

# Hepatitis B Fact Sheet

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a series of fact sheets written by experts in the field of liver disease

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## What Happens When Drug Resistance Develops?

**W**hen patients infected with the hepatitis B virus (HBV) are treated with antiviral medications for several years, their HBV is able to develop resistance to the treatment. Antivirals are drugs that interfere with the replication process, but HBV mutates easily. Over time certain mutations can “resist” the antiviral, increase rapidly in number, and start causing liver damage again.

Unfortunately, the first antivirals used to treat chronic hepatitis B had high rates of “resistance.” For example, about 70% of patients treated with the antiviral lamivudine (Epivir-HBV) develop resistance to the drug within five years.

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**Lamivudine (Epivir-HBV) should be avoided because of its high resistance rate.**

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Avoiding antiviral resistance is very important because some people will have to take antiviral medications for many years to keep their viral load (HBV DNA) low.

Because of the risk of drug resistance doctors are very careful about what to prescribe when treating hepatitis B. And, if antiviral resistance has developed, they would have to prescribe antivirals that will work against the drug-resistant HBV.

This fact sheet is an overview of the sequence of drugs that should be used to avoid or address drug resistance.

### Which drug to use first?

Of the seven drugs available, experts recommend pegylated interferon (Pegasys), and the antivirals tenofovir (Viread) and entecavir (Baraclude) as the best drugs to treat HBeAg-positive or -negative patients who have never been treated before. Furthermore, these drugs are the most potent, and the two antivirals have been shown to carry very low rates of viral or drug resistance.

### Which antiviral drugs to avoid

Lamivudine (Epivir-HBV) should be avoided because of its high resistance rate. Telbivudine (Tyzeka) has a moderate resistance rate, causing resistance in 25% of HBeAg-positive patients and 11% in HBeAg-negative patients after two years. Adefovir (Hepsera) also poses a moderate risk, causing resis-



**Hepatitis B: Drug Resistance**

tance in 29% of patients after five years.

**Treatment options recommended when viral resistance has developed:<sup>1</sup>**

- If lamivudine resistance occurs: Continue lamivudine and add tenofovir (preferred) or adefovir. Or, switch to a combination of the experimental antiviral emtricitabine and tenofovir.

- If adefovir resistance occurs: Continue adefovir and add lamivudine or telbivudine. Or, switch to or add entecavir if lamivudine has not been used in the past. A third option is switching to emtricitabine plus tenofovir.
- If entecavir resistance occurs: Switch to or add adefovir or tenofovir. Another option is to switch to an emtricitabine/tenofovir combination.

- If telbivudine resistance occurs: Continue telbivudine and add tenofovir (preferred) or adefovir. Another option is to switch to a combination of emtricitabine and tenofovir.

<sup>1</sup>Keeffe E, Dietrich D, Han S, et al. A treatment algorithm for the management of chronic hepatitis B virus infection in the United States: 2008 Update. *Clinical Gastroenterology and Hepatology*. 2008;6:1315-1341.

Drug/Brand name	Type	Year Approved	Resistance
Interferon alfa-2a (Intron A)	Interferon	1991	None
Lamivudine (Epivir-HBV)	Nucleoside reverse transcriptase inhibitor	1998	23% at Year 1; ~70% at year 5
Adefovir (Hepsera)	Nucleoside reverse transcriptase inhibitor	2002	0% at year 1; 29% at year 5
Entecavir (Baraclude)	Nucleoside reverse transcriptase inhibitor	2005	1.2% in treatment naïve at year 5; 46% in lamivudine resistant at year 5
Peginterferon alfa-2a (Pegasys)	Interferon	2005	None
Telbivudine (Tyzeka)	Nucleoside reverse transcriptase inhibitor	2006	25% in HBeAg positive at year 2; 11% in HBeAg negative at year 2
Tenofovir (Viread)	Nucleoside Reverse transcriptase Inhibitor	2006	0% at year 2; adefovir resistant HBV should be treated with tenofovir and another HBV antiviral

The information in this fact sheet is designed to help you understand and manage HBV and is not intended as medical advice. All persons with HBV should consult a medical practitioner for diagnosis and treatment of HBV.

For more information about hepatitis B, visit the following websites.  
**Hepatitis B Foundation: [www.hepb.org](http://www.hepb.org) • [HIVandHepatitis.com](http://HIVandHepatitis.com)**

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