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A.17 - Glecaprevir + pibrentasvir fixed dose combination (100 mg + 40 mg) tablet and 50 mg glecaprevir granules + 20 mg pibrentasvir granules co-packaged in sachet

MSF has noticed the application for the inclusion of the fixed-dose combination (FDC) of glecaprevir + pibrentasvir (100 mg + 40 mg) tablet and the 50 mg glecaprevir + 20 mg pibrentasvir granules co-packaged in sachet in the core list of the WHO Model List of Essential Medicines for Children (EMLc) in section 6.4.4.2 Medicines for hepatitis C, sub-section 6.4.4.2.1, Pangenotypic direct-acting antiviral combinations, for the treatment of chronic hepatitis C virus (HCV) infection among paediatric patients. As no medicines for hepatitis C are currently included in the WHO Model List of Essential Medicines for Children, these section and sub-section must be created.

Since 2019, the FDC of glecaprevir + pibrentasvir **(**100 mg + 40 mg) tablet is included in the WHO Model List of Essential Medicines for the treatment of chronic HCV infection in adults.

According to WHO, 71 (62–79) million people worldwide were living with chronic HCV infection and 1.75 (1.57–2.12) million people were newly infected with HCV in 2015. At least 400 000 people died each year, due to liver cancer and cirrhosis caused by untreated HCV infections, 62% of people living with HCV are living in low- and middle-income countries (LMICs) and approximately 93% of the people infected with HCV are not receiving treatment. Although the prevalence of chronic HCV infection is lower in children than adults, an estimated 3.5 to 5 million children worldwide have chronic HCV infection.
The 2016 World Health Assembly has adopted targets for the elimination of chronic HCV as a public health threat by 2030. A global elimination strategy cannot succeed unless it includes treatment of children living with chronic HCV infection.

The combination of glecaprevir + pibrentasvir was already included as one of the three recommended pan-genotypic regimens for adults in the 2018 WHO “Guidelines for the care and treatment of persons diagnosed with chronic HCV infection” and this combination is expected to be added as a treatment for children with chronic HCV infection in the 2021 planned update of these guidelines.

The combination of glecaprevir + pibrentasvir, as well as other pangenotypic DAA regimens (sofosbuvir + velpatasvir and sofosbuvir + daclatasvir) presents the advantage of reducing the need for genotyping to guide treatment decisions.

According to the DORA study, glecaprevir + pibrentasvir is effective for the treatment of all HCV genotypes, in children aged 3 years and older, for whom dosing recommendations and appropriate formulation are available. The good tolerability allows a complete treatment course of 8 to 16 weeks.

MSF would like to draw the attention of the Expert Committee to the following points:

- Glecaprevir + pibrentasvir is not the first line regimen for children, sofosbuvir + daclatasvir and sofosbuvir + velpatasvir are the preferred regimens. Glecaprevir + pibrentasvir can be used in case of failure of these regimens.

- Glecaprevir + pibrentasvir is not ideal for patients living with HIV / HCV co-infection, due to its drug interactions with lopinavir/ritonavir (first-line treatment for children under 3 years of age) and efavirenz (used in children older than 3 years of age). Only dolutegravir can be used with glecaprevir + pibrentasvir but the dolutegravir regimen is not yet implemented for children in most countries.

- Following the initial marketing authorization (Europe in 2017), the glecaprevir + pibrentasvir (100 mg + 40 mg) FDC is approved and commercially available in many countries, but mostly in high-income countries.

- The Medicines Patent Pool has signed in November 2018 a royalty-free license agreement with the originator manufacturer of glecaprevir + pibrentasvir to enable generic manufacturers to develop, manufacture, license, submit for WHO prequalification, and supply this generic medicine at an affordable price, in 99 LMICs. There is a single generic supplier who has obtained the sublicense in December 2019 and there are currently no WHO-prequalified products.

- The film-coated granules formulation of 50 mg glecaprevir + 20 mg pibrentasvir is currently under review for approval by the US Food and Drug Administration (FDA) and not yet widely available. The 2 products are co-packaged in a sachet as a child-friendly formulation, allowing a once-daily administration after the granules are mixed with a small amount of food. Until this film-coated granules formulation is widely affordable and available, the film-coated tablet FDC of glecaprevir + pibrentasvir (100 mg + 40 mg), not a child-friendly formulation, can be used at the dosing of 1 or 2 tablets, once a day. Once again, MSF would like to emphasize that access to child-friendly (ideally scored dispersible tablets), quality-assured generic formulations

should be promoted, as they are essential to increase ease and safety of administration as well as adherence to treatment.

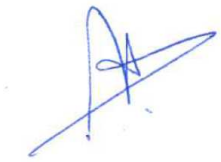
- The inclusion of the combination of glecaprevir + pibrentasvir in the EMLc will serve as a basis for National Essential Medicines Lists and increase interest in paediatrics formulations. The inclusion will therefore attract additional manufacturers, facilitate importation, alert manufacturers about the need for local registrations, allow for better competition between manufacturers in order to reduce price, and thus improve accessibility overall, particularly in LMICs.

- Previously all products listed in the WHO Model List of Essential Medicines for Children were also listed in the WHO Model List of Essential Medicines: if this logic is maintained, the 50 mg glecaprevir + 20 mg pibrentasvir granules co-packaged in sachet should also be added in the WHO Model List of Essential Medicines.

Since January 2015, in collaboration with Health Authorities, MSF provided treatments with DAAs to more than 35 800 people living with HCV, in 15 countries.

MSF recommends that the 23rd Expert Committee on the Selection and Use of Essential Medicines consider all these elements in its decision-making process.

For Médecins Sans Frontières



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