva: World Health Organization; 2010 (http://www.who.int/mediacentre/factsheets/fs164/en/, accessed 28 December 2013). 2. Foster G, Mathurin P. Hepatitis C virus therapy to date. Antivir Ther. 2008;13 Suppl 1:3-8. PMID:18432157 3. Foster GR. Pegylated interferons for the treatment of chronic hepatitis C: pharmacological and clinical differences between peginterferon-alpha-2a and peginterferon-alpha-2b. Drugs. 2010;70(2):147-65. http://dx.doi.org/10.2165/11531990-000000000-00000 PMID:20108989 4. Zeuzem S, Hultcrantz R, Bourliere M, Goeser T, Marcellin P, Sanchez-Tapias J, et al. Peginterferon alfa-2b plus ribavirin for treatment of chronic hepatitis C in previously untreated patients infected with HCV genotypes 2 or 3. J Hepatol. 2004;40(6):993-9. http://dx.doi.org/10.1016/j.jhep.2004.02.007 PMID:15158341 5. Hadziyannis SJ, Sette H Jr, Morgan TR, Balan V, Diago M, Marcellin P, et al.; PEGASYS International Study Group. Peginterferon-alpha2a and ribavirin combination therapy in chronic hepatitis C: a randomized study of treatment duration and ribavirin dose. Ann Intern Med. 2004;140(5):346-55. http://dx.doi.org/10.7326/0003-4819-140-5-200403020-00010 PMID:14996676 6. Ford N, Kirby C, Singh K, Mills EJ, Cooke G, Kamarulzaman A, et al. Chronic hepatitis C treatment outcomes in low- and middle-income countries: a systematic review and meta-analysis. Bull World Health Organ. 2012;90(7):540-50. http://dx.doi.org/10.2471/BLT.11.097147 PMID:22807600 7. Toyoda H, Kumada T. Pharmacotherapy of chronic hepatitis C virus infection - the IDEAL trial: ‘2b or not 2b (= 2a), that is the question’. Expert Opin Pharmacother. 2009;10(17):2845-57. http://dx.doi.org/10.1517/14656560903321521 PMID:19891593 8. Chou R, Hartung D, Rahman B, Wasson N, Cottrell EB, Fu R. Comparative effectiveness of antiviral treatment for hepatitis C virus infection in adults: a systematic review. Ann Intern Med. 2013;158(2):114-23. http://dx.doi.org/10.7326/0003-4819-158-2-201301150-00576 PMID:23437439. 9. Kieran J, Schmitz S, O’Leary A, Walsh C, Bergin C, Norris S, et al. The relative efficacy of boceprevir and telaprevir in the treatment of hepatitis C virus genotype 1. Clin Infect Dis. 2013;56(2):228-35. http://dx.doi.org/10.1093/cid/cis880 PMID:23074309 10. Hepatitis C − peginterferon alfa and ribavirin (TA 200). London: National Institute for Health and Care Excellence; 2010 (http://guidance.nice.org.uk/TA200, accessed 28 December 2013). 11. European Association for the Study of the Liver (EASL). EASL Clinical Practice Guidelines: management of hepatitis C virus infection. J Hepatol. 2011;55(2):245-64. http://dx.doi.org/10.1016/j.jhep.2011.02.023 PMID:21371579 12. Ghany MG, Strader DB, Thomas DL, Seeff LB; American Association for the Study of Liver Diseases. Diagnosis, management, and treatment of hepatitis C: an update. Hepatology. 2009;49(4):1335-74. http://dx.doi.org/10.1002/hep.22759 PMID:19330875