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Enfuvirtide
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Enfuvirtide (Fuzeon™[1], T-20, DP178) is a fusion inhibitor which was approved in the US in March 2003 for treatment of HIV infections in antiretroviral-experienced patients with evidence of active HIV replication despite ongoing antiretroviral therapy. It has thus joined the anti-HIV armamentarium consisting of the nucleoside reverse transcriptase (RT) inhibitors zidovudine, didanosine, zalcitabine, stavudine, lamivudine, abacavir and emtricitabine, the nucleotide RT inhibitor tenofovir, the non-nucleoside RT inhibitors nevirapine, delavirdine and efavirenz, and the protease inhibitors saquinavir, ritonavir, indinavir, nelfinavir, amprenavir, lopinavir and atazanavir.

Enfuvirtide is the first anti-HIV agent to be licensed that acts at a viral entry step. It is also the first anti-HIV drug that requires parenteral administration (for adults, 90mg [in 1mL] twice daily subcutaneously). In phase III clinical trials, enfuvirtide, when added to optimised background antiretroviral therapy, produced a significant reduction in viral load and a significant increase in CD4+ cell counts. Enfuvirtide should be recommended for salvage therapy in antiretroviral-experienced patients not responding to their existing drug regimens.

There are some limitations inherent to the therapeutic use of polypeptides like enfuvirtide (which is 36 amino acids long), such as production costs, lack of oral bioavailability and potential for immunogenicity. However, immunogenicity may be less of a problem in patients with advanced immunodeficiency, who are most likely to need salvage therapy. The necessity of repeated subcutaneous injections inevitably leads to local injection-site reactions (pain, erythema, induration and the presence of nodules or cysts). The delivery problems may perhaps be circumvented by the design of long-acting drug forms, as has been achieved with the pegylated interferons. Finally, there is the possibility of pre-existing viral drug resistance or potential for development of such resistance and this should be carefully assessed, both phenotypically and genotypically, in future clinical studies.

While these different issues, particularly production costs and delivery problems, are likely to limit the clinical use of enfuvirtide to specific indications, they should not detract from the fact that as the first viral entry inhibitor to be licensed for clinical use, enfuvirtide offers a new dimension to the therapy of HIV infections. ▲

1 Use of a tradenames is for product identification purposes only and does not imply endorsement.