

Drugs recently approved or pending approval

AGENERASE

The United States Food and Drug Administration approved marketing of Agenerase (amprenavir) by GlaxoWellcome (Research Triangle Park, NC). Agenerase is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection. Drug effectiveness was measured in an ongoing, double-blind, placebo-controlled study. Therapy-naive adults ($n = 232$) with median CD4 cell counts of 416 cells/mm³ and median plasma HIV-1 RNA levels of 4.67 log₁₀ copies/mL were randomized to receive Agenerase (1200 mg twice daily) plus lamivudine (150 mg twice daily) plus zidovudine (300 mg twice daily) or lamivudine (150 mg twice daily) plus zidovudine (300 mg twice daily). After 24 weeks of therapy, differences in the mean CD4 cell count between the two treatment arms were not significant. However, the proportion of patients reaching HIV-1 RNA plasma levels less than 400 copies/mL was 53% in the Agenerase/lamivudine/zidovudine arm compared with 11% in the lamivudine/zidovudine arm. Agenerase should not be coadministered with the following drugs: astemizole, bepridil, cisapride, dihydroergotamine, ergotamine, midazolam, and triazolam. Potential adverse events associated with Agenerase include nausea, diarrhea, oral/perioral paresthesia, and rash. The recommended adult dose is 1200 mg (eight 150-mg tablets) twice daily in combination with other antiretroviral agents. The recommended pediatric dose depends on individual patient weight and means of administration.



DEPOCYT

Chiron (Emeryville, CA) received approval to market DepoCyt (cytarabine liposome injection). DepoCyt is indicated for the intrathecal treatment of lymphomatous meningitis. Drug efficacy was evaluated in a randomized multi-center study. Patients with neoplastic meningitis caused by lymphoma ($n = 33$) were randomized to DepoCyt (50 mg administered every 2 weeks) or standard unencapsulated cytarabine (50 mg twice/week) for 4 weeks. The study's endpoint was an absence of neurologic progression during the treatment period and an increase in complete response, defined as conversion confirmed by a blinded central pathologist from a positive examination of cerebrospinal fluid for malignant cells to a negative examination on two separate occasions (at least 3 days apart, on day 29 and later) at all initially positive sites. A

complete response was reached in 7 of 17 (41%) patients in the DepoCyt arm compared with 1 of 16 (6%) in the standard unencapsulated cytarabine arm. DepoCyt is contraindicated in patients with active meningeal infection. Adverse reactions associated with DepoCyt may include arachnoiditis, headache, asthenia, and confusion. Recommended dosing regimen for DepoCyt is 50 mg administered intrathecally every 14 days for five doses (weeks one, three, five, seven, nine), then every 28 days for five doses (weeks 13, 17, 21, 25, 29). Dexamethasone (4 mg twice daily) should be administered for 5 days beginning on the day of DepoCyt injection.

XENICAL

The Food and Drug Administration granted approval to Roche Pharmaceuticals (Nutley, NJ) to market Xenical (orlistat). Xenical is indicated for obesity management, including weight loss and weight maintenance, when used in conjunction with a reduced-calorie diet in obese patients with an initial body mass index equal to or greater than 30 kg/m² or equal to or greater than 27 kg/m² in the presence of other risk factors (eg, hypertension, diabetes, dyslipidemia). Xenical is also indicated to

reduce the risk of weight regain. Drug efficacy was measured in seven multicenter, double-blind, placebo-controlled studies of 1 to 2 years' duration. Obese patients were randomized to Xenical (120 mg three times/day) plus reduced-calorie diet or placebo plus reduced-calorie diet. Data combined from five studies demonstrated that the overall mean weight loss after 1 year of treatment was 13.4 lb. in the Xenical arms and 5.8 lb. in the placebo arms. Data combined from four studies demonstrated that after 2 years of treatment, 40% of patients in the Xenical arms had lost 5% or more body weight compared with 24% of patients in the placebo arms. Xenical is contraindicated in patients with chronic malabsorption syndrome or cholestasis. Commonly observed adverse reactions associated with Xenical include gastrointestinal events such as oily spotting, flatus with discharge, fecal urgency, and fatty/oily stool. The recommended dose of Xenical is one 120-mg capsule three times/day with each meal that contains fat.

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