

Hepatitis antivirals

Two pharmacologically distinct groups sharing one page for teaching purposes - hepatitis C direct-acting antivirals, which cure most patients within eight to twelve weeks, and hepatitis B nucleos(t)ide analogues, which suppress the virus for as long as they are taken but do not cure it.

Online guide: <https://www.medguideglobal.com/pharmacology/antivirals-antifungals-antiparasitics/hepatitis-antivirals>

Content updated: 2026-09-15

Quick revision

One Liner: Hepatitis C direct-acting antivirals achieve sustained virologic response - undetectable HCV RNA 12 weeks after finishing an 8- to 12-week course - in more than 95% of patients, which counts as a cure; hepatitis B nucleos(t)ide analogues like entecavir and tenofovir suppress viral replication for as long as they are taken but do not eliminate the virus, and relapse is expected if treatment stops.

1. Hepatitis C is treated with combinations of three direct-acting antiviral (DAA) classes: NS3/4A protease inhibitors, NS5A inhibitors and NS5B polymerase inhibitors, each blocking a different HCV non-structural protein needed for replication. [5]
2. Sustained virologic response (SVR), defined as undetectable HCV RNA 12 or more weeks after completing therapy, is considered a virologic cure and is achieved in roughly 95% or more of patients on a currently recommended pangenotypic 8- to 12-week regimen. [7]
3. EPCLUSA (sofosbuvir/velpatasvir) and MAVYRET (glecaprevir/pibrentasvir) are both pangenotypic, covering HCV genotypes 1 through 6, which is why they have largely replaced older genotype-specific regimens. [1][2]
4. Chronic hepatitis B has no approved cure with currently available agents; entecavir and tenofovir are the preferred nucleos(t)ide analogues because of their high barrier to resistance, but withdrawal of therapy usually leads to relapse. [6]
5. All HCV DAA regimens and hepatitis B nucleos(t)ide analogues carry an HBV reactivation warning for coinfecting patients: DAA treatment of HCV in an HBV/HCV-coinfecting patient not on HBV-active therapy has been linked to fulminant HBV reactivation, and stopping an HBV-suppressive drug in a chronic HBV patient can trigger a severe hepatitis flare. [1][2][3]
6. All patients should be tested for HBsAg and anti-HBc before starting HCV DAA therapy specifically because of this reactivation risk. [1]
7. Entecavir and tenofovir alafenamide (Vemlidy) both require baseline and periodic renal monitoring, and hepatic function must be followed closely for months after either drug is discontinued. [4][3]

Overview

1. This page groups two pharmacologically separate fields under one teaching umbrella because they are so often confused with each other: antivirals for hepatitis C and antivirals for hepatitis B. The single most important distinction a student needs is the treatment endpoint each achieves. Hepatitis C direct-acting antivirals (DAAs) can cure the infection outright within a matter of weeks. Hepatitis B nucleos(t)ide analogues suppress viral replication for as long as the drug is taken, but do not currently cure chronic infection, and relapse is the expected outcome of stopping treatment without another reason (such as achieving specific, guideline-defined stopping criteria) to do so. [7][6]
2. Modern HCV therapy is built from three DAA classes acting on different non-structural proteins the virus needs to replicate: NS3/4A protease inhibitors (e.g. glecaprevir), which block cleavage of the HCV polyprotein; NS5A inhibitors (e.g. velpatasvir, pibrentasvir), which interfere with the viral replication complex; and NS5B polymerase inhibitors (e.g. sofosbuvir), which block the enzyme that synthesises the negative-strand RNA intermediate needed to make new viral genomes. Current regimens combine two of these mechanisms in one pill, taken once daily, and current pangenotypic

options such as EPCLUSA (sofosbuvir/velpatasvir) and MAVYRET (glecaprevir/pibrentasvir) cover HCV genotypes 1 through 6 rather than requiring genotype-specific drug selection. [5][1][2]

3. The outcome that makes this class remarkable is sustained virologic response (SVR): continued absence of detectable HCV RNA 12 or more weeks after finishing therapy. AASLD-IDSA guidance treats SVR as tantamount to virologic cure, and currently recommended 8- to 12-week pangenotypic regimens achieve it in more than 95% of treated patients - a cure rate essentially unheard of for a chronic viral infection before DAAs became available in the early 2010s. [7]

4. Hepatitis B is managed differently because the virus persists as covalently closed circular DNA in hepatocyte nuclei, a reservoir current oral agents do not eliminate. Entecavir and tenofovir (in either its disoproxil fumarate or newer alafenamide form) are the preferred nucleos(t)ide analogues for chronic HBV specifically because of their high genetic barrier to resistance relative to older agents such as lamivudine, but their labelling is explicit that stopping therapy can result in a severe, sometimes fatal, hepatitis flare and that ongoing suppression, not cure, is the realistic goal. [6][3]

5. The two fields intersect at one clinically important safety issue: hepatitis B virus reactivation during hepatitis C treatment. Both EPCLUSA and MAVYRET carry warnings that HBV reactivation, in some cases fulminant, has occurred in HCV/HBV-coinfected patients treated with a DAA regimen while not also receiving HBV-active antiviral therapy - which is why all patients are tested for HBsAg and anti-HBc before starting an HCV DAA, regardless of which regimen is chosen. [1][2]

Classification and drug examples

Intro: Hepatitis C therapy is classified by which HCV non-structural protein a DAA targets; hepatitis B therapy is classified separately, by nucleos(t)ide analogue generation and genetic barrier to resistance.

1. Name: HCV NS5B polymerase inhibitors

1. Note: Block the viral RNA-dependent RNA polymerase that synthesises the negative-strand RNA template needed to make new HCV genomes.

Name: Sofosbuvir

1. Sovaldi

2. component of Epclusa

Route: Oral

Note: Nucleotide analogue NS5B inhibitor; the backbone of most modern pangenotypic HCV regimens. [1] [5]

2. Name: HCV NS5A inhibitors

2. Note: Interfere with the NS5A protein's role in assembling the HCV replication complex, blocking viral RNA replication and virion assembly.

1. Name: Velpatasvir

component of Epclusa

1. Route: Oral

1. Note: Pangenotypic NS5A inhibitor, co-formulated with sofosbuvir. [1]

2. Name: Pibrentasvir

component of Mavyret

2. Route: Oral

2. Note: Pangenotypic NS5A inhibitor with a high resistance barrier, co-formulated with glecaprevir. [2] [5]

3. Name: HCV NS3/4A protease inhibitors

3. Note: Block the NS3/4A serine protease responsible for cleaving the HCV polyprotein into functional viral proteins.

Name: Glecaprevir

component of Mavyret

Route: Oral

Note: Pangenotypic protease inhibitor, co-formulated with pibrentasvir as MAVYRET. [2] [5]

4. Name: Hepatitis B nucleos(t)ide analogues

4. Note: Suppress HBV reverse transcriptase/DNA polymerase; entecavir and the tenofovir salts are preferred for their high barrier to resistance.

1. Name: Entecavir

Baraclude

1. Route: Oral

1. Note: Guanosine nucleoside analogue activated by viral polymerase; taken on an empty stomach. [3]

2. Name: Tenofovir disoproxil fumarate

Viread

2. Route: Oral

2. Note: Also used in HIV regimens; carries renal and bone-density warnings. [6]

3. Name: Tenofovir alafenamide

Vemlidy

3. Route: Oral

3. Note: Lower-dose prodrug approved specifically for chronic HBV with compensated liver disease; not recommended in decompensated (Child-Pugh B or C) hepatic impairment. [4] [6]

Mechanism of action

Summary: HCV and HBV are treated by entirely different mechanisms because they replicate differently: HCV is a positive-strand RNA virus that DAAs attack at three distinct non-structural proteins, while HBV is a DNA virus that replicates through an RNA intermediate via reverse transcription, which nucleos(t)ide analogues block by acting as faulty substrates for the viral polymerase.

Target: HCV NS3/4A protease, NS5A protein and NS5B polymerase (DAAs); HBV reverse transcriptase/DNA polymerase (nucleos(t)ide analogues)

Cidal Static: HCV DAAs are effectively curative when SVR is achieved because HCV has no latent reservoir once replication is fully suppressed for the treatment course; HBV analogues are virustatic - they suppress replication of circulating and template DNA but do not eliminate the intranuclear cccDNA reservoir

Kill Kinetics: HCV RNA typically becomes undetectable within the first few weeks of DAA therapy; HBV DNA suppression with entecavir or tenofovir also occurs over weeks to months but is lost on treatment discontinuation

1. Step: 1

1. Title: NS3/4A protease inhibitors block HCV polyprotein processing

1. Detail: HCV translates its genome as a single long polyprotein that the NS3/4A protease must cleave into individual functional proteins; glecaprevir blocks this cleavage. [5]

2. Step: 2

2. Title: NS5A inhibitors disrupt the HCV replication complex

2. Detail: NS5A is a structural component of the membrane-associated replication complex; velpatasvir and pibrentasvir interfere with its role in complex assembly and RNA replication. [5]

3. Step: 3

3. Title: NS5B polymerase inhibitors block new HCV RNA synthesis

3. Detail: Sofosbuvir, once triphosphorylated intracellularly, is incorporated by the NS5B RNA-dependent RNA polymerase and terminates the growing RNA chain, halting production of new viral genomes. [5]

4. Step: 4

4. Title: Entecavir is phosphorylated intracellularly and inhibits HBV polymerase

4. Detail: Entecavir triphosphate competes with the natural substrate for HBV reverse transcriptase/DNA polymerase and, once incorporated, terminates the growing DNA chain, inhibiting priming, reverse transcription of the pregenomic RNA, and second-strand DNA synthesis. [3]

5. Step: 5

5. Title: Tenofovir competitively inhibits HBV reverse transcriptase after activation

5. Detail: Tenofovir, delivered as either the disoproxil or alafenamide prodrug, is converted intracellularly to its active diphosphate form, which competitively inhibits HBV reverse transcriptase and causes DNA chain termination after incorporation. [4]

Spectrum of activity

Intro: HCV DAAs and HBV nucleos(t)ide analogues each cover a specific virus and, within it, a specific range of genotypes or strains rather than a broad range of unrelated pathogens.

1. Subclass: Sofosbuvir/velpatasvir (Epclusa)
 1. Coverage: Pangenotypic: HCV genotypes 1, 2, 3, 4, 5 and 6 in adults and pediatric patients 6 years and older. [1]
2. Subclass: Glecaprevir/pibrentasvir (Mavyret)
 2. Coverage: Pangenotypic: HCV genotypes 1, 2, 3, 4, 5 and 6, without cirrhosis or with compensated (Child-Pugh A) cirrhosis, in patients 3 years and older. [2]
3. Subclass: Entecavir, tenofovir disoproxil fumarate, tenofovir alafenamide
 3. Coverage: Chronic hepatitis B virus infection; entecavir and tenofovir are the preferred agents given their higher barrier to resistance than lamivudine or adefovir. [6]

Major clinical uses

1. Drug: Sofosbuvir/velpatasvir
 1. Organism: Hepatitis C virus, genotypes 1-6
 1. Indication: Chronic HCV infection without cirrhosis or with compensated cirrhosis; with ribavirin in decompensated cirrhosis
 1. Line: pangenotypic first-line option
 1. Note: One tablet (400 mg sofosbuvir/100 mg velpatasvir) once daily, typically for 12 weeks, per label. [1]
 2. Drug: Glecaprevir/pibrentasvir
 2. Organism: Hepatitis C virus, genotypes 1-6
 2. Indication: Acute or chronic HCV infection without cirrhosis or with compensated (Child-Pugh A) cirrhosis
 2. Line: pangenotypic first-line option, including as short as 8 weeks in eligible patients
 2. Note: Not recommended in patients with moderate to severe (Child-Pugh B or C) hepatic impairment. [2]
 3. Drug: Entecavir
 3. Organism: Hepatitis B virus
 3. Indication: Chronic HBV infection in adults and pediatric patients 2 years and older with evidence of active viral replication and either persistent ALT/AST elevation or histologically active disease
 3. Line: preferred first-line HBV suppressive agent
 3. Note: Administered on an empty stomach; higher dose used for decompensated liver disease. [3]
 4. Drug: Tenofovir alafenamide
 4. Organism: Hepatitis B virus
 4. Indication: Chronic HBV infection in adults and pediatric patients 6 years and older weighing at least 25 kg, with compensated liver disease
 4. Line: preferred first-line HBV suppressive agent
 4. Note: Not recommended in decompensated (Child-Pugh B or C) hepatic impairment; patients must be tested for HIV before starting, since it should not be used alone in HIV-infected patients. [4]

Pharmacokinetics

1. Drug: Sofosbuvir/velpatasvir
 1. Route: Oral, with or without food
 1. Absorption: Well absorbed orally

1. Csf Penetration: See prescribing reference
1. Metabolism: Sofosbuvir: intracellular activation to the active triphosphate; velpatasvir: minimal metabolism
1. Elimination: Sofosbuvir metabolite predominantly renal; velpatasvir predominantly biliary/fecal
1. Dose Adjust: Not recommended in severe renal impairment for sofosbuvir-containing products per label caution [1]
2. Drug: Glecaprevir/pibrentasvir
2. Route: Oral, taken with food
2. Absorption: Absorption increased with food; label specifies dosing with a meal
2. Csf Penetration: See prescribing reference
2. Metabolism: Minimal metabolism; both are substrates of hepatic transporters
2. Elimination: Predominantly biliary/fecal, largely as unchanged drug
2. Dose Adjust: Not recommended with moderate to severe (Child-Pugh B or C) hepatic impairment [2]
3. Drug: Entecavir
3. Route: Oral, on an empty stomach
3. Absorption: Reduced absorption with food; label specifies dosing at least 2 hours after and 2 hours before a meal
3. Csf Penetration: See prescribing reference
3. Metabolism: Minimal hepatic metabolism
3. Elimination: Predominantly renal
3. Dose Adjust: Renal impairment is the principal dose-adjustment driver [3]
4. Drug: Tenofovir alafenamide
4. Route: Oral
4. Absorption: Well absorbed orally
4. Csf Penetration: See prescribing reference
4. Metabolism: Intracellular conversion to active tenofovir diphosphate
4. Elimination: Predominantly renal, with lower plasma tenofovir exposure than tenofovir disoproxil fumarate
4. Dose Adjust: Renal function assessed at baseline and periodically; not recommended in decompensated hepatic impairment [4]
1. This page gives no dose regimens by design. Regimen duration for HCV DAAs (8 vs 12 vs 16 weeks) and dosing for HBV analogues depend on genotype, prior treatment, cirrhosis status, renal function and, for HBV, HBeAg status, and belong in a current prescribing reference or AASLD/hcvguidelines.org resource used by the treating clinician.
2. HCV DAAs are notable for comparatively few hepatic or renal dose-adjustment requirements at compensated liver disease stages relative to older interferon-based regimens, one of the practical reasons they largely replaced those regimens. [7]

Adverse effects

1. Effect: Headache and fatigue
1. Detail: Commonly reported with sofosbuvir/velpatasvir and with glecaprevir/pibrentasvir. [1][2]
2. Effect: Headache, nausea and diarrhea with entecavir/tenofovir
2. Detail: Generally well tolerated; these are the most frequently reported adverse effects with entecavir and tenofovir salts. [6]
1. Effect: Hepatitis B virus reactivation during HCV DAA therapy
1. Detail: HBV reactivation, in some cases resulting in fulminant hepatitis, hepatic failure and death, has been reported in HCV/HBV-coinfected patients undergoing or having completed DAA treatment without concurrent HBV-active antiviral therapy.
1. Action: All patients are tested for HBsAg and anti-HBc before starting HCV DAA therapy; HBV/HCV-coinfected patients are monitored for HBV reactivation during and after treatment. [1][2]
2. Effect: Severe acute exacerbation of hepatitis B after stopping anti-HBV therapy
2. Detail: Discontinuing entecavir or a tenofovir salt in a patient with chronic HBV can cause a severe, sometimes fatal,

hepatitis flare.

2. Action: Hepatic function is monitored closely, clinically and by laboratory testing, for at least several months after stopping anti-HBV therapy. [3]

3. Effect: Lactic acidosis and severe hepatomegaly with steatosis

3. Detail: Reported with nucleoside analogues including entecavir, alone or combined with other antiretrovirals, and can be fatal.

3. Action: Treatment is suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity. [3]

4. Effect: Renal impairment with tenofovir-containing products

4. Detail: New onset or worsening renal impairment, including cases requiring monitoring of serum creatinine, creatinine clearance, urine glucose and protein, is described for tenofovir alafenamide.

4. Action: Renal function is assessed before starting and on a clinically appropriate schedule during treatment. [4]

1. Drug: Sofosbuvir/velpatasvir

1. Effect: Amiodarone co-administration has been associated with serious symptomatic bradycardia in patients also taking a sofosbuvir-containing regimen; concomitant use requires caution and monitoring per label. [1]

2. Drug: Glecaprevir/pibrentasvir

2. Effect: Contraindicated with atazanavir or rifampin, and not recommended with moderate to severe hepatic impairment, distinguishing it from sofosbuvir/velpatasvir's broader hepatic-impairment tolerance for compensated disease. [2]

3. Drug: Entecavir

3. Effect: Cross-resistance exists with lamivudine-experienced patients, who require a higher entecavir dose and have reduced response rates compared with nucleoside-naïve patients. [6]

Contraindications, precautions and interactions

1. Glecaprevir/pibrentasvir: coadministration with atazanavir or rifampin. [2]

2. Sofosbuvir/velpatasvir with ribavirin (for decompensated cirrhosis) carries ribavirin's own contraindications, including pregnancy. [1]

1. All patients should be tested for HBsAg and anti-HBc before starting an HCV DAA regimen because of the HBV reactivation risk. [1]

2. Tenofovir alafenamide should not be used alone in patients with untreated HIV infection; HIV testing is done before starting. [4]

3. Entecavir and tenofovir require close hepatic monitoring for several months after discontinuation because of the flare risk. [3]

1. With: Amiodarone

1. Effect: Serious symptomatic bradycardia reported with concomitant sofosbuvir-containing regimens. [1]

2. With: P-glycoprotein and BCRP inducers (e.g. rifampin, St John's wort)

2. Effect: Can substantially reduce sofosbuvir, velpatasvir, glecaprevir or pibrentasvir concentrations, risking treatment failure. [1][2]

3. With: Nephrotoxic drugs

3. Effect: Concurrent use with tenofovir salts increases the risk of renal impairment. [4]

Resistance mechanisms

Intro: HCV resistance-associated substitutions can pre-exist at baseline in some patients or emerge on treatment, while HBV resistance to nucleos(t)ide analogues is primarily a function of drug generation and prior nucleoside exposure.

1. Mechanism: Baseline and treatment-emergent HCV resistance-associated substitutions

1. Detail: Mutations at NS3/4A positions such as V36, Q80, T54, R155 and A156 and the NS5B substitution S282T are

the most clinically relevant resistance-associated variants; some agents (e.g. elbasvir) can face enough pre-existing baseline resistance in certain genotypes to affect regimen choice. [5]

2. Mechanism: Cross-resistance and higher genetic barrier of entecavir/tenofovir for HBV

2. Detail: Entecavir and tenofovir have a relatively high genetic barrier to resistance compared with lamivudine or adefovir monotherapy; however, patients with prior lamivudine resistance mutations need a higher entecavir dose and show reduced response, reflecting some cross-resistance between older and newer nucleoside analogues. [6]

Comparison tables

Title: Cure versus suppression: the defining distinction of this page

Caption: HCV DAAs and HBV nucleos(t)ide analogues are grouped here for teaching convenience, but they achieve fundamentally different treatment endpoints.

1. Key: virus

1. Label: Virus

2. Key: example_regimen

2. Label: Example regimen

3. Key: endpoint

3. Label: Treatment endpoint

4. Key: duration

4. Label: Typical duration

1. Virus: Hepatitis C

1. Example Regimen: Sofosbuvir/velpatasvir or glecaprevir/pibrentasvir

1. Endpoint: Sustained virologic response (SVR) - considered a virologic cure

1. Duration: 8 to 12 weeks, then stop [7]

2. Virus: Hepatitis B

2. Example Regimen: Entecavir or tenofovir (disoproxil fumarate or alafenamide)

2. Endpoint: Ongoing viral suppression - not a cure with currently available oral agents

2. Duration: Typically indefinite; relapse expected if stopped without meeting specific stopping criteria [6]

High-yield exam pearls

1. Pearl: SVR12 (undetectable HCV RNA 12 weeks after finishing therapy) is treated as a cure; there is no equivalent cure endpoint for chronic HBV with currently available oral agents.

1. Why: This is the single most exam-relevant distinction between the two halves of this page and is frequently tested directly. [7][6]

2. Pearl: Both EPCLUSA and MAVYRET are pangenotypic (genotypes 1-6), unlike older genotype-specific HCV regimens.

2. Why: Pangenotypic coverage is why genotype testing is no longer a prerequisite for choosing a regimen the way it once was. [1][2]

3. Pearl: HBV reactivation during HCV DAA therapy is a named boxed-warning-level concern, not a theoretical one.

3. Why: It is specifically why HBsAg and anti-HBc testing precedes every HCV DAA regimen, regardless of which one is chosen. [1][2]

4. Pearl: Entecavir must be taken on an empty stomach, unlike glecaprevir/pibrentasvir, which needs food to be adequately absorbed.

4. Why: These are opposite administration requirements within the same broad hepatitis-antiviral page, a detail exam questions can exploit directly. [3][2]

5. Pearl: Stopping entecavir or tenofovir in a chronic HBV patient can cause a severe hepatitis flare, mirroring the same phenomenon seen when antiretrovirals with anti-HBV activity are stopped in HIV/HBV coinfection.

5. Why: It reinforces that these are the same mechanism (loss of HBV suppression) appearing in two different clinical

contexts covered on two different pages of this site. [3]

Common exam traps

1. Trap: Assuming hepatitis B antivirals cure chronic HBV the way hepatitis C DAAs cure HCV.
 1. Correction: Entecavir and tenofovir suppress HBV replication for as long as they are taken; they do not eliminate the intranuclear cccDNA reservoir, and relapse is the expected outcome of stopping therapy outside specific guideline-defined stopping criteria. [6]
2. Trap: Assuming a patient with HCV/HBV coinfection only needs HCV treatment.
 2. Correction: Treating HCV alone with a DAA in an untreated HBV/HCV-coinfected patient risks HBV reactivation, in some cases fulminant; HBsAg/anti-HBc testing and, if positive, appropriate HBV management are part of standard pre-DAA workup. [1][2]
3. Trap: Treating all HCV DAA regimens as interchangeable regardless of hepatic function.
 3. Correction: Glecaprevir/pibrentasvir is not recommended with moderate to severe hepatic impairment, while sofosbuvir/velpatasvir (with ribavirin) is used specifically in decompensated cirrhosis - hepatic status, not just genotype, drives regimen selection. [2][1]

Self-test questions

1. Question: What does sustained virologic response (SVR) mean for hepatitis C treatment?
 1. A temporary drop in viral load during treatment
 2. Continued absence of detectable HCV RNA 12 or more weeks after completing therapy, considered a virologic cure
 3. A measure of liver fibrosis only
 4. The point at which treatment must be extended
 1. Explanation: SVR12 - undetectable HCV RNA 12 or more weeks after finishing therapy - is treated by AASLD-IDSA guidance as equivalent to virologic cure. [7]
2. Question: Which of the following best describes the treatment endpoint for chronic hepatitis B with entecavir or tenofovir?
 1. Cure, equivalent to HCV DAA therapy
 2. Ongoing viral suppression, not a cure, with relapse expected if therapy is stopped
 3. Complete clearance of cccDNA from hepatocytes
 4. No monitoring required once started
 2. Explanation: Current oral HBV nucleos(t)ide analogues suppress replication but do not eliminate the intranuclear cccDNA reservoir, so withdrawal of therapy usually results in relapse. [6]
3. Question: Why must patients be tested for HBsAg and anti-HBc before starting a hepatitis C DAA regimen?
 1. To determine HCV genotype
 2. Because HBV reactivation, in some cases fulminant, has occurred in coinfecting patients treated with a DAA without concurrent HBV-active therapy
 3. It is not actually required
 4. To rule out hepatitis A
 3. Explanation: Both EPCLUSA and MAVYRET labelling warn of HBV reactivation in HCV/HBV-coinfecting patients not receiving HBV-active antiviral therapy, so HBV status is checked before starting. [1][2]
4. Question: What distinguishes a pangenotypic HCV regimen such as glecaprevir/pibrentasvir?
 1. It only treats genotype 1
 2. It covers HCV genotypes 1 through 6, removing the need for genotype-specific drug selection
 3. It requires interferon co-administration
 4. It is used only for hepatitis B
 4. Explanation: MAVYRET (glecaprevir/pibrentasvir) and EPCLUSA (sofosbuvir/velpatasvir) are both labelled for HCV genotypes 1-6, which is what "pangenotypic" means in this context. [2]

5. Question: Which three HCV non-structural proteins do direct-acting antivirals target?

1. NS1, NS2, NS3
2. NS3/4A protease, NS5A, and NS5B polymerase
3. Core, E1 and E2 envelope proteins
4. Only the RNA genome directly

5. Explanation: The three DAA classes target the NS3/4A protease (polyprotein cleavage), NS5A (replication complex assembly) and NS5B polymerase (RNA synthesis). [5]

6. Question: What is a key administration difference between entecavir and glecaprevir/pibrentasvir?

1. Both must be taken with food
2. Entecavir is taken on an empty stomach, while glecaprevir/pibrentasvir must be taken with food for adequate absorption
3. Both must be taken on an empty stomach
4. Neither has a food requirement

6. Explanation: Entecavir's label specifies dosing at least 2 hours after and before a meal, while MAVYRET's label specifies dosing with food to achieve adequate absorption - opposite requirements. [3][2]

Frequently asked questions

1. Question: Is hepatitis C curable?

1. Answer: Yes, in the large majority of patients. Current direct-acting antiviral regimens such as sofosbuvir/velpatasvir or glecaprevir/pibrentasvir achieve sustained virologic response - undetectable HCV RNA 12 or more weeks after finishing an 8- to 12-week course - in more than 95% of treated patients, and AASLD-IDSA guidance treats this as a virologic cure. [7]

2. Question: Is hepatitis B curable in the same way?

2. Answer: No, not with currently available oral agents. Entecavir and tenofovir suppress HBV replication effectively and for as long as they are taken, but they do not eliminate the virus's intranuclear cccDNA reservoir, so stopping treatment usually leads to relapse. Suppression, not cure, is the realistic treatment goal for most patients with chronic HBV today. [6]

3. Question: Why does starting hepatitis C treatment sometimes require a hepatitis B test first?

3. Answer: Because HBV reactivation - in some cases fulminant, leading to hepatic failure and death - has been reported in patients coinfecting with HCV and HBV who were treated with a direct-acting antiviral for HCV without also receiving HBV-active antiviral therapy. Both EPCLUSA and MAVYRET labelling recommend testing all patients for HBsAg and anti-HBc before starting. [1][2]

4. Question: Why are entecavir and tenofovir preferred over older hepatitis B drugs like lamivudine?

4. Answer: Entecavir and tenofovir have a substantially higher genetic barrier to resistance than lamivudine or adefovir, meaning resistance mutations are far less likely to emerge during long-term therapy. Patients with prior lamivudine resistance do respond less well to entecavir and need a higher dose, reflecting some cross-resistance, but tenofovir generally remains an effective option in that setting. [6]

References

[1] EPCLUSA (sofosbuvir and velpatasvir) - prescribing information. DailyMed, U.S. National Library of Medicine . <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=7f30631a-ee3b-4cfe-866b-964df3f0a44f>

[2] MAVYRET (glecaprevir and pibrentasvir) - prescribing information. DailyMed, U.S. National Library of Medicine . <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=7bf99777-0401-9095-8645-16c6e907fcc0>

[3] BARACLUDE (entecavir) - prescribing information. DailyMed, U.S. National Library of Medicine . <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=046e61c9-9298-4b2e-b76e-b26b81fec20>

[4] VEMLIDY (tenofovir alafenamide) - prescribing information. DailyMed, U.S. National Library of Medicine . <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=72e6b33c-0351-4070-9172-eeaa186c01d2>

[5] Hepatitis C. StatPearls Publishing / NCBI Bookshelf 2026. <https://www.ncbi.nlm.nih.gov/books/NBK430897/>

[6] Hepatitis B. StatPearls Publishing / NCBI Bookshelf 2026. <https://www.ncbi.nlm.nih.gov/books/NBK555945/>

[7] HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C - Overview. AASLD-IDSA HCV Guidance Panel . <https://www.hcvguidelines.org/>

For education only. This guide does not replace professional medical advice. Do not use it to choose or change treatment.