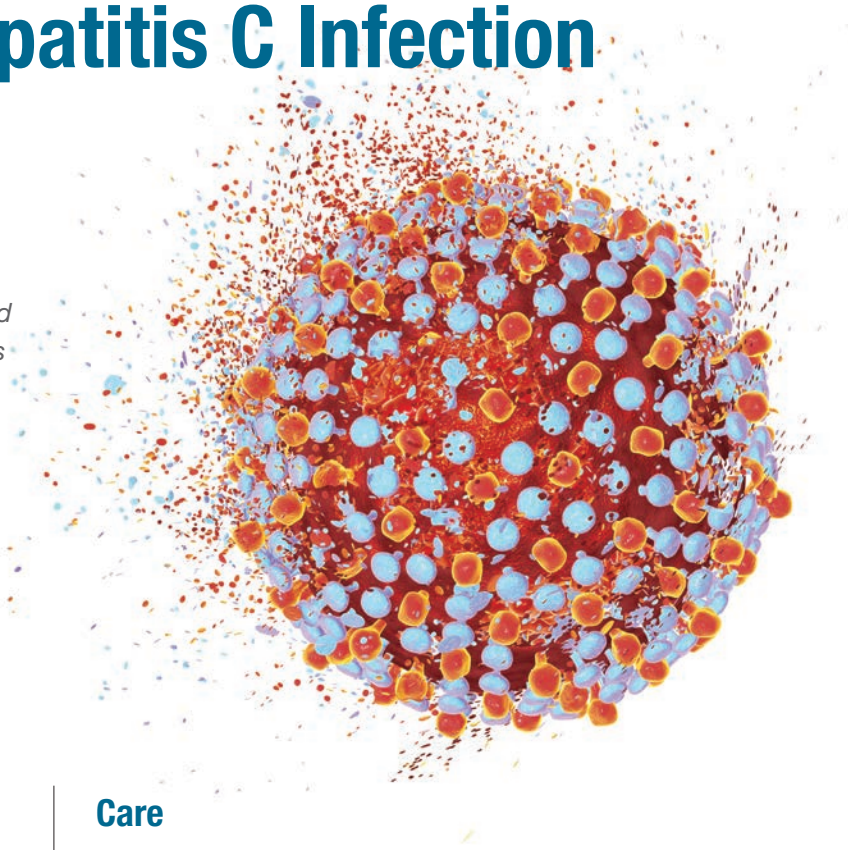
TREATASIA

November 2018

# Fact Sheet: WHO Guidelines for the Screening, Care, and Treatment of Persons with Hepatitis C Infection

*In July 2018, the World Health Organization (WHO) updated its guidelines on care and treatment of hepatitis C virus infection, which are aimed at helping policy makers and healthcare providers in low- and middle-income countries establish screening, care, and treatment programs. While the 2017 recommendations on laboratory testing remain unchanged, this updated version provides evidence-based recommendations for treating hepatitis C virus using only direct-acting antivirals (DAAs). The guidelines can be used by civil society, community organizations, and patient groups to advocate for access to testing, diagnostics, and treatment of hepatitis C. This fact sheet summarizes the major recommendations.*



## WHAT DO THE GUIDELINES SAY?

### Screening

Screening is the process that helps individuals know if they have been infected with the hepatitis C virus.

- All individuals who have ever been part of a population with high rates of hepatitis C infection should be screened with an antibody test. This includes people who inject drugs (PWID) and people living with HIV (PLHIV).
- Among the general population, in settings where the hepatitis C antibody prevalence is ≥2% or ≥5%, all adults should have access to and be offered the antibody test.
- Anyone who has a positive antibody test should have a hepatitis C viral load test (also known as an HCV RNA test) to confirm whether or not there is ongoing chronic infection.
- Genotype testing of the hepatitis C virus is not needed before treatment with a "pan-genotypic" DAA regimen (see **Treatment** section below).

### Care

All individuals with chronic hepatitis C infection can take steps to prevent liver damage and should have access to appropriate medical care to monitor the condition of their livers.

- An alcohol use assessment should be done for people who have confirmed hepatitis C infection, followed by an alcohol reduction intervention for those with moderate or high levels of alcohol use (defined as drinking more than nine glasses of beer or wine per week, regardless of age or sex).
- PWID should be offered information on how to prevent hepatitis B and C infection, including being offered vaccination against hepatitis B virus to avoid the risk of having two liver infections at the same time.
- Liver damage should be assessed using the APRI and FIB-4 scores, which are calculated using a combination of liver enzyme levels, platelet level, and the person's age.[1] A special ultrasound of the liver that assesses liver stiffness (called a FibroScan®) can be used, if available.

## Treatment

Medical treatment is available that can cure chronic hepatitis C infection.

- All adults and children aged 12 years and above with chronic hepatitis C infection should be offered treatment with DAAs, regardless of how serious their liver disease is.
  - ✔ For people aged 18 years and above, "pan-genotypic" DAA regimens should be used. These are specific 2-drug combinations that can cure infections of all types of hepatitis C virus.
  - ✔ For adolescents aged 12 to 17 years who weigh at least 35 kilograms, DAA regimens can be chosen based on the genotype.
    - o None of the currently recommended pan-genotypic DAAs in the 2018 guidelines are yet approved for use in both adolescents and children. Clinical research trials are ongoing, and results are anticipated in 2019 that will help guide future recommendations.
  - ✔ For children under 12 years of age, treatment may be deferred until they are older and it is safe to use DAA regimens.
  - ✔ Interferon should no longer be used for the treatment of chronic hepatitis C infection.

The guidelines make the following recommendations about the pan-genotypic regimens used to treat hepatitis C and their duration of use for adults and adolescents.

### Regimens for treating adults with chronic hepatitis C infection who do not have cirrhosis*

| Regimen | Duration |
|---|---|
| Glecaprevir/pibrentasvir | 8 weeks** |
| Sofosbuvir/daclatasvir | 12 weeks |
| Sofosbuvir/velpatasvir | 12 weeks |

**Treatment for both hepatitis C mono-infection and HIV co-infection.*

***Adults with genotype 3 who have previously received interferon and/or ribavirin should be treated for 16 weeks.*

### Regimens for treating adults with chronic hepatitis C infection who have compensated cirrhosis*

| Regimen | Duration |
|---|---|
| Glecaprevir/pibrentasvir | 12 weeks** |
| Sofosbuvir/daclatasvir | 24 weeks*** |
| Sofosbuvir/velpatasvir | 12 weeks |

**Treatment for both hepatitis C mono-infection and HIV co-infection.*

***Adults with genotype 3 who have previously received interferon and/or ribavirin should be treated for 16 weeks.*

****12 weeks may be considered in countries where genotype 3 distribution is known and its prevalence is less than 5%.*

### Regimens for treating adolescents 12 to 17 years of age with chronic hepatitis C infection*

| Genotype | Regimen | Duration |
|---|---|---|
| Genotypes 1, 4, 5, 6 | Sofosbuvir/ ledipasvir | 12 weeks** |
| Genotype 2 | Sofosbuvir/ribavirin | 12 weeks |
| Genotype 3 | Sofosbuvir/ribavirin | 24 weeks |

**In those without cirrhosis or with compensated cirrhosis. Adolescents must weigh at least 35 kilograms.*

***24 weeks for those who are treatment experienced and have compensated cirrhosis.*

### Monitoring for treatment response

Frequent monitoring of hepatitis C viral load is not required during treatment with DAAs. The guidelines suggest a simplified monitoring schedule.

| Time point | If treated with DAAs alone | If treated with DAAs and ribavirin* |
|---|---|---|
| Baseline, pre-treatment | Full blood count, kidney and liver function** | Full blood count, kidney and liver function |
| Week 4 | *Refer to footnotes below table* | Full blood count, kidney and liver function |
| Week 12 (after the last day of treatment) | Full blood count, kidney and liver function | Full blood count, kidney and liver function |

**Recommended treatment for adolescents with genotypes 2 and 3.*

***If the baseline hemoglobin is more than 10 g/dl, there is no need to repeat these tests at week 4.*

## Drug–drug interactions between hepatitis C and HIV medicines[2]

Some HIV medicines can interact with the DAAs used to treat hepatitis C. When these drug-drug interactions are anticipated, substitutions for HIV medications should be made before starting hepatitis C treatment.

| DAAs | ABC | ATZ/r | DRV/r | DTG | EFV | LPV/r | NVP | RAL | TDF | TAF | ZDV | XTC |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Daclatasvir | | | | | | | | | | | | |
| Gleceprevir/pibrentasvir | | | | | | | | | | | | |
| Sofosbuvir | | | | | | | | | | | | |
| Sofosbuvir/ledipasvir | | | | | | | | | | | | |
| Sofosbuvir/velpatasvir | | | | | | | | | | | | |

*Do not co-administer.*
*May need dose adjustment for DAAs.*
*No known interaction; can be co-administered.*

ABC: abacavir; ATZ/r: atazanavir/ritonavir; DRV/r: darunavir/ritonavir; DTG: dolutegravir; EFV: efavirenz; LPV/r: lopinavir/ritonavir; NVP: nevirapine; RAL: raltegravir; ZDV: zidovudine; TDF: tenofovir disoproxil fumarate; XTC: emtricitabine or lamivudine; TAF: tenofovir alafenamide.

Key populations with different co-infections need to have special considerations while being provided with care and treatment.

- HIV co-infection causes more rapid progression of hepatitis C infection. While DAA treatment should be considered and prioritized for all co-infected individuals, drug-drug interactions with antiretroviral medications need to be taken into account.
- Stabilization of HIV disease with antiretroviral therapy is advisable prior to starting hepatitis C treatment.
- Treating PWID for hepatitis C is both effective and cost-effective, and it prevents transmission of hepatitis C.
- Treatment of active tuberculosis infection should be considered prior to starting hepatitis C treatment.

## Regional relevance

The WHO's Regional Offices of the Western Pacific (WPRO)[3] and South East Asia (SEARO)[4] have both published regional action plans for viral hepatitis, which have been validated by member states. National governments are developing and finalizing their own strategies to address their local hepatitis C epidemics. India, Mongolia, and Thailand have started national programs to support diagnosis and treatment.

High-quality generic DAAs manufactured in the region are now available. The WHO prequalification (PQ) program and the Global Fund/WHO Expert Review Panel (ERP) have certified the quality of multiple generic DAA formulations.

The availability of generic DAAs is slowly increasing in the region while the costs are falling. Generic companies are working to complete regulatory requirements in more countries to facilitate registration of the medicines prior to marketing and distribution. National regulatory bodies need to provide fast-track registration of DAAs to allow for large-scale and more rapid treatment implementation.

The full guidelines can be accessed at http://www.who.int/hepatitis/publications/hepatitis-c-guidelines-2018/en/

[1] Online score calculators are available at http://gihep.com/calculators/hepatology/fibrosis-4-score/ and http://www.hepatitisc.uw.edu/page/clinical-calculators/apri

[2] For more information on potential drug-drug interactions please refer to https://www.hep-druginteractions.org/

[3] http://www.wpro.who.int/hepatitis/resource/features/regional_action_plan/en/

[4] http://www.searo.who.int/entity/hiv/documents/hap/en/

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