Ombitasvir + paritaprevir + ritonavir

NOT RECOMMENDED AS AN ESSENTIAL MEDICINE

Section: 6. Anti-infective medicines > 6.4. Antiviral medicines > 6.4.4. Antihepatitis medicines > 6.4.4.2. Medicines for hepatitis C > 6.4.4.2.2. Medicines for hepatitis C > Non-pangenotypic direct-acting antiviral combinations

ATC codes: J05AP53

Indication	Chronic hepatitis C ICD11 code: 1E51.1
INN	Ombitasvir + paritaprevir + ritonavir
Medicine type	Chemical agent
List type	Core
Formulations	**Oral > Solid:** 12.5 mg + 75 mg + 50 mg tablet
EML status history	First added in 2015 (TRS 994) Removed in 2023 (TRS 1049)
Sex	All
Age	Adolescents and adults
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Main patent is active in several jurisdictions. For more information on specific patents and license status for developing countries visit www.MedsPal.org Read more about patents.
Wikipedia	Ombitasvir + paritaprevir + ritonavir
DrugBank	Ombitasvir, Paritaprevir, Ritonavir

Expert Committee recommendation

The Expert Committee noted that pangenotypic direct-acting antiviral regimens are now the standard for treatment of chronic HCV infection as recommended in current WHO guidelines for treatment of HCV infection. They offer the advantages of simplifying the care pathway by removing the need for genotype testing and focusing procurement, thereby facilitating treatment expansion worldwide. The Committee noted that dasabuvir, used in combination with ombitasvir + paritaprevir + ritonavir, is not a pangenotypic regimen. The Committee also noted that interferon-based regimens have low efficacy and are associated with significant toxicity. These treatments are no longer recommended in WHO guidelines. The Committee therefore recommended the deletion from the EML of dasabuvir, ombitasvir + paritaprevir + ritonavir, and pegylated interferon alfa 2a and 2b from the core list of the EML.

Background

Pegylated interferon alfa has been included on the EML for use in combination with ribavirin for the treatment of chronic HCV infection since 2013. Dasabuvir and the fixed=dose combination of ombitasvir + paritaprevir + ritonavir were added in 2015. Listings of antivirals on the EML for the treatment of chronic HCV infection were

differentiated in 2019, to distinguish between pangenotypic and non-pangenotypic treatments. With pangenotypic regimens now recommended by WHO as the standard of care, the Expert Committee recommended that non-pangenotypic treatments could be considered for future deletion from the EML (1).

Public health relevance

It is estimated that 58 million people are chronically infected with HCV worldwide, with higher burdens in low and middle-income countries (2). However, in 2019 about 79% of people infected with HCV were unaware of their infection status and only about 13% of all infected people received treatment (2). An estimated 290 000 people died as a result of hepatitis C in 2019, mostly from liver cancer and cirrhosis caused by untreated HCV infections. In this context, the WHO goal is still to eliminate HCV as a public health threat by 2030, that is, a 90% reduction in chronic infections and 65% reduction in mortality compared to 2015.

Benefits

In 2018, WHO issued updated guidelines on care and treatment of chronic HCV infection (3). Key changes made were the following. • The adoption of a “treat all” approach: the use of safe and highly effective direct-acting antiviral regimens for all persons with HCV infection improves the balance of benefits and harms of treating persons with little or no fibrosis, thus supporting a strategy of treating all persons with chronic HCV infection, rather than reserving treatment for persons with more advanced disease. • The recommendation for the use of three pangenotypic direct-acting antiviral regimens for the treatment of persons with chronic HCV infection aged 18 years and above: o sofosbuvir/velpatasvir 12 weeks o sofosbuvir/daclatasvir 12 weeks and o glecaprevir/pibrentasvir 8 weeks. In 2022, this was updated to include adolescents and children down to the age of 3 years (4,5). Since 2016, several new, pangenotypic direct-acting antiviral medicines had been approved by at least one stringent regulatory authority, reducing the need for genotyping to guide treatment decisions. A WHO-commissioned systematic review identified 142 clinical studies that evaluated the safety and efficacy of various direct-acting antiviral regimens approved by the United States Food and Drug Administration and the European Medicines Agency. In 2018, the Guidelines Development Group made a recommendation to use pangenotypic regimens for the treatment of HCV infection. The Guidelines Development Group acknowledged that the potential clinical benefits of pangenotypic regimens were similar to those of non-pangenotypic regimens. However, pangenotypic regimens present an opportunity to simplify the care pathway by removing the need for expensive genotyping and so simplifying procurement and supply chains. These regimens offer an important opportunity to facilitate treatment expansion worldwide. These factors shift the balance of benefits and harms in favour of the use of pangenotypic regimens. Interferon-based regimens also have low efficacy and are associated with considerable toxicity.

Harms

Pegylated interferon alfa and ribavirin are associated with prominent side-effects during treatment and potentially irreversible long-term side-effects, such as thyroid disease, type 1 diabetes, ophthalmological complications and growth impairment in children (5).

WHO guidelines

Pegylated interferon alfa 2a and 2b and the non-pangenotypic regimen of dasabuvir with ombitasvir + paritaprevir + ritonavir are no longer recommended treatments in current WHO guidelines for treatment of chronic HCV infection (3,4).

Other considerations

Dasabuvir, ombitasvir, paritaprevir and ritonavir have been removed from expressions of interest issued for WHO prequalification of active pharmaceutical ingredients and finished pharmaceutical products.

1. The selection and use of essential medicines. Report of the WHO Expert Committee, 2019 (including the 21st WH

O Model List of Essential Medicines and the 7th WHO Model List of Essential Medicines for Children). Geneva: World Health Organization; 2019 (WHO Technical Report Series, No. 1021; https://apps.who.int/iris/handle/10665/330668, accessed 6 October 2023).
2. Hepatitis C – fact sheet [internet]. Geneva: World Health Organization; 2022 (https://www.who.int/news-room/fact-sheets/detail/hepatitis-c, accessed 6 October 2023).
3. Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. Geneva: World Health Organization; 2018. (https://apps.who.int/iris/handle/10665/273174, accessed 6 October 2023).
4. Updated recommendations on treatment of adolescents and children with chronic HCV infection, and HCV simplified service delivery and diagnostics. Geneva: World Health Organization; 2022 (https://apps.who.int/iris/handle/10665/363590, accessed 6 October 2023).
5. Indolfi G, Easterbrook P, Dusheiko G, El-Sayed MH, Jonas MM, Thorne C, et al. Hepatitis C virus infection in children and adolescents. Lancet Gastroenterol Hepatol. 2019;4(6):477–87.

