Enfuvirtide *(Fuzeon)*

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Drug Summary

Enfuvirtide (also known as T-20), is the only FDA-approved HIV fusion inhibitor. Enfuvirtide is a potent antiretroviral agent that must be delivered by twice-daily subcutaneous injections. Use of enfuvirtide frequently results in painful injection site reactions, such as subcutaneous nodules and irritation. Because these reactions limit enfuvirtide tolerability, the use of enfuvirtide is generally limited to salvage therapy for patients with extensive treatment history, multiclass antiretroviral resistance, and few antiretroviral therapy options. The need for enfuvirtide decreased dramatically following the approval of multiple potent antiretroviral agents that have activity in the setting of common HIV resistance-associated mutations.

Key Clinical Trials

Approval of enfuvirtide by the FDA was based on studies in heavily treatment-experienced individuals, in which enfuvirtide was added to an optimized background regimen. Most notably, two randomized, open-label, phase III studies enrolled persons with HIV RNA levels above 5,000 copies/mL and prior treatment with (or documented resistance to) each of the NRTI, NNRTI, and PI antiretroviral classes [TORO 1 and TORO-2]. Participants in these trials received enfuvirtide plus an optimized background regimen or the background regimen alone. In an analysis of the combined data, the groups that received enfuvirtide had higher rates of HIV RNA below 400 copies/mL at 48 weeks and greater increases in CD4 cell count. Several trials have examined switching from enfuvirtide to raltegravir for patients who had not previously been treated with integrase inhibitors. In both a randomized trial and a single-arm study of patients with multiclass resistance but suppressed HIV RNA on an enfuvirtide-containing regimen, substitution of raltegravir for enfuvirtide resulted in high rates of continued viral suppression [EASIER and CHEER].

Adverse Effects

Enfuvirtide causes reactions at the sites of injection in up to 98% of individuals using the drug. These reactions often include development of bothersome subcutaneous nodules and may include redness, pain, tenderness, swelling, itching, or hardening of the skin. A needle-free gas-powered injection device (Biojector 2000) was used in the past as an alternative for administering enfuvirtide; persons using it had fewer local reactions, but can get more serious adverse effects, such as long-lasting nerve pain and hematomas. Less commonly, enfuvirtide may cause a generalized hypersensitivity reaction, eosinophilia, or nausea.

Use In Pregnancy

In the HHS Perinatal Guidelines section Recommendations for Use of Antiretroviral Drugs During Pregnancy (last updated October 19, 2017), **enfuvirtide** is in the category Not Recommended for Initial ART in Pregnancy.

- For additional information regarding the safety and toxicity of enfuvirtide in pregnancy see the HHS Perinatal Guidelines summary on Enfuvirtide.

Key Drug Interactions

For complete information on enfuvirtide-related drug interactions, see the Drug Interactions section in the Enfuvirtide (*Fuzeon*) Prescribing Information.