Application for Inclusion of Sofosbuvir/Velpatasvir on the WHO Model List of Essential Medicines for Children (EMLc)

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General Information

1. Summary statement of the proposal for inclusion, change or deletion.

This document proposes the inclusion of sofosbuvir/velpatasvir, as a fixed dose combination (FDC) product, for treatment of chronic hepatitis C infection among pediatric patients on the core list of the Model List of Essential Medicines for Children (EMLc). The regimen of sofosbuvir (SOF) plus velpatasvir (VEL) represents the combination of two direct-acting antiviral drugs. SOF/VEL tablets are currently included in the WHO Model List of Essential Medicines (EML) for treatment of chronic hepatitis C virus (HCV) in adults. This application proposes to add the SOF/VEL FDC tablet to the Model List of Essential Medicines for Children (EMLc) to span the pediatric ages and weight bands for which this product provides appropriate dosing.

The principal reasons for requesting this inclusion are as follows:

- The combination SOF/VEL provides effective treatment for all common genotypes of HCV, with high rates of sustained virologic response (SVR) measured at 12 weeks after the completion of therapy in children 3 years of age or older for whom an appropriate formulation is available.
- Treatment with SOF/VEL is well-tolerated and the great majority of patients are able to complete a treatment course of 12 weeks.
- The combination of SOF/VEL has a relatively low or manageable risk of drug-drug interactions and can be used in patients receiving antiretroviral therapy for HIV infection.
- SOF/VEL 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. SOF/VEL is expected to be added as a treatment for adolescents and children with chronic HCV infection in the planned update to the chapter on treatment in adolescents and children in the 2018 WHO Guidelines for the Care and Treatment of Persons Diagnosed with Chronic Hepatitis C Virus Infection. The regimen will be recommended as therapy for pediatric patients for whom dosing recommendations and an appropriate formulation are available. This will be published in Q2/Q3 2021 as a rapid communication policy brief, and will also be included in the overall WHO consolidated guidelines on testing, care and treatment of viral hepatitis to be published end 2021.

2. Relevant WHO technical department and focal point (if applicable).

Philippa Easterbrook, WHO Global Hepatitis Program

3. Name of organization(s) consulted and/or supporting the application.

Clinton Health Access Initiative, Inc.
Boston, MA USA

4. International Nonproprietary Name (INN) and Anatomical Therapeutic Chemical (ATC) code of the medicine.

INN: sofosbuvir velpatasvir

ATC: J05AP55

5. Dose forms(s) and strength(s) proposed for inclusion; including adult and age-appropriate paediatric dose forms/strengths (if appropriate).

SOF/VEL is available as an FDC oral tablet containing either SOF 400mg/VEL 100mg or SOF 200mg/VEL 50mg produced by:

- Gilead Sciences Ireland UC
  IDA Business & Technology Park
  Carrigtohill, County Cork, Ireland

- Viatris Inc. (formerly Mylan Laboratories Limited)
  Plot No. 564/A/22
  Road No. 92
  Jubilee Hills, Hyderabad – 500096, India

6. Whether listing is requested as an individual medicine or as representative of a pharmacological class.

We request inclusion of SOF/VEL in the EMLc as an FDC product in the "Medicines for Hepatitis C" category (6.4.4.2), in the sub-category: "Pangenotypic direct-acting antiviral combinations" (6.4.4.2.1) without a square box. There are other direct acting antivirals listed for the treatment of chronic HCV, but these are not considered therapeutic equivalents.

Treatment details, public health relevance and evidence appraisal and synthesis

7. Treatment details (requirements for diagnosis, treatment and monitoring).

The current EML listing for DAAs recommends genotype-specific treatment for adolescents aged 12-17 years or weighing at least 35 kg with chronic HCV infection and further notes that SOF/VEL is a pan-genotypic DAA combination. The recommended dose for adults and adolescents (12-17 years and >35kg) without cirrhosis is SOF 400mg/VEL 100mg for 12 weeks. The approved dose for children 6 years to 12 years of age is SOF 400mg/VEL 100mg for those 30kg or more and SOF 200mg/VEL 50mg for those weighing 17kg up to 30kg. For children with cirrhosis, weight-based ribavirin dosing is added to the 12-week regimen. The innovator is proposing these weight based-doses be extended to children 3 to 5 years of age and a dose of SOF 150mg/VEL 37.5mg in children < 17kg. Regulatory submissions are pending at this time.

Dose adjustment is not needed for patients with renal impairment, including those requiring dialysis, or for patients with moderate to severe liver impairment. Drug concentrations of both SOF and VEL may be significantly decreased in those receiving P-gp inducers and/or moderate to strong CYP450 enzyme inducers, and concomitant use with these inducers is not recommended.[1]

Dosing recommendations for children are planned for the 2021 update to the chapter on treatment in adolescents and children in the 2018 WHO Guidelines for the Care and Treatment of Persons Diagnosed with Chronic Hepatitis C Virus Infection, based on a meta-analysis of recent clinical trials conducted in children and clinical trials performed by the innovator manufacturer, Gilead Sciences. The dose to be recommended in children without cirrhosis will be SOF 400mg/VEL 100mg given once daily for 12 weeks for children weighing

more than 30kg and SOF 200/VEL 50mg for children weighing 17kg up to 30kg. WHO dosing recommendations for children weighing less than 17kg will be made pending regulatory approval.

Identification of children with chronic HCV infection is frequently made on the basis of diagnosis of an infected parent and subsequent testing of the child. Diagnosis of chronic HCV requires testing to identify viral RNA by PCR in the blood, as antibody testing may indicate past or cleared infection. An HCV-infected woman may transmit the virus to her infant in about 5% of affected pregnancies (about 10% in HIV/HCV co-infected women) but 25-40% of children infected via mother-to-child-transmission of HCV will clear virus spontaneously in the first 4 years of life.[2] For this reason, treatment is not recommended for children younger than 3 years of age. Assessment of liver function is recommended at the time of diagnosis and liver transaminases should be monitored throughout treatment. A combined assessment of AST and platelet count, the AST to platelet ratio index (APRI) can provide an indication of the degree of liver fibrosis and liver biopsy is not routinely recommended in children. Transient elastography (FibroScan®) can also be considered to assess stage of fibrosis but is not widely available for children in LMIC. Children found to have cirrhosis generally require more intensive therapy, often including the addition of ribavirin to the DAA regimen. Undetectable HCV RNA 12 (or 24) weeks after the completion of treatment (SVR) is indicative of treatment success and considered a functional cure. However, specialized testing is not required for patient management prior to initiating or while receiving SOF/VEL therapy.

8. Information supporting the public health relevance.

Chronic HCV infection remains a major cause of liver disease globally, with an estimated 71 million people living with chronic HCV overall as of 2015 and an estimated 1.75 million new cases per year.[3] Previously, interferon-based therapy was long and difficult to tolerate, had a low success rate, and required extensive clinical and laboratory monitoring during treatment. The introduction of multiple all-oral, DAA regimens has led to SVR rates > 90% with treatment courses of 12 weeks and greatly improved safety profile. With these improved characteristics acknowledged, in 2016, the World Health Assembly adopted targets for the elimination of chronic HCV as a public health threat by 2030.[4] Treatment of chronic HCV in adults in LMIC has scaled up as availability of DAA treatments has increased.

Little emphasis has been placed on chronic HCV in children and the prevalence, epidemiology, and natural history of infection are less well understood in children than in adults. A recently-published modeling exercise, estimated 3.26 million children are living with chronic HCV infection; 20 countries account for 80% of all cases in patients 0-18 years of age. Countries with the highest number of children with chronic HCV include: Pakistan, China, India, Nigeria, and Egypt.[5] The predominant mode of acquisition of HCV infection in children is mother-to-child transmission, although older children and adolescents may become infected via unsafe injection practices or poor infection control practices. About 5% of infants born to mothers with HCV infection will acquire infection, up to 10% if the mother is co-infected with HIV. The risk of transmission increases with increasing maternal HCV RNA levels.[2] Fortunately, asymptomatic or minimally symptomatic liver disease is common in pediatric patients and cirrhosis and hepatocellular carcinoma are rare in this age group, allowing treatment to be deferred in younger children according to previous treatment guidelines. As noted in a recent publication, including children and adolescents in national HCV surveillance, testing, and treatment programs can eventually help achieve the goal of HCV elimination.[6] Indeed, many academic and non-governmental organizations suggest that a global HCV elimination strategy cannot succeed unless it includes treatment of children and, increasingly, countries with a high burden of HCV infection are developing case finding strategies and treatment programs for children as well as adults.

9. Review of benefits: summary of evidence of comparative effectiveness.

- *Identification of clinical evidence (search strategy, systematic reviews identified, reasons for selection/exclusion of particular data)*

  Evidence of effectiveness of SOF/VEL in children is based on information gathered from the scientific literature and review of treatment guidelines discussions. A recently published systematic review with meta-analysis assessed the efficacy and safety of DAAs in children and adolescents and was used to justify this EMLc request.[6] Description of the registrational trials in adults and children and information regarding the metabolism of SOF/VEL and expected or known drug-drug interactions are summarized in the Epclusa® (sofosbuvir and velpatasvir, Gilead Sciences) U.S. package insert.[1] Based on accumulated data from interferon-based treatment trials and other DAA treatment trials to date suggesting that children responded to treatment as well or better than adults, it is also expected that effectiveness of SOF/VEL in children can be extrapolated from larger adult efficacy trials using pharmacokinetic bridging and small confirmatory trials. Extrapolation of efficacy is an approach endorsed by the U.S. Food and Drug Administration for chronic HCV because the course of the infection and the effects of DAAs are considered sufficiently similar between adult and pediatric populations to allow approval of DAAs on the basis of matching pharmacokinetic parameters after the critical parameters are identified in adult patients.[8]

- *Summary of available data (appraisal of quality, outcome measures, summary of results)*

  A review of the available clinical trials data in adults was submitted to the Expert Committee with the request for addition of SOF/VEL to the 2017 EML and these data will not be repeated in this dossier. This dossier will focus on what is known regarding the use of SOF/VEL in patients younger than 18 years of age. A SOF/VEL innovator-sponsored pediatric registrational trial (for Epclusa, Gilead Sciences) is ongoing and has completed cohorts in children 6 to 18 years of age in high-income countries and provides most of the currently available data. Although use of a medication in adolescents is usually included in the EML, discussion of dosing in this age group is necessary in this dossier in order to support pediatric weight-based dosing.

  Gilead Sciences is conducting a pediatric trial of Epclusa® (sofosbuvir and velpatasvir) in patients < 18 years of age as part of the development programs for their sofosbuvir-containing regimens. To date, their registrational study has enrolled children with chronic HCV infection at sites in the U.S., U.K., Italy, and Belgium in three cohorts: 12-17 years (n=102), 6-11 years (n=73) and 3-5 years (n=41). The two older cohorts have been submitted for regulatory review and led to the approval of SOF/VEL for use in children 6 years of age and older or weighing at least 17kg. Across the 2 older cohorts about 75% were infected with genotype 1 HCV, 13% had genotype 3, and smaller numbers had genotypes 2, 4, and 6. Children 6-11 years old received 200mg/50mg and those 12-17 received 400mg/100mg once daily for 12 weeks, after which they were monitored for 12 weeks to assess treatment response. Overall, 93.7% of the study participants achieved SVR. Of the children who did not achieve SVR, only 2 experienced virologic failure; in others failure was due to participants being lost to follow-up (n=8) or spitting up or being unable to swallow the study drug tablets (n=2). The authors demonstrated that the plasma concentrations of SOF and VEL in the study participants were comparable to those observed in adults receiving the recommended dose.[9]

  The third cohort in the study, enrolling children 3-5 years of age, was recently reported. This group received either SOF/VEL dosed as in the earlier cohorts if at least 17kg or SOF/VEL 150mg/37.5mg

administered using an investigational granule formulation if < 17kg. Mean weight in this cohort was 19kg with a range of 13kg to 35kg, although it is not clear whether all children received the investigational granule formulation. The cohort was comprised of patients with genotype 1 (78%), genotype 2 (15%), genotype 3 (5%) and genotype 4 (2%). SVR was achieved in 83% (34/41) of patients in the cohort, however, no virologic failures were documented, and the seven treatment failures were described as nonvirologic failures, either early treatment discontinuation or lost to follow-up. Regulatory submission of this third cohort is described as pending.[10]

An additional observational study evaluating SOF/VEL in a small cohort of complex pediatric patients undergoing allogeneic hematopoietic cell transplant was recently published. These investigators reported their experience using SOF/VEL to treat five children with active genotype 1b HCV in the setting of relapsed/refractory leukemia and allogeneic hematopoietic cell transplantation. No major drug interactions were observed with either cyclosporine or sirolimus. All patients achieved virologic response and normalization of liver enzymes without significant adverse events during treatment. After a median of 15 months of follow-up, four of the patients remained disease free and with SVR.[11]

The systematic review and meta-analysis conducted by Indolfi et al identified near 100% success in achieving SVR with SOF-containing regimens administered to a total of 1674 patients; the review includes only the study by Jonas et al in listing SOF/VEL.[7]

- *Summary of available estimates of comparative effectiveness*

In the clinical studies to date, SOF/VEL has not been compared to other DAA regimens regardless of the population being studied. In its guidance for industry on developing DAAs, the U.S. FDA notes that a development plan containing at least one comparative trial is preferred but non-comparative studies using historical controls may be acceptable.[8] The standard basis for assessing efficacy across all ages and weights is achieving SVR in a high proportion of participants; > 95% SVR was achieved in almost all reported studies of SOF/VEL across all ages and genotypes studied. There are no comparative pediatric trials available.

10. Review of harms and toxicity: summary of evidence of safety.

- *Estimate of total patient exposure to date*

To date, the number of children treated with SOF/VEL is very small. As noted above, the systematic review identified only one reviewable study that included 175 children. Non-cirrhotic children receiving their initial treatment with SOF/VEL received a 12-week course. The Epclusa® package insert recommends adding weight-based ribavirin in children known to have cirrhosis.

- *Description of the adverse effects/reactions and estimates of their frequency*

DAAs in general, and SOF/VEL in particular, are well-tolerated and serious adverse events are uncommon. In ASTRAL-1, the large adult registrational trial employing a placebo control, the most commonly observed adverse reactions (all severity grades) in participants receiving 12 weeks of SOF/VEL treatment included headache (22%), fatigue (15%), nausea (9%), asthenia (5%), and insomnia (5%). However, among study participants experiencing adverse reactions, 79% had only mild events. Additionally, with the exception of asthenia, each of these adverse reactions occurred at a similar frequency or more frequently in subjects treated with placebo. Subjects with cirrhosis receiving

SOF/VEL plus ribavirin were more likely to have hematologic abnormalities during treatment but these laboratory abnormalities occurred in less than 1% of study participants in the placebo-controlled ASTRAL-1 trial.[1,12]

SOF/VEL was generally well-tolerated in the pediatric registrational trial. The most common adverse events among the 175 participants in the two older cohorts included headache (in 23% of patients), fatigue (18%), nausea (13%), vomiting (12%), and cough (11%). Four patients had serious adverse events reported during the trial: auditory hallucinations, constipation (both in the younger cohort) and two adolescents with suicidal ideation, exacerbation of bipolar disorder, and suicide attempts. Additional assessment of the psychiatric events revealed that 27% of the study participants had some relevant psychiatric medical history.[9] The most common adverse events observed among the 41 patients in the youngest cohort included vomiting (27%), cough (15%), pyrexia (15%), rhinorrhea (15%), fatigue (12%), nasal congestion (12%), and diarrhea (12%). One patient in this age group discontinued treatment due to an adverse event but there were no serious adverse events. Additionally, the later abstract reported no negative effects on weight gain, height, BMI, radiographic bone age, or sexual maturation from treatment initiation to 24 weeks post-treatment completion in either boys or girls 3-17 years of age.[10]

- *Summary of available data (appraisal of quality, summary of results)*

  Overall, the quality and quantity of data supporting the safety of SOF/VEL in adults is good and includes both clinical trials and observational cohorts in a variety of settings. One pediatric registrational trial has been reported including patients from 3 to 17 years of age in three age cohorts. The full study report for the pediatric trial has not been published but results of the three cohorts have been presented at international meetings.[9,10]

- *Summary of comparative safety against comparators*

  There is no comparative safety data in pediatric patients but all DAA regimens included in the Indolfi systematic review were reported to be well-tolerated.[7]

- *Identification of variation in safety that may relate to health systems and patient factors*

  No specific safety issues associated with SOF/VEL are expected to pose a differential risk in the international health setting. No special laboratory monitoring is required that might result in potential harm to patients if not available in LMIC clinic setting.

11. Summary of available data on comparative cost and cost-effectiveness of the medicine.

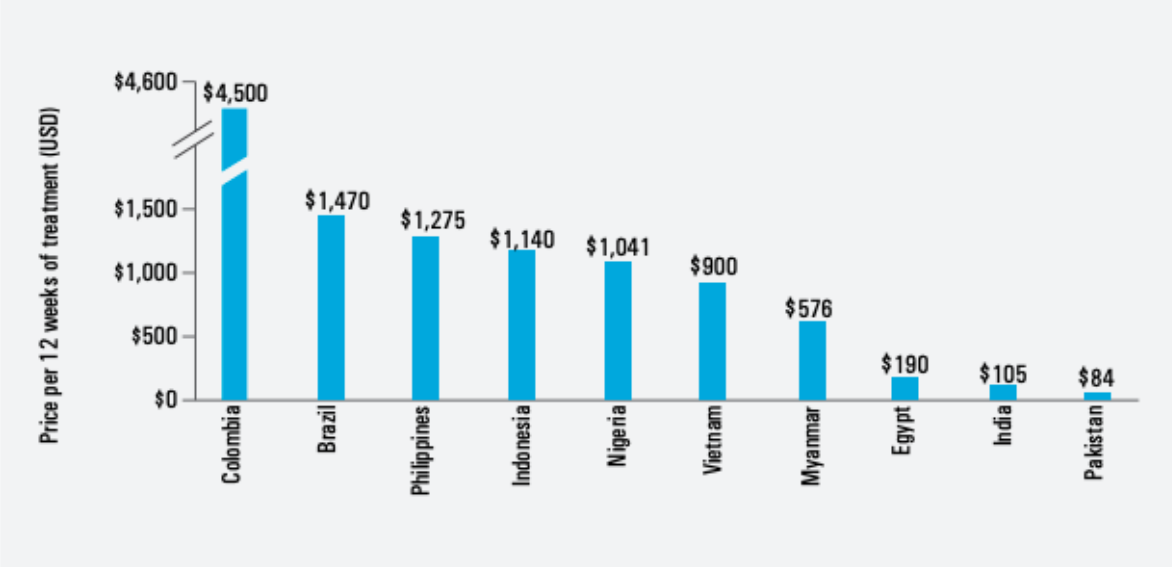
SOF/VEL 400mg/100mg and SOF/VEL 200mg/50mg

At present, there is a single generic formulation of SOF/VEL 400mg/100mg which is now widely available. SOF alone is manufactured by several generic manufacturers but VEL is not available as a single drug product. The UNDP Health Procurement Mechanism lists the price for Mylan's SOF/VEL 400mg/100mg tablets as $270 for a 12-week course.[13]

Epclusa® is registered by Gilead Sciences as a full-strength 400mg/100mg tablet for adults and adolescents and a half-strength 200mg/50mg tablet for children weighing from 17kg to 30kg. Gilead offers "access pricing" for their branded Epclusa® to government programs in 101 selected LMIC at a flat price of $300/28-tablet bottle, or $900 for a full treatment course.[14]

The introduction of additional generic SOF/VEL products has the potential to substantially lower the cost of SOF/VEL, as in India and Pakistan where local generic products are available. Barber et al documented the variability in cost of originator DAA products, reported on the availability of generic DAAs globally, and estimated the cost of production of some DAAs. They estimated manufacturing cost-based price for a 12-week course of SOF/VEL could be as low as $85.[15] These availability and cost concepts appear to be realistic as the CHAI HCV Market Analysis published in 2020 found the following in-country-specific pricing (Figure 1).[13]

Figure 1: In-country Price for 12 Weeks of Treatment with SOF/VEL FDC[13]



The prices are public sector prices paid by govt. to the supplier if available, or lowest identified private sector prices if public sector in-country prices not available; Prices shown can be for originator or generic product; Amongst generic products, prices can be for WHO PQ'd/ ERP reviewed or locally quality assured products; Prices as of 2019.
Source: CHAI Analysis for India, Nigeria, Indonesia, Vietnam, Myanmar; Coalition PLUS for Colombia and Brazil; World Health Alliance member for Philippines; mapCrowd for Egypt (mapCrowd accessed on 29th April 2020); Aga Khan University for Pakistan.

While there is currently no SOF/VEL 200mg/50mg generic product available and, therefore, no pricing information available, it is a similar composition formulation and should cost slightly less than the full-strength product because of lower amount of active ingredient, if both products are being sold (or used) at similar volumes.

Special Pricing Arrangements
There are no known special pricing arrangements other than Gilead's access pricing.

Country Level Cost Effectiveness Analyses
At the time of submission, no known country level cost-effectiveness studies have been conducted for SOF/VEL tablets for children.

Regulatory information

12. Summary of regulatory status and market availability of the medicine.

Epclusa® (sofosbuvir and velpatasvir), registered by Gilead Sciences, is approved by FDA and EMA; voluntary licenses are available in some LMIC through the company.

To date there is a single generic supplier with a WHO-prequalified SOF/VEL product (Viatris, formerly Mylan Laboratories Ltd) available in the international setting. India and Pakistan are reported to have locally manufactured generic products as well.

13. Availability of pharmacopoeial standards (British Pharmacopoeia, International Pharmacopoeia, United States Pharmacopoeia, European Pharmacopeia).

These products are not listed in any of the pharmacopoeia standards.

References: Comprehensive reference list and in-text citations.

1. U.S. Food and Drug Administration. Epclusa (sofosbuvir and velpatasvir) tablets, for oral use, package insert. 2020. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/208341s015lbl.pdf
2. Indolfi G, Easterbrook P, Dusheiko G, El-Sayed MH, Jonas MM, Thorne C, Bulterys M, Siberry G, Walsh N, Chang M-H, Meyers T, Giaquinto C, Wirth S, Chan P-L, and Penazzato M. 2019. Hepatitis C virus infection in children and adolescents. Lancet Gastroenterol Hepatol, Published Online, April 11, 2019, http://dx.doi.org/10.1016/ S2468-1253(19)30046-9
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/bitstream/handle/10665/273174/9789241550345-eng.pdf?ua=1
4. World Health Organization. Global health sector strategy on viral hepatitis 2016–2021: towards ending viral hepatitis, June 2016. https://apps.who.int/iris/bitstream/handle/10665/246177/WHO-HIV-2016.06-eng.pdf?sequence=1
5. Schmelzer J, Dugan E, Blach S, Coleman S, Cai Z, DePaola M, Estes C, Gamkrelidze I, Jerabek K, Ma S, Montoya S, Razavi-Shearer D, Razavi-Shearer K, Robbins-Scott S, Razavi H, and El Sayed MH. Global prevalence of hepatitis C virus in children in 2018: a modelling study. Lancet Gastroenterol Hepatol 2020; 5: 374–92.
6. El-Sayed MH and Indolfi G. Hepatitis C virus treatment in children: a challenge for hepatitis C virus elimination. *Semin Liver Dis* 2020; 40:213-224.
7. Indolfi G, Giometto S, Serranti D, Bettiol A, Bigagli E, De Masi S, Lucenteforte E. Systematic review with meta-analysis: the efficacy and safety of direct-acting antivirals in children and adolescents with chronic hepatitis C virus infection. Aliment Pharmacol Ther. 2020;52:1125–1133.
8. U.S. Food and Drug Administration. Guidance for Industry: Chronic Hepatitis C Virus Infection: Developing Direct-Acting Antiviral Drugs for Treatment Guidance for Industry. Nov 2017. https://www.fda.gov/media/79486/download
9. Jonas MM, Romero R, Sokal EM, Rosenthal P, Verucchi G, Lin C-H, Wen JW, Narkewicz MR, Bansal S, Shao J, Hsueh C, Gaggar A, Kersey K, Gonzalez-Peralta RP, Leung DH, Balistreri WF, Murray KF, and Schwarz KB. Abstract 748: Safety and efficacy of Sofosbuvir/Velpatasvir in pediatric patients 6 to < 18 Years old with chronic hepatitis C infection. Presented at The Liver Meeting (AASLD), November 8-12, 2019, Boston MA.
10. Sokal E, Schwarz KB, Rosenthal P, Verucchi G, Lin C-H, Balistreri W, Wen J, Whitworth S, Leung DH, Bansal S, Karnsakul W, Mangia A, Rao GS, Shao J, Hsueh C-H, Parhy B, Gaggar A, Kersey K, Narkewicz MR, Gozalex-Peralta RP, Murray KF, Romero R, and Jonas MM. Abstract 931: Safety and efficacy of sofosbuvir/velpatasvir for the treatment of chronic hepatitis C infection in adolescents and children aged 3 to 17 years old through 24 weeks post-treatment. Presented at the Liver Meeting (Virtual, AASLD), November 13-16, 2020.
11. Jaiswal SR, Bhakuni P, Soni M, Gupta M, Thatai A, and Chakrabarti S. Safety and efficacy of Sofosbuvir and Velpatasvir in children with active hepatitis C virus infection undergoing haploidentical transplantation. *Transpl Infect Dis*. 2020 Oct 10:e13490. doi: 10.1111/tid.13490. Epub ahead of print. PMID: 33037697.
12. J.J. Feld, I.M. Jacobson, C. Hézode, T. Asselah, P.J. Ruane, N. Gruener, A. Abergel, A. Mangia, C.-L. Lai, H.L.Y. Chan, F. Mazzotta, C. Moreno, E. Yoshida, S.D. Shafran, W.J. Towner, T.T. Tran, J. McNally, A. Osinusi, E. Svarovskaia, Y. Zhu, D.M. Brainard, J.G. McHutchison, K. Agarwal, and S. Zeuzem, for the ASTRAL-1 Investigators. Sofosbuvir and Velpatasvir for HCV Genotype 1, 2, 4, 5, and 6 Infection. *N Engl J Med* 2015;373:2599-607. DOI: 10.1056/NEJMoa1512610

13. Clinton Health Access Initiative. Hepatitis C Market Report. May 2020. https://3cdmh310dov3470e6x160esb-wpengine.netdna-ssl.com/wp-content/uploads/2020/05/Hepatitis-C-Market-Report_Issue-1_Web.pdf

14. Gilead Sciences. HCV Access Fact Sheet: Expanding Chronic Hepatitis C Treatment in Low- and Middle-Income Countries. 2019. https://www.gilead.com/-/media/files/pdfs/other/hcv-access-fact-sheet-061219.pdf?la=en&hash=ECF6F2AE73040656D7313C2D1BB27812

15. Barber MJ, Gotham D, Khwairakpam G, and Hill A. Price of a hepatitis C cure: Cost of production and current prices for direct-acting antivirals in 50 countries. 2020 *J Virus Eradication* https://doi.org/10.1016/j.jve.2020.06.001