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The information contained in this publication is intended for medical professionals, as a quick reference to the national guidelines. This resource does not replace nor represent the comprehensive nature of the published guidelines. Recognizing the rapid changes that occur in this field, clinicians are encouraged to consult with their local experts or research the literature for the most up-to-date information to assist with individual treatment decisions for their patient. If your patient should experience a serious adverse event, please report the event to the FDA (*www.fda.gov/Safety/MedWatch/HowToReport/default.htm*) to help increase patient safety.

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Hepatitis in HIV/AIDS

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Editors: Jeffrey Beal, MD, AAHIVS
Maribel Gonzalez, MSN, ARNP
Joanne J. Orrick, PharmD, AAHIVP
Elizabeth Sherman, PharmD, AAHIVP
Todd S. Wills, MD

Managing Editor: Kimberly Molnar, MAcc
Layout: Adrian Green, BS

This guide is intended to assist clinicians in the diagnosis, prevention, and/or treatment of hepatitis A virus (HAV), hepatitis B virus (HBV), and hepatitis C virus (HCV) infection in HIV-infected patients (pts). **As the treatment recommendations for hepatitis are rapidly changing, providers are urged to regularly refer to the guidelines listed below.**

Unless otherwise noted, all information is adapted from:

1. Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at *www.aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf*. Accessed July 15, 2015

2. Lok AS, McMahon BJ. AASLD Practice Guideline Update. Chronic Hepatitis B: Update 2009. Hepatology; 2009; 50:1-36. Available at *http://www.idsociety.org/uploadedFiles/IDSA/Guidelines-Patient_Care/PDF_Library/Chronic_Hep_B_Update_2009%208_24_2009.pdf*. Accessed July 15, 2015

3. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. *http://www.hcvguidelines.org*. Accessed August 28, 2015.

ASSESSING HAV, HBV, AND HCV INFECTION STATUS

- Screen all HIV-infected pts for HAV, HBV, and HCV at baseline
- HAV testing: HAV total or IgG antibody (not IgM)
- HBV testing: Hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs) hepatitis B core antibody (anti-HBc)
  - If HBsAg (+), order HBV DNA viral load
- HCV testing: HCV antibody
  - If HCV antibody (+), order HCV RNA viral load and reflex to genotype

HEPATITIS A VACCINATION

- Recommended in chronic liver disease, MSM, IDU (AIII)
- Response best with CD4 > 200 cells/mm^3; revaccinate after reaching ≥ 200 cells/mm^3 if vaccinated at a lower CD4 and still Ab negative (BIII)

HEPATITIS B VIRUS (HBV)

Preventing HBV Infection

Indications for HBV Vaccination:
- Pts without chronic hepatitis B or without immunity from prior HBV vaccination (anti-HBs < 10 IU/mL) (AII)
- Pts with isolated anti-HBc and with negative HBV DNA (BII)
- Early vaccination is recommended before CD4 count falls below 350 cells/mm^3 (AII)
- Vaccination should not be deferred until CD4 reaches > 350 cells/mm^3; initiate series at entry to care (AII)

Vaccination Schedule:
- Hepatitis B vaccine IM (Engerix-B® 20 µg/mL or Recombivax HB® 10 µg/mL) at 0, 1, and 6 months (AII), **or**
- Hepatitis A/B vaccine (Twinrix®) 1 mL IM at 0, 1, and 6 months (or) at days 0, 7, 21 to 30, and 12 months (AII)
- Anti-HBs drawn 1 month after completion; anti-HBs < 10 IU/mL denotes non-responder (BIII)

For Vaccine Non-Responders:
- Revaccinate with a second vaccine series (BIII)
- Consider delay revaccination until a sustained CD4 increase if low CD4 count at the time of first vaccination (CIII)

Alternative Vaccine Dose for Non-Responders:
- Some experts recommend revaccinating with 40 µg doses of either hepatitis B vaccine (CIII)

Treating Chronic HBV Infection

Indication for Therapy:
- All HIV/HBV co-infected pts, regardless of CD4 count or HBV treatment status (AII). Treatment should be used for both HIV and HBV infections (AIII)

Preferred Therapy (ART regimen should include 2 drugs active against HBV):
- Tenofovir 300 mg + (emtricitabine 200 mg or lamivudine 300 mg) po once daily (AIII)

Duration of Therapy:
- Pts on treatment for HBV and HIV will receive therapy indefinitely (CIII)

Alternative Therapy:
If pts do not want to or are unable to take ART:
- Anti-HBV therapy is indicated if active liver disease, elevated ALT, and HBV DNA > 2,000 IU/mL, or significant liver fibrosis (AI)
- Peginterferon alfa 2a 180 mcg SQ once weekly for 48 weeks (CIII) **or**
- Peginterferon alfa 2b 1.5 mcg/kg SQ once weekly for 48 weeks (CIII)

If tenofovir cannot be used as part of the ART regimen:
- Fully suppressive ART + entecavir should be used (BIII)

NOTE: Single drug HBV therapy should be avoided due to high rate of HBV drug resistance (AI).

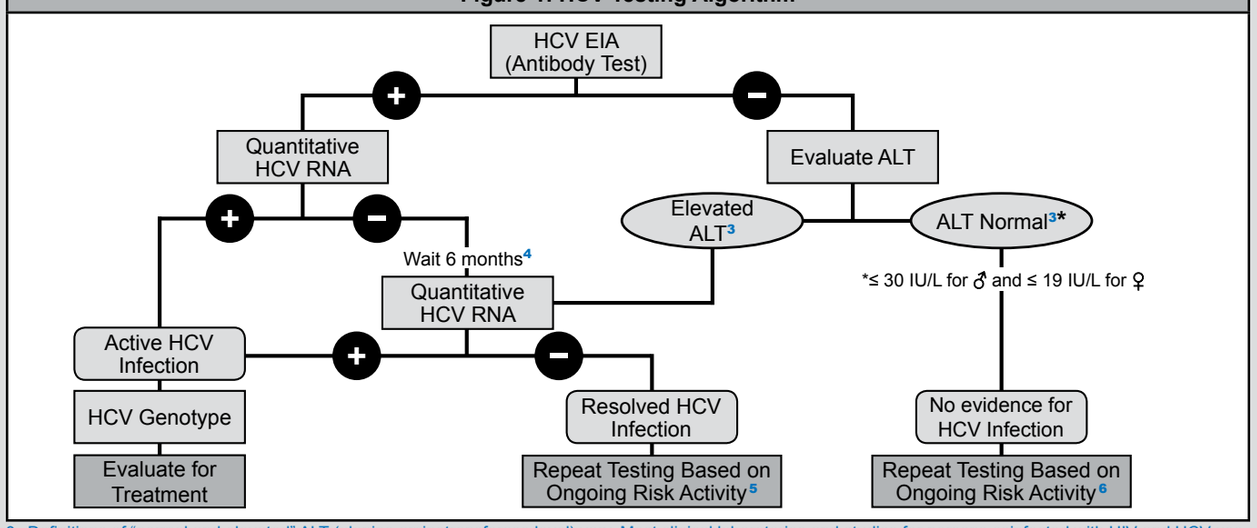
Other Considerations:
- Adefovir, emtricitabine, entecavir, lamivudine, telbivudine, or tenofovir should not be used for the treatment of HBV infection in pts who are not also receiving combination ART (AII)
- As pts with HBV/HCV/HIV co-infection appear to have accelerated liver fibrosis progression, high risk of hepatocellular carcinoma, and increased mortality, treatment for both HBV and HCV infection should be initiated, if feasible
- When changing ART regimens, continue agents with anti-HBV activity because of the risk of IRIS (BIII)
- If anti-HBV therapy is discontinued and a flare occurs, therapy should be re-instituted (AIII)

Table 1: Antiviral Agents for the Treatment of HBV
Information adapted from references listed above and Han Y, Zhang Y, Wang Y, et al. Analysis of hepatitis B virus genotyping and drug resistance gene mutations based on massively parallel sequencing. J Virol Methods. 2013 Nov;193(2):341-7.

Name	Dose	Considerations	Renal Dose Adjustment	HBV mutation sites associated with antiviral resistance
Emtricitabine/tenofovir (Truvada®)	200/300 once daily	• Treatment of choice & preferred NRTI backbone for HIV/HBV co-infected pts	CrCL 30-49: 1 tab every 48 hours CrCL < 30 **or** HD: do not use	A194T, V173L, L180M, M204V/I
Adefovir dipivoxil (Hepsera®)	10 mg once daily	• Generally less efficacious	CrCL 30-49: 10 mg every 48 hours; CrCL 10-29: 10 mg every 72 hours; HD[1]: 10 mg every 7 days	A181T/V, N236T
Emtricitabine (Emtriva®)[2]	200 mg once daily		CrCL 30-49: 200 mg every 48 hours; CrCL 15-29: 200 mg every 72 hours; CrCL < 15 **or** HD[1]: 200 mg every 96 hours	V173L, L180M, M204V/I
Entecavir (Baraclude®)	1 mg once daily (if lamivudine/ emtricitabine resistant)	• High barrier to resistance	CrCL 30-49: 0.5 mg once daily or 1 mg every 48 hours; CrCL 10-29: 0.3 mg once daily or 1 mg every 72 hours; CrCL < 10 **or** HD[1]: 0.1 mg once daily or 1 mg every 7 days[1]	I169T, L180M, M204V, S202I/G, T184G/S/A/I/L/F, M250V/I/L
Lamivudine (Epivir®)	300 mg once daily	• Lower barrier to resistance	CrCL 30-49:150 mg once daily CrCL 15-29: 150 mg x 1, then 100 mg once daily; CrCL 5-14: 150 mg x 1, then 50 mg once daily; CrCL < 5 **or** HD[1]: 50 mg x 1, then 25 mg once daily	L80I/V, V173L, L180M, M204V/I
Telbivudine (Tyzeka®)[2]	600 mg once daily	• Lower barrier to resistance	CrCL 30-49: 600 mg every 48 hours; CrCL < 30 (not requiring HD): 600 mg every 72 hours; HD[1]: 600 mg every 96 hours	M204I
Tenofovir (Viread®)	300 mg once daily	• If tenofovir cannot be used as part of the ART regimen because of current or high risk of renal dysfunction: a fully suppressive ART regimen without tenofovir should be used, with the addition of entecavir to the regimen. • High barrier to resistance	CrCL 30-49: 300 mg every 48 hours; CrCL 10-29: 300 mg twice weekly every 72-96 hours; CrCL < 10 and not on HD: not recommended; HD[1]: 300 mg every week (assumes 3 HD sessions per week of approximately 4 hours each)	A194T
Pegylated IFN alfa-2a (Pegasys®)	180 mcg SQ weekly	• Side effects • Subcutaneous injection	CrCL < 30 or HD[1]: 135 mcg SQ weekly	

1. Dose after hemodialysis (HD) on HD days.
2. Dose differs for solution, see package insert or guidelines.

Figure 1: HCV Testing Algorithm



3. Definitions of "normal and elevated" ALT (alanine aminotransferase level) vary. Most clinical laboratories and studies for persons coinfected with HIV and HCV use ALT > 40 IU/L as the cut-off for elevated ALT. Prior studies in monoinfected pts have defined elevated ALT as > 30 IU/L (for men) and > 19 IU/L (for women).
4. See *www.hcvguidelines.org* for treatment and monitoring recommendations if a decision is made to initiate treatment during the acute infection period.
5. Positive HCV EIA, but confirmed negative RNA, indicates resolved HCV infection. Pts may become reinfected; repeat HCV RNA annually if pt has ongoing risk (e.g., unprotected sex, exposure to blood or instruments that could be contaminated with blood, risky behavior).
6. For persons without HCV infection, repeat HCV EIA should be done annually only in those individuals with ongoing risk for acquiring HCV.

Table 2: Evaluation of Liver Disease Stage

Liver Biopsy	Noninvasive Tests
• Not required; consider if more accurate staging could impact tx decision • Provides information on the state of intensity of liver inflammation, degree of fibrosis, amount of steatosis, and may identify other causes of liver disease	• Most common noninvasive tests include HCV FibroSURE™, ALT, AST, platelet count, AST-Platelet Ratio Index (APRI), and FIB-4 • Useful in differentiating minimal fibrosis from advanced fibrosis (i.e., cirrhosis), but not as useful in pts with intermediate stages • Considered in pts who refuse liver biopsy (when recommended)

ALCOHOL AND SUBSTANCE ABUSE

- Do not exclude pts from treatment due to a history of alcohol or drug use; heavy use can accelerate liver disease progression impacting treatment response
- Instruct pts with chronic HCV infection to avoid alcohol consumption particularly during HCV treatment
- Active drug use may negatively impact adherence and pts should receive counseling and/or be referred to treatment programs

TREATMENT CONSIDERATIONS

The goal of therapy for hepatitis C is to achieve a sustained virologic response (SVR). This is defined as an undetectable HCV RNA viral load 12 weeks after completion of treatment. An SVR is considered evidence of cure. Those with advanced fibrosis or compensated cirrhosis and/or are HIV coinfected have a high priority for immediate treatment.

Tools to Improve Treatment Success

• Substance abuse counselors • Pt education • Opioid dependence treatment • Peer-based counseling • Group counseling

Table 3: AASLD Treatment Guidelines Initial Therapy (Treatment Naïve)

Genotype	Recommended Treatment	Alternative Treatment
GT 1a	Daily DCV + SOF x 12 weeks; 24 weeks if cirrhotic ± RBV Rating: BI (not cirrhotic) , BIIa (cirrhotic) Daily LDV/SOF x 12 weeks Rating: AI Daily PTV/r/OBV + twice daily DSV + RBV x 12 weeks; 24 weeks if cirrhotic Rating: AI Daily SOF + SMV x 12 weeks; 24 weeks if cirrhotic and absent Q80K polymorphism (± RBV) Rating: AI	
GT 1b	Daily DCV + SOF x 12 weeks; 24 weeks if cirrhotic ± RBV Rating: BI (not cirrhotic), BIIa (cirrhotic) Daily LDV/SOF x 12 weeks Rating: AI Daily PTV/r/OBV + twice daily DSV x 12 weeks Rating: AI Daily SOF + SMV x 12 weeks; 24 weeks if cirrhotic ± RBV Rating: AI	
GT 2	Daily DCV + SOF x 12 weeks if intolerant of RBV Rating: BIIa Daily SOF + RBV x 12 weeks; Rating: AI Extend treatment to 16 weeks if cirrhotic; Rating: CIIb	
GT 3	Daily DCV + SOF x 12 weeks; 24 weeks if cirrhotic ± RBV Rating: AI (not cirrhotic), CIIa (cirrhotic) Daily SOF + RBV + weekly PEG-IFN (if IFN eligible) x 12 weeks Rating: AI	Daily SOF + RBV x 24 weeks if IFN-ineligible Rating: AI
GT 4	Daily LDV/SOF x 12 weeks; Rating: BIIb Daily PTV/r/OBV + RBV x 12 weeks; Rating: BI Daily SOF + RBV x 24 weeks; Rating: BIIa	Daily SOF + RBV + weekly PEG-IFN x 12 weeks Rating: BII
GT 5 or 6	Daily LDV/SOF x 12 weeks Rating: BIIa	Daily SOF + RBV + weekly PEG-IFN x 12 weeks Rating: BIIa

TREATMENT CONSIDERATIONS

See Table 3 for the recommended regimens based on genotype. See Table 9 for drug-drug interactions with antiretrovirals.
Before prescribing, the clinician should refer to the product label for each drug to review contraindications/precautions, adverse effects, and drug interactions.
Also see *www.hep-druginteractions.org* and *http://www.hcvguidelines.org/full-report/unique-patient-populations-patients-renal-impairment* for a comprehensive hepatitis C drug interaction database and recommended dose adjustments for pts with renal impairment.

= Take with food = Take without food = Take with or without food

Daclatasvir (Daklinza™, DCV)

(dak-LAT-as-vir)

Drug Classes: NS5A inhibitor
Dosage Form: 30, 60 mg tab
Adult dose:
- 60 mg once daily
- 30 mg once daily with strong CYP3A inhibitors
- 90 mg once daily with moderate CYP3A inducers

Important Points:
- AEs: headache, fatigue
- Metabolism: CYP3A4
- Drug interaction potential: CYP3A4 substrate [levels may be ↑ by strong CYP3A inhibitors (e.g., ritonavir, itraconazole, clarithromycin), levels may be ↓ by moderate/strong CYP3A inducers (e.g., phenytoin, carbamazepine, rifampin, St. John's wort). **Contraindicated with strong CYP3A inducers**. ↑ dose with moderate CYP3A inducers. Inhibits P-glycoprotein, organic anion transporting polypeptide (OATP) 1B1 and 1B3, and breast cancer resistance protein (BCRP) and may ↑ levels of drugs that are substrates of these transporters.
- No dosage adjustment for mild, moderate, or severe renal or hepatic impairment
- Serious symptomatic bradycardia may occur when combined with amiodarone due to interaction with sofosbuvir

Ledipasvir/Sofosbuvir (Harvoni®, LDV/SOF)

(led-i-pas-vir/soe-FOS-bue-vir)

Drug Classes: NS5A/NS5B polymerase inhibitor
Dosage Form: 90, 400 mg tab
Adult dose: 90, 400 mg po once daily

Important Points:
- AEs: Fatigue, headache, insomnia
- Metabolism: LDV: unknown, primarily oxidative metabolism, biliary elimination; SOF: dephosphorylation, renal elimination (80%)
- Drug interaction potential: LDV may increase TDF levels (monitor for TDF related renal adverse effects); P-glycoprotein inducers (e.g. carbamazepine, phenytoin, rifampin, TPV/r) can ↓ SOF levels; LDV requires an acidic environment for absorption
- No dose adjustment for mild or moderate renal impairment. Dose not established for CrCL < 30 mL/min or ESRD requiring HD.
- No dose adjustment for mild, moderate or severe hepatic impairment (Child-Pugh Class A, B or C). Dose not established in pts with decompensated cirrhosis.

Table 4: LDV/SOF Dosing with Acid-reducing agents

Acid-reducing Agents	Dosing Recommendations
Antacids	Separate antacid and LDV/SOF administration by 4 hours
H2 Receptor Antagonists (H2RAs)	Give simultaneously with or 12 hours apart from LDV/SOF. Max dose of famotidine 40 mg bid [or equivalent].
Proton Pump Inhibitors (PPIs)	Give simultaneously with LDV/SOF under fasted conditions. Max dose of omeprazole 20 mg [or equivalent].

Paritaprevir/Ritonavir/Ombitasvir (Technivie™, PTV/r/OBV)

(par-i-TA-pre-vir/ri-TOE-na-veer/om-BIT-as-vir)

Drug Classes: NS3/4A protease inhibitor (PTV)/PK enhancer (RTV)/ NS5A inhibitor (OBV)
Dosage Form: PTV/r/OBV 75/50/12.5 mg tab
Adult dose: PTV/r/OBV 2 tabs (150/100/25 mg) po once daily

Important Points:
- Take with food
- AEs: asthenia, fatigue, nausea, insomnia
- Metabolism: PTV: CYP3A4 major, CYP3A5 minor; RTV: CYP3A4 major, 2D6 minor; OBV: amide hydrolysis
- Drug interaction potential: PTV levels may be ↑ or ↓ by drugs that inhibit or induce metabolism. RTV is a potent CYP3A4 inhibitor. OBV and PTV also inhibit UGT1A1.
  - The dose of ritonavir used for boosting of HIV protease inhibitors may need to be adjusted (or held) when administered with PTV/r/OBV and then restored when HCV treatment is completed. The HIV protease inhibitor should be administered at the same time as the fixed-dose HCV combination.
- No dosage adjustment for mild, moderate, or severe renal impairment
- No dosage adjustment for mild hepatic impairment (Child-Pugh Class A), not recommended in pts with moderate hepatic impairment (Child-Pugh Class B), contraindicated in pts with severe hepatic impairment (Child-Pugh Class C)

TREATMENT CONSIDERATIONS (Continued)

Paritaprevir/Ritonavir/Ombitasvir plus Dasabuvir (Viekira Pak™, PTV/r/OBV plus DSV)

(par-i-TA-pre-vir/ri-TOE-na-veer/om-BIT-as-vir/da-SA-bue-vir)

Drug Classes: NS3/4A protease inhibitor (PTV) / PK enhancer (RTV) / NS5A inhibitor (OBV) / NS5B polymerase inhibitor (DSV)
Dosage Form: PTV/r/OBV 75/50/12.5 mg tab plus DSV 250 mg tab
Adult dose: PTV/r/OBV 2 tabs (150/100/25 mg) po once daily plus DSV 250 mg po twice daily

See Paritaprevir/Ritonavir/Ombitasvir section for other important points

Important Points:
- Take with food
- AEs: nausea, pruritus, insomnia, asthenia, fatigue
- Metabolism: PTV: CYP3A4 major, CYP3A5 minor; RTV: CYP3A4 major, 2D6 minor; OBV: amide hydrolysis; DSV: CYP2C8 major, CYP3A4 minor
- Drug interaction potential: PTV and DSV levels may be ↑ or ↓ by drugs that inhibit or induce their metabolism. RTV is a potent CYP3A4 inhibitor. OBV and PTV also inhibit UGT1A1.

Ribavirin (Copegus®, RBV)

(rye-ba-VYE-rin)

Drug Classes: Antiviral (mechanism not fully established)
Dosage Form: 200 mg tab or cap, 400 mg tab, 40 mg/mL oral solution
Adult dose:
- < 75 kg: 1000 mg per day in 2 divided doses (e.g. 400 mg QAM + 600 mg QPM)
- ≥ 75 kg: 1200 mg per day in 2 divided doses (e.g. 600 mg QAM + 600 mg QPM)

Important Points:
- Contraindicated in women who are pregnant and in male partners of women who are pregnant
- AEs: fatigue/asthenia, pyrexia, myalgia, headache, hemolytic anemia, rash
- Metabolism: Unknown, not a CYP substrate
- Drug interaction potential: Primarily related to overlapping toxicities.
  - Do not use with didanosine, stavudine, or zidovudine
- Reduce dose in pts with CrCL < 50 mL/min (See Table 8)

Simeprevir (Olysio®, SMV)

(sim-E-pre-vir)

Drug Classes: NS3/4A protease inhibitor
Dosage Form: 150 mg cap
Adult dose: 150 mg po once daily

Important Points:
- Take with food
- Pt should use sunscreen to ↓ risk of photosensitivity
- Contains a sulfa component but history of sulfa allergy is not a contraindication as it does not correlate with rash or photosensitivity
- AEs: rash, photosensitivity, pruritus
- Metabolism: CYP3A4 and possibly CYP2C8 and CYP2C19
- Drug interaction potential: SMV levels may be ↑ or ↓ by drugs that inhibit or induce CYP3A4
- No dosage adjustment for mild, moderate, or severe renal impairment
- No dosage adjustment for mild hepatic impairment (Child-Pugh Class A), not recommended in pts with moderate or severe hepatic impairment (Child-Pugh Class B or C)

Sofosbuvir (Sovaldi®, SOF)

(soe-FOS-bue-vir)

Drug Classes: NS5B polymerase inhibitor
Dosage Form: 400 mg tab
Adult dose: 400 mg po once daily

Important Points:
- AEs: Fatigue, headache, insomnia, asthenia
- Metabolism: Dephosphorylation, renal elimination (80%)
- Drug interaction potential: P-glycoprotein inducers (e.g. carbamazepine, phenytoin, rifampin, TPV/r) can decrease SOF levels
- No dose adjustment for mild or moderate renal impairment. Dose not established for CrCL < 30 mL/min or ESRD requiring HD.
- No dose adjustment for mild, moderate or severe hepatic impairment (Child-Pugh Class A, B or C). Dose not established in pts with decompensated cirrhosis.

TREATMENT RELATED BONE MARROW TOXICITY

Ribavirin therapy is primarily associated with anemia. In many cases, dose reduction of the implicated drug can stabilize or reverse the cytopenia; however, in some cases erythrocyte stimulating factors [(epoetin alfa or darbepoetin alfa) and/or granulocyte colony-stimulating factor (G-CSF, filgrastim)] are required.

Use of Erythrocyte Stimulating Factors

Dosing
- Epoetin alfa 40,000 IU SC/week **or**
- Darbepoetin alfa 200 mcg SC every other week
- Goal: 1 g/dL or more increase in Hgb in 2 weeks, if goal not achieved:
  - Epoetin alfa 60,000 IU per week **or**
  - Darbepoetin alfa 300 mcg every other week

Outcome Goal
- Hgb between 10-12 g/dL, but not exceeding 12 g/dL
  - Hgb of > 13 g/dL resulting from erythrocyte stimulating agents has been linked to increased mortality and cardiovascular complications
  - Some experts will maintain the use of erythrocyte stimulating agents and slowly increase ribavirin dose when Hgb is between 10-12 g/dL

Table 5: Prior to Starting Treatment

At any time prior to starting treatment:	
HCV Genotype and Subtype	HCV VL quantitative
Immediately prior to starting treatment:	
Assess for potential drug-drug interactions	Serum pregnancy testing in women of childbearing potential, if ribavirin to be used
Within 12 weeks of starting treatment:	
CBC, INR	TSH (if using IFN)
Hepatic function panel (albumin, total and direct bilirubin, ALT, AST, and Alk Phos)	Calculated GFR

Table 6: On Treatment and Post-Treatment

4 Weeks	6 Weeks	8 Weeks	12 Weeks Post-Treatment	When to Stop Treatment
CBC, serum creatinine, calculated GFR	As clinically indicated			
Hepatic function panel	if < 10-fold ↑ ALT and asymptomatic	if < 10-fold ↑ ALT and asymptomatic		10-fold ↑ ALT or any ↑ ALT + weakness, nausea, vomiting, jaundice, ↑ Bili, ↑ Alk Phos, or ↑ INR
HCV VL quantitative	HCV VL quantitative if not undetectable at 4 weeks		HCV VL quantitative[6]	> 10-fold ↑ HCV VL quantitative at week 6
Clinic visit or telephone contact	As clinically indicated to evaluate: Medication adherence Monitor for adverse events Monitor for drug-drug interactions			
• Ongoing contraception assessment and pregnancy testing if using RBV through 6 months post treatment • TSH every 12 weeks for patients on IFN				

6. Consider HCV viral load quantitative at end of treatment and 24 week or longer following completion

Table 7: Ongoing Monitoring Post-Treatment

Failed Treatment		Achieved SVR	
All Patients		Metavir F0-F2 (No advanced fibrosis)	
CBC	Every 6-12 months	Follow up as if never infected	
Hepatic function panel		HCV VL quantitative to assess for recurrence or reinfection based on ongoing risk factors or presence of unexplained hepatic dysfunction	
INR			
Advanced Fibrosis (Metavir F3 or F4)		Advanced Fibrosis (Metavir F3 or F4)	
Hepatic Ultrasound	Every 6 months	Hepatic Ultrasound	Every 6 months
Cirrhosis		Cirrhosis	
Endoscopic surveillance for esophageal varices		Baseline endoscopy	
Evaluate for retreatment as alternative treatment becomes available.		If elevated liver enzymes, assess for other causes	

Table 8: Ribavirin Dosing in Renal Impairment

Creatinine Clearance	Ribavirin dose
30-50 mL/min	200 mg alternating with 400 mg every other day
< 30 mL/min	200 mg daily
Hemodialysis	200 mg daily
NOTE: Copegus® is the only ribavirin formulation approved for pts with CrCL < 50 mL/min	

Table 9: HCV Direct Acting Antivirals Interactions with Antiretrovirals

Information adapted from DHHS Adult/Adolescent Antiretroviral Guidelines, package inserts and *www.hep-druginteractions.org*. Review references for any drug interactions not listed.

✓ = ARV agent and HCV drug can be used concomitantly | X = Concomitant use of ARV agent and HCV drug **is not recommended**

? = Data on PK interactions with the ARV drug are unavailable or insufficient to make a recommendation

Select ARVs by Drug Classes	HCV Direct-Acting Antiviral Agents				
	NS5A Inhibitor	NS5B Inhibitor	Co-Formulated NS5A/NS5B Inhibitor	HCV Protease Inhibitor[7]	Co-Formulated NS3/4A protease inhibitor/PK enhancer (PTV/r)/ NS5A inhibitor (OBV) ± NS5B polymerase inhibitor (DSV)
	Daclatasvir (DCV)	Sofosbuvir (SOF)	Ledipasvir/ sofosbuvir (LDV/ SOF)	Simeprevir (SMV)	Paritaprevir (PTV) / Ritonavir (RTV) / Ombitasvir (OBV) ± Dasabuvir (DSV)
Nucleoside Reverse Transcriptase Inhibitors					
Emtricitabine (FTC)	✓	✓	✓	✓	✓
Lamivudine (3TC)	✓	✓	✓	✓	✓
Abacavir (ABC)	✓	✓	✓	✓	✓
Tenofovir (TDF)	✓	✓	✓[8]	✓	✓
Zidovudine (ZDV)	✓	✓	✓	✓	✓
HIV Protease Inhibitors (PIs) | NOTE: /r indicates ritonavir (RTV) and /c indicates cobicistat (COBI) for boosting					
Atazanavir (ATV) Unboosted	✓	✓	✓	X	✓[10] (+ DSV) / X (- DSV)
ATV/r, ATV/c	✓[9]	✓	✓[8]	X	✓[11] (+ DSV) / X (- DSV)
Darunavir (DRV)/r or DRV/c	✓	✓	✓[8]	X	X (+ DSV) / ✓[12] (- DSV)
Fosamprenavir/r (FPV/r)	✓[9]	✓	✓[8]	X	X
Lopinavir/r (LPV/r)	✓	✓	✓[8]	X	X
Saquinavir/r (SQV/r)	✓[9]	✓	✓[8]	X	X
Tipranavir/r (TPV/r)	✓[9]	X	X	X	X
Non-nucleoside Reverse Transcriptase Inhibitors					
Efavirenz (EFV)	✓[13]	✓	✓[14]	X	X
Etravirine (ETR)	✓[13]	✓	✓	X	X
Nevirapine (NVP)	?	✓	✓	X	X
Rilpivirine (RPV)	✓	✓	✓	✓	X
Integrase Strand Transfer Inhibitors					
Dolutegravir (DTG)	✓	✓	✓	✓	✓
Elvitegravir (EVG)/c/TDF/FTC	✓[9]	✓	X	X	X
EVG + PI/r (without c)	Refer to recommendation for specific ritonavir-boosted PI				
Raltegravir (RAL)	✓	✓	✓	✓	✓
CCR5 Antagonist					
Maraviroc (MVC)	✓	✓	✓	✓	?

7. Boceprevir and telaprevir are no longer recommended by HCV guidelines. Telaprevir was discontinued from U.S. market in October 2014).
8. Concomitant LDV/SOF with TDF and a ritonavir boosted PI or cobicistat boosted ATV or DRV may ↑ TDF exposure. Consider alternative HCV or ART, especially in pts with ↑ risk for renal insufficiency. If concomitant use necessary, monitor for TDF-associated adverse reactions (i.e., estimated creatinine clearance, serum phosphorous, urine glucose, and urine protein) before and periodically during HCV treatment.
9. Reduce DCV dose to 30 mg once daily.
10. Reduce ATV dose to 300 mg and take in AM at same time as Paritaprevir/Ritonavir/Ombitasvir plus Dasabuvir. **Do not use ATV unless DSV included in regimen.**
11. Take ATV 300 mg in AM at same time as Paritaprevir/Ritonavir/Ombitasvir plus Dasabuvir; discontinue RTV or COBI in HIV regimen until HCV therapy completed. **Do not use ATV unless DSV included in regimen.**
12. Take darunavir 800 mg once daily with food at the same time as PTV/r/OBV; discontinue RTV or COBI in the regimen until HCV therapy completed.
13. Increase DCV dose to 90 mg once daily.
14. Monitor for TDF-associated toxicity if EFV used with TDF/FTC due to ↑ TDF level.

EVALUATION OF LIVER STATUS AND TRANSPLANTATION REFERRAL

- Pts with documented or possible cirrhosis should have periodic assessment of liver status
- Model for End-Stage Liver Disease (MELD) score and the Child-Pugh (CP) score can predict mortality risk and can be used to determine the need for liver transplantation referral
  - Refer pt to hepatologist for transplantation evaluation if MELD > 10 and/or CP > 7
- See *www.mayoclinic.org/meld/mayomodel6.html* for MELD score calculation and see Table 10 for CP score calculation

Table 10: Child-Pugh (CP) Score Calculation[15]

Score	1	2	3
Encephalopathy[16]	None	Grade 1-2	Grade 3-4
Ascites	None	Mild or controlled by diuretics	Moderate or refractory to diuretics
Albumin	> 3.5 g/dL	2.8-3.5 g/dL	< 2.8 g/dL
Total Bilirubin **or**	< 2 mg/dL	2-3 mg/dL	> 3 mg/dL
Modified Total Bilirubin[17]	< 4 mg/dL	4-7 mg/dL	> 7 mg/dL
Prothrombin Time	< 4	4-6	> 6
or INR	< 1.7	1.7-2.3	> 2.3

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. Department of Health and Human Services. *Page P-20*. Available at: *http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf*. Accessed November 4, 2014.

15. Class A: Score 5-6; Class B: Score 7-9; Class C: Score > 9.
16. Grade 1: mild confusion, anxiety, restlessness, fine tremor, slowed coordination; Grade 2: drowsiness, disorientation, asterixis; Grade 3: somnolent but rousable, marked confusion, incomprehensible speech, incontinent, hyperventilation; Grade 4: coma, decerebrate posturing, flaccidity.
17. Modified total bilirubin used to score pts with Gilbert's Syndrome or in those taking IDV or ATV.

EVALUATION FOR HEPATOCELLULAR CARCINOMA (HCC)

- Pts with advanced fibrosis (e.g., bridging fibrosis and cirrhosis)should have hepatic ultrasound every 6 mos to assess for HCC
- Alpha-fetoprotein (AFP) alone is inadequate to assess for HCC and is not recommended