Emerging Drug List
ALEMTUZUMAB

CANADIAN COORDINATING OFFICE FOR HEALTH TECHNOLOGY ASSESSMENT

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Generic (Trade Name)**:** Alemtuzumab (Campath-1)

Manufacturer: Berlex

Indication: In the U.S. alemtuzumab is indicated for the treatment of B-cell chronic lymphocytic leukemia
(B-CLL) patients who have been treated with alkylating agents and who have failed fludarabine therapy.

Current Regulatory Status: In Canada, alemtuzumab is currently under review by Health Canada and the company is expecting approval in 2002. It is currently available in the U.S. and was approved by the FDA in May, 2001.

Description: Alemtuzumab is a recombinant (DNA-derived) humanized monoclonal antibody. It is directed against the 21-28 kD cell surface glycoprotein CD52. CD52 is a nonmodulating antigen that is found on the surface of essentially all B- and T-lymphocytes, most monocytes, macrophages, and natural killer (NK) cells and some granulocytes. Alemtuzumab is believed to cause lysis of leukemic cells following cell surface binding via an antibody dependent reaction. A portion of bone marrow cells (including some $CD34^+$ cells) express CD52 antigens.

The initial dose of alemtuzumab is 3 mg as a two hour intravenous infusion. The dose is increased to 10 mg and then 30 mg, as tolerated. The maintenance dose is 30 mg/day, given three times per week for up to 12 weeks.

Current Existing Treatments: Chronic lymphocytic leukemia (CLL) is the most common form of leukemia in the Western hemisphere, affecting approximately six people out of 100,000. The disease is characterized by the clonal proliferation and accumulation of neoplastic B-lymphocytes (incidence 95%) or T-lymphocytes (incidence 5%). Hence B-CLL is the predominant form of CLL. There are various chemotherapeutic regimens available for the treatment of B-CLL. These include chlorambucil, chlorambucil/prednisone, fludarabine, cladribine, cyclophosphamide/vincristine/ prednisone (COP), cyclophosphamide/doxorubicin/ vincristine/prednisone (CHOP), and myeloablative therapy with stem cell support.

Cost: A cost for alemtuzumab is not available at this time.

Evidence: The U.S. approval of alemtuzumab was based on three multicentre, open-label, noncomparative trials in a total of 149 patients. Patients had failed to respond to prior treatment with fludarabine and had been treated with an alkylating agent. Patients were started on a low dose of alemtuzumab and then escalated to the maintenance dose of 30 mg per day for three days per week for a duration of 4 to 12 weeks. A partial response rate was observed in 31% (29 of 93 patients) in Study 1, 21% (7 of 32 patients) in Study 2,

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and 29% (7 of 24 patients) in Study 3. A complete response was seen in only 2% (2 of 93 patients) in Study 1. The mean duration of response (in months) was seven months in Studies 1 and 2 and 11 months in Study 3. Progression-free survival was four months in Study 1, five months in Study 2, and seven months in Study 3.

Adverse Effects: Adverse effects observed in patients treated with B-CLL include rigors (86%), fever (85%), neutropenia (85%), anemia (80%), thrombocytopenia (72%), nausea (54%), vomiting (41%), rash (40%), fatigue (34%), hypotension (32%), urticaria (30%), dyspnea (26%), cough (25%), headache (24%), pain (24%), pruritus (24%), diarrhea (22%), bronchitis (21%), anorexia (20%), sweating (19%), pneumonia (16%), dysesthesias (15%), sepsis (15%), stomatitis (14%), edema (13%), asthenia (13%), pharyngitis (12%), dizziness (12%), abdominal pain (11%), tachycardia (11%), hypertension (11%), myalgias (11%), herpes simplex (11%), insomnia (10%), dyspepsia (10%), chest pain (10%), constipation (9%), back and malaise (9%), bronchospasm (9%), purpura (8%), moniliasis (8%), depression (7%), tremor (7%), epistaxis (7%), rhinitis (7%), other infections (7%), somnolence (5%), and pancytopenia (5%).

Infusion related reactions can be minimized by premedicating with diphenhydramine 50 mg and acetaminophen 650 mg, administered 30 minutes before alemtuzumab infusion. Anti-infective prophylaxis with trimethoprim/sulfamethoxazole DS twice daily for three days per week and famciclovir 250 mg twice daily is recommended during, and for two months after treatment, with alemtuzumab.

Conclusion: First line agents for the treatment of B-CLL are relatively effective and inexpensive. Alemtuzumab may offer some advantage in cases where patients have failed prior treatment with fludarabine and have been treated with alkylating agents. Alemtuzumab's toxicities and potentially significant cost will most likely limit its use in clinical practice. Clearly more research is needed to better determine its place in therapy.

References:

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