

# NEW DRUG REVIEW

## Tenofovir Disoproxil Fumarate for Chronic Hepatitis B

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The recent US Food and Drug Administration (FDA) approval of tenofovir disoproxil fumarate (Viread, Gilead Sciences) for the treatment of chronic hepatitis B (CHB) adds a potent nucleotide analog to our armamentarium of first-line therapies for hepatitis B. In phase III clinical trials, tenofovir has demonstrated an excellent profile in terms of resistance development (0% at 2 years), safety, and robust suppression of virus (complete suppression achieved at 1 year among e antigen-positive patients and e antigen-negative patients: 76% and 93%, respectively). In these trials, tenofovir was compared to the first-line oral antiviral therapy adefovir (Hepsera, Gilead Sciences) and showed significantly improved efficacy, leading to its approval for the treatment of CHB by the FDA. Along with the nucleoside agent entecavir (Baraclude, Bristol-Myers Squibb), tenofovir should be considered a viable therapeutic option in both e antigen-positive and e antigen-negative patients who are good candidates for therapy.

In treatment-naïve patients, the decision to commence treatment is predicated on a number of patient factors, including levels of hepatitis B viral DNA and alanine aminotransferase, age, disease history, family history of hepatic illness or malignancy, and severity of liver disease. Decisions regarding what agent to administer are based on efficacy, side effects, and physician and patient preference, as well as cost. As an agent previously approved for use in the management of HIV, tenofovir has over 2 million documented patient-years of experi-

ence and has maintained a favorable safety profile. Although all nucleotide agents carry some concern regarding possible renal toxicities, these have yet to be observed in association with tenofovir therapy in CHB. Tenofovir is also generally less expensive than other first-line therapies and may be more convenient to administer, as it does not require dosing on an empty stomach, whereas some nucleoside agents, such as entecavir, do.

In the large cohort of patients with previous exposure and resistance to lamivudine, tenofovir could also impart a considerable cost savings, as it can be dosed in combination with lower-cost lamivudine. Due to issues of cross-resistance, entecavir should not be added to lamivudine and would need to be administered as a monotherapy or paired with a nucleotide such as tenofovir or adefovir, in patients requiring combination therapy. Another option for combination therapy would be the off-label prescription of Truvada (Gilead Sciences), which combines tenofovir with emtricitabine, in a single pill.

For patients co-infected with hepatitis B and HIV, a logical choice is combination tenofovir/emtricitabine. With the understanding that tenofovir is beneficial in both disease states, the days of treating one disease while the other continues to progress are over. We now have the tools available to orchestrate simultaneous treatment and management of both viruses, in order to optimize outcomes for our patients.

### Suggested Reading

Marcellin P, Heathcote EJ, Buti M, Gane E, de Man RA, et al. Tenofovir disoproxil fumarate versus adefovir dipivoxil for chronic hepatitis B. *N Engl J Med*. 2008;359:2488-2491.

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