A.31	Sofosbuvir + velpatasvir – hepatitis C infection (children)
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: An estimated 115 million people are infected with HCV and 11 million are <15 years. 80 million are viremic, and 5-million of these are <15 years old. Over 80% reside in LMICs Maternal fetal transmission rates are approximately 5% of affected pregnancies, but 25% of infected infants will clear the virus spontaneously by age4. Largest number of infected children reside in Africa, Asia and Middle East. Global health care costs for HCV infected children and their families are hundreds of millions of dollars annually.
Briefly summarize the role of the proposed medicine(s) relative to other therapeutic agents currently included in the Model List, or available in the market.	• Most commonly used combination for treatment of Hepatitis C in adult and children are 1. Velpatasvir plus sofosbuvir is used for the treatment of chronic HCV infection. • With this combination sustained viral responses are seen in over 95% children with mild side effects. • It is approved by FDA in adults and children over 3 or older who meet specific requirements as determined by a health care provider. • Several trials have been conducted in LMICs • NO drugs are listed in EMLc at present for treatment of HCV in children.
Have all important studies and all relevant evidence been included in the application?	☒ Yes ☐ No ☐ Not applicable If no, please provide brief comments on any relevant studies or evidence that have not been included:

Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed indication?	☒ Yes ☐ No ☐ Not applicable Briefly summarize the reported benefits (e.g. hard clinical versus surrogate outcomes) and comment, where possible on the actual magnitude and clinical relevance of benefit associated with use of the medicine(s). • FDA approved Sofosbuvir-velpatasvir on the basis of an open label trial in 173 patients >6 years or weighing >36 pounds/17 kilograms with chronic HCV. They were infected through vertical transmission and were treatment naïve (NCT03022981). • SVR for all genotypes was >90% Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)? YES. Several trials have been conducted in low resource settings.
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: Side effects are mild and generally well tolerated.
Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments:
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	• It is essential that treatment be given to children >3 years who have maternal-fetal transmission and have unable to clear HCV infection spontaneously. • Long term side effects of untreated HCV are well known liver fibrosis, cirrhosis leading to decompensated liver disease and cancer also. • Treatment of these long-term complications costs millions of dollars to patients and society annually
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	HIGH

Are there any special requirements for the safe, effective and appropriate use of the medicine(s)**?** (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	☒ Yes ☐ No ☐ Not applicable Comments: Monitoring viral load during and after treatment and liver function tests. Hepatitis B testing should be performed prior to start of therapy.
Are you aware of any issues regarding the registration of the medicine by national regulatory authorities? (e.g. accelerated approval, lack of regulatory approval, off-label indication)	☐ Yes ☒ No ☐ Not applicable Comments:
Is the proposed medicine recommended for use in a current WHO Guideline approved by the Guidelines Review Committee? (refer to: https://www.who.int/publications/who-guidelines)	☒ Yes ☐ No ☐ Not applicable Comments: for adults infected with HCV.
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	Very good combination of short duration with sustained viral response. Side effects not significant. Cheap and generics available.
Any additional comments	
Based on your assessment of the application, and any additional evidence / relevant information identified during the review process, briefly summarize your proposed recommendation to the Expert Committee, including the supporting rationale for your conclusions, and any doubts/concerns in relation to the listing proposal.	APPROVED. Short term treatment of 12 weeks. Cost of treatment not expensive. Generics are available in all resource settings.
References (if required)	