Enfuvirtide (Fuzeon®, T-20)

Class:
Enfuvirtide is a fusion inhibitor.

Antiviral Activity:
Enfuvirtide has activity against HIV-1 but not HIV-2.

Mechanism of Action:
Enfuvirtide binds to a region of the gp41 subunit of the HIV-1 envelope glycoprotein (first heptad repeat domain – HR1), that mediates a conformational change required for viral and host-cell membrane fusion. This conformational change is essential to bring the viral and cellular membranes into close enough proximity for fusion and subsequent viral entry into the host-cell. Enfuvirtide prevents this step and thus also the infection of the cell by HIV-1.

Mechanism of Resistance:
Resistance to enfuvirtide appears to develop through substitutions in viral DNA that lead to changes in the enfuvirtide HR1 domain of gp41.

Pharmacokinetics:
The absolute bioavailability is 84.3% ± 15.5%. It is 92% bound to plasma proteins, primarily albumin with a lower extent of binding to alpha-1 acid glycoprotein. Enfuvirtide catabolism is believed to be via amino acid breakdown and recycling. In vitro experiments indicate that enfuvirtide is hydrolyzed to a deamidated metabolite (M3).

Adverse Effects:
The most common adverse reaction is injection site reaction, which can include erythema, induration, nodules and cysts, edema and hemorrhage. Peripheral neuropathy, decreased appetite and eosinophilia are other adverse effects. Hypersensitivity reactions (rash, fever, nausea and vomiting, chills, rigors, hypotension, and elevated serum liver transaminases) as well as other immune mediated reactions (primary immune complex reaction, respiratory distress, glomerulonephritis, and Guillain-Barre syndrome) have been seen. In phase III clinical trials an increased rate of bacterial pneumonia was observed in the enfuvirtide group as compared to the control group.

Dosage:
90mg powder for infection

Adult dose: 90mg subcutaneously twice a day
Children 4-16 years old: 2 mg/kg subcutaneously twice a day (maximum dose of 90mg)

Disease state based dosing:
There are no specific guidelines for dosage adjustment in renal or hepatic failure.

Contraindications/Warnings/Precautions:
Systemic hypersensitivity reactions (<1%) include combinations of rash, fever, nausea and vomiting, chills, rigors hypotension, and/or elevated serum liver transaminase. These reactions may recur on re-challenge, so enfuvirtide should not be restarted following a hypersensitivity reaction.

Enfuvirtide must be injected subcutaneously. It should not be administered intramuscularly nor intravenously. Complications can be minimized by varying the injection sites (abdomen, upper thighs, upper arms). An overview of the injection technique can be found on: http://www.fuzeon.com/pdfs/pii.pdf

Drug Interactions:
There are no documented drug interactions with enfuvirtide.

Pregnancy:
Category B: No evidence of risk in humans but studies inadequate.

Monitoring Requirements:
An increased rate of bacterial pneumonia was observed in the Phase 3 clinical trials although its association with enfuvirtide remains unclear. Thus, patients should be carefully monitored for signs and symptoms for pneumonia.

Brand names/Manufacturer:
Fuzeon®
Hoffmann La Roche Inc