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**A.30 - Sofosbuvir + daclatasvir fixed dose combination (400 mg + 60 mg tablet), sofosbuvir 200 mg and 400 mg tablets, daclatasvir 30 and 60 mg tablets**

MSF strongly supports the inclusion of sofosbuvir and daclatasvir, either as a 400 mg + 60 mg tablet fixed dose combination (FDC) or as single medicines (sofosbuvir 200 mg and 400 mg tablets, daclatasvir 30 and 60 mg tablets) 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 2015, as single drugs, sofosbuvir 400 mg tablet and daclatasvir 30 and 60 mg tablet are 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 sofosbuvir + daclatasvir 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 hepatitis C virus infection” and this combination is expected to be to be added as a treatment for children with chronic HCV infection, in the 2021 planned update of these guidelines.

The combination of sofosbuvir and daclatasvir, as well as 2 other pangenotypic DAA regimens (sofosbuvir + velpatasvir and glecaprevir + pibrentasvir) presents the advantage of reducing the need for genotyping to guide treatment decisions.

According to a recent systematic review with meta-analysis of clinical trials conducted in children and adolescents, published in 2020, and to pharmacokinetic modeling and simulation, sofosbuvir + daclatasvir is effective, for the treatment of all HCV genotypes, in children weighing 14 to 35 kg, for whom dosing recommendations and appropriate formulation are available. The good tolerability of this regimen allows a complete treatment course of 12 weeks. HIV/HCV co-infected children receiving antiretroviral therapy can be treated with the combination of sofosbuvir + daclatasvir due to its low or manageable risk of drug-drug interactions.

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

- In low-and middle-income countries, sofosbuvir + daclatasvir is the regimen of choice for adults, due to its effectiveness, safety profile and availability of WHO-prequalified and affordable products from multiple manufacturers.

- Using the FDC of sofosbuvir and daclatasvir (400 mg + 60 mg tablet) will allow to reduce the pill-burden: the once-daily intake of one tablet increases ease of administration and therefore adherence to treatment.

- The film-coated tablets are not child-friendly formulations. Again, MSF would like to emphasize that paediatric dosage forms like scored dispersible tablets, or granules easily dissolved in water or food should be promoted and should reach internationally agreed quality standards. Access to child-friendly formulations is essential to increase ease and safety of administration as well as adherence to treatment.

- Since April 2020, the European Medicines Agency (EMA) has approved pediatric film-coated granules of sofosbuvir 150 mg and 200 mg, supplied by the originator manufacturer, for the treatment of children at least 3 years and weighing at least 17 kg. These film-coated granules are child-friendly formulations; they can be taken with or without a small amount of water, non-acid liquid or non-acid food. Currently, the originator manufacturer is also the only supplier of sofosbuvir 200 mg tablet for the treatment of children weighing from 17 kg to 35 kg. The inclusion of sofosbuvir and daclatasvir 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 importations, 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. Therefore, these inclusions will allow to scale-up treatment in children with chronic HCV infection.

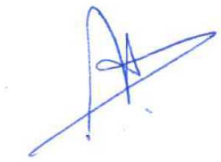
- Previously all products listed in the WHO Model List of Essential Medicines for Children were also listed in the WHO Model List of Essential Medicines: if this logic is maintained, the FDC of sofosbuvir and daclatasvir (400 mg + 60 mg) tablet and sofosbuvir 200 mg tablet should also be added in the 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 has been using sofosbuvir + daclatasvir in its programs since 2015.

MSF urges the 23rd Expert Committee on the Selection and Use of Essential Medicines to include sofosbuvir and daclatasvir, either as a fixed dose combination (400 mg + 60 mg tablet) or as single drugs (sofosbuvir 200 mg and 400 mg tablets, daclatasvir 30 and 60 mg tablets) in the EMLc for the treatment of chronic HCV infection in paediatric patients and to include sofosbuvir + daclatasvir (400 mg + 60 mg) FDC and sofosbuvir 200 mg tablet in the EML.

For Médecins Sans Frontières



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