antiretroviral regimen. Evaluation must continue, including monitoring for adverse effects and the emergence of viral resistance.

©Review prepared and translated by the Prescrire Editorial Staff (no conflicts of interest)

Literature search

Our literature search was based on continuous prospective scrutiny of contents listings of the main international journals, Current Contents-Clinical Medicine, and member bulletins of the International Society of Drug Bulletins (ISDB) at the Prescrire library; routine consultation of Martindale The Complete Drug Reference; and routine consultation of the websites of the European Medicines Agency (EMEA) and the Food and Drug Administration (FDA) up to 25 January 2008.
We also examined the following databases: Embase/Excerpta Medica Drugs and Pharmacology (1991-4th quarter 2007), Medline (1966-January week 1, 2008), Reactions (1983-October 2007), The Cochrane Library (CDSR, DARE, Central, HTA, Nhseed; 2007 issue 4), and the following websites: Cadth, CVZ, DERP, Inami, Iqwig, NICE, Scottish Consortium and SIGN, up to 15 January 2008.

In response to our request for information, Merck Sharpe and Dohme-Chibret sent us some basic administrative documents, published documents, and packaging items.

1- U.S. Office of AIDS Research Advisory Council "Guidelines for the use of antiretroviral agents in HIV-1 infected adults and adolescents" October 2006: 116 pages.
2- Prescrire Editorial Staff "Enfuvirtide" *Prescrire Int* 2005; **14** (76): 60.
3- Prescrire Rédaction "tipranavir-Aptivus°. Un inhibiteur de la protéase du HIV en dernier recours" *Rev Prescrire* 2006; **26** (275): 573.
4- Prescrire Rédaction "darunavir-Prezista°. Après échecs multiples des antirétroviraux: une option de plus" *Rev Prescrire* 2007; **27** (289): 812-813.
5- Grinsztejn B et al. "Safety and efficacy of the HIV-1 integrase inhibitor raltegravir (MK-0518) in treatment-experienced patients with multidrug-resistant virus: a phase II randomised controlled trial" *Lancet* 2007; **369**: 1261-1269.
6- Highleyman L and Carter M "CROI: integrase inhibitor raltegravir (MK-0518) doubles HIV suppression in treatment-experienced patients at 16 weeks". www.aidsmap.com accessed 26 April 2007: 3 pages.
7- Merck "Isentress (raltegravir) 400 mg for treatment of HIV (NDA 22-145). Briefing document (background package)" 6 August 2007: 160 pages.
8- Markowitz M et al. "Rapid and durable antiretroviral effect of the HIV-1 integrase inhibitor raltegravir as part of combination therapy in treatment-naive patients with HIV-1 infection" *J Acquir Immun Defic Syndr* 2007; **46** (2): 125-133.
9- "Lipid levels were not increased in patients taking MK-0518 an investigational HIV integrase inhibitor, in combination therapy after 24 weeks of therapy". www.merck.com accessed 26 April 2007: 2 pages.
10- "L'inhibiteur d'intégrase MK-0518 en essai de phase III" *Moniteur Hospitalier* 2006; (186): 6.
11- European Commission "Résumé des caractéristiques-Isentress" 20 December 2007: 13 pages.
12- Prescrire Editorial Staff "Maraviroc" *Prescrire Int* 2008; **17** (95): 98-101.

Assessment elsewhere

Raltegravir is marketed in several countries. Evidence has been assessed by drug bulletins independent of the pharmaceutical industry. Below are selected excerpts from their conclusions (our translations when necessary).

The Medical Letter (United States): "*Raltegravir (Isentress), the first integrase strand transfer inhibitor, taken with other active antiretroviral drugs is effective in patients infected with treatment-refractory HIV-1 infection*" (1).

Australian Prescriber (Australia): "(…) *raltegravir has a significant effect on the markers of HIV infection. Whether this improves the patient's prognosis remains to be seen. Longer-term follow-up is also needed to assess the development of viral resistance and long-term adverse events such as cancer*" (2).

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1- "Two New Drugs for HIV Infection" *Med Lett Drugs Ther* 2008; **50** (1277): 2-4.
2- "Newly marketed drugs-Raltegravir" *Australian Prescriber* 2008. www.australianprescriber.com accessed 5 February 2008: 2 pages.

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adalimumab

New Indication

Severe Crohn's disease: a second TNF alpha antagonist, subcutaneous administration

see also page 145

● **No direct comparison with intravenous infliximab.**

Adalimumab (Humira°, Abbott) is the second TNF alpha antagonist immunosuppressant, after infliximab, to be marketed for the treatment of adults with severe Crohn's disease (1,2).

Clinical evaluation is mainly based on a randomised, double-blind, placebo-controlled trial in 499 patients who "responded" to 2 injections of adalimumab (2,3). After one year of treatment, 36% of patients who received adalimumab were still in remission, versus 12% of patients on placebo (p<0.001). Data concerning complications of Crohn's disease (e.g. fistulae) are not very convincing (2).

Adalimumab has the adverse effects common to all TNF alpha antagonists, notably serious infections, lymphoma and worsening heart failure. Adalimumab has a different mode of administration: it is injected subcutaneously while infliximab is administered by intravenous infusion, in hospital (1,2).

In conclusion, the only (minor) advantage of adalimumab is its convenience of use, but only in patients with non-fistulated forms of Crohn's disease.

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Selected references from Prescrire's literature search.

In response to our request for information, Abbott only provided us with published documents.

1- Prescrire Editorial Staff "Infliximab in long-term use in Crohn's disease" *Prescrire Int* 2004; **13** (76): 205.
2- European Medicines Agency - CHMP "European Public Assessment Report (EPAR) (rev. 9) - Humira. Scientific discussion H-C-481-482-II-33" 26 April 2007: 20 pages.
3- Colombel JF et al. "Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: the CHARM trial" *Gastroenterology* 2007; **132** (1): 52-65.

adalimumab
(Humira°)

Solution for SC injection

• **40 mg** of adalimumab per prefilled syringe

■ **New indication:** *"(…) severe, active Crohn's disease, in patients who have not responded despite a full and adequate course of therapy with a corticosteroid and/or an immunosuppressant; or who are intolerant to or have medical contraindications for such therapies".*
[EU marketing authorisation, centralised procedure]

immunosuppressant;
TNF alpha antagonist