Selected Properties of Enfuvirtide

Other names	Fuzeon®, T20
Manufacturer	Hoffmann- La Roche Limited
Pharmacology/Mechanism of Action	Enfuvirtide is an inhibitor of HIV-1 gp41 mediated fusion. Enfuvirtide binds to the first heptad-repeat (HR1) in the gp41 subunit of the viral envelope glycoprotein and prevents the conformational changes required for the fusion of viral and cellular membranes, and thus interferes with the entry of HIV-1 into cells.
Activity	The IC50 (50% inhibitory concentration) for enfuvirtide in laboratory and primary isolates representing HIV-1 clades A to G ranges from 4 to 280 nM (18 to 1260 ng/mL).
Resistance - genotypic	Mutations in the gp41 envelope gene associated with resistance (IAS-USA Fall 2005 Resistance Mutations): G36D/S, I37V, V38A/M/E, Q39R, Q40H, N42T, N43D
Resistance - phenotypic	In site-directed mutagenesis experiments, isolates with a single mutation display one- to 21-fold reductions in susceptibility, whereas isolates with two mutations display 15- to 500-fold reductions in susceptibility.
Cross-Resistance	No cross-resistance with other antiretroviral drug classes.
Oral Bioavailability	Not orally absorbed. SC: 84.3% compared to IV
Effect of Food	Not applicable
Protein Binding	92% bound to plasma proteins in HIV infected plasma over a concentration range of 2 to 10 µg/mL. It is bound predominantly to albumin and to a lower extent to alpha-1 acid glycoprotein.
Vd	5.5 ± 1.1 L
Tmax	Not available
serum T ½	3.8 hours
Drug Concentrations	Plasma Ctrough(ss): 2.6 to 3.4 µg/mL Single dose kinetics, mean (±SD): Cmax 4.59 ±1.5 µg/mL, AUC 55.8 ± 12.1 µg•h/mL
Minimum target trough concentrations (for wildtype virus)	The IC50 for baseline clinical isolates ranged from 0.089 to 107 nM (0.4 to 480 ng/mL) by the cMAGI assay (n=130).
CSF (% of serum)	N/a 2010 CNS Penetration Effectiveness (CPE) Score: 1 [Letendre S et al. 2010]
Metabolism	Catabolism to constituent amino acids.
Excretion	N/a
Dosing – Adult	90 mg (1 mL) subcutaneously (SC) BID. Inject into upper arm, anterior thigh or abdomen. Case report of a 70 year old HIV-infected male who received enfuvirtide 180 mg daily via continuous IV administration

	because of inability to continue with SC injections due to severe injection site reactions. Therapeutic enfuvirtide plasma concentrations (3519 ng/mL) were achieved, which were approximately 4 times higher than Ctrough concentrations achieved with SC administration (755 ng/mL).[Neijzen et al. 2013]
Dosing – Pediatric	Neonatal/Infant: not approved for < 6 years old. Pediatric (6-16 y.o.): 2mg/kg SC BID to a maximum of 90 mg (1 mL) BID. Inject into upper arm, anterior thigh or abdomen. Monitor weight closely and adjust dose accordingly.
Special instructions	Educate patients regarding sterile technique. It may take up to 45 minutes for the powder to solubilize. The reconstituted solution is stable for 24 hours in the fridge. It should be brought to room temperature prior to usage. Unused portions should be discarded. Ensure there are no bubbles or particulate matter prior to injection. Injection sites should be rotated. Avoid injecting into moles, scar tissue, bruises, the navel, sites with little SC fat, or sites of existing or previous reactions. Massage area after injection to reduce pain. Wear loose clothing around site of injection. A warm compress of analgesics may be required. Monitor carefully for local infection or cellulitis.
Adjust in Liver Dysfunction	No dosage recommendation available.
Adjust in Renal Failure/Dialysis	No dosage adjustment necessary in impaired renal function or hemodialysis.
Toxicity	Diarrhea, nausea, fatigue, eosinophilia Local injection site reactions (98%): pain, erythema, induration, cysts and nodules, pruritis, ecchymosis Increased rate of bacterial pneumonia (5.6% vs. 0.3% without enfuvirtide) Hypersensitiviy reaction (<1%): rash, fever, nausea & vomiting, chills, rigors, hypotension, and increased LFTs; may recur on re-challenge. D/C drug and seek immediate medical attention. Avoid re-challenge if possible. One report of successful desensitization protocol in a monitored ICU setting (Desimone et al. 2004). Immune-mediated reactions: primary immune complex reaction, respiratory distress, glomerulonephritis, Guillain-Barre syndrome have been reported.
Pregnancy & Lactation	Pregnancy risk category B. No human studies in pregnancy, therefore not recommended.
Drug Interactions	Unlikely to have significant drug interactions with concomitantly administered CYP450 substrates. No significant interactions identified with other antiretroviral agents.
Baseline Assessment	CBC/diff , LFTs, CK, electrolytes, glucose, fasting cholesterol profile.
Routine Labs	CBC/diff monthly, CK/LFTs, electrolytes, glucose q3 months.
Dosage Forms	Single-use vial: enfuvirtide 108 mg. Reconstitute with 1.1 mL of Sterile Water for infection. Final concentration 90 mg/mL. DIN

	02247725 One-month convenience kit includes: 60 single use efuvirtide vials, 60 vials of diluent (sterile water for injection), 60 reconstitution syringes, 60 administration syringes (1 mL), and alcohol wipes.
Storage	Store powder for solution at room temperature. The reconstituted solution is stable for 24 hours in the fridge.

References:

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