



JANUARY

2004

FORMULARY ADDITIONS

**Aprepitant (*EMEND*[®])
80 mg and 125 mg capsules**

Aprepitant is a selective high-affinity antagonist of human substance P/neurokinin 1 (NK₁) receptors. Aprepitant has little or no affinity for serotonin (5-HT₃), dopamine, and corticosteroid receptors, the targets of existing therapies for chemotherapy-induced nausea and vomiting (CINV). Aprepitant, in combination with other antiemetic agents, is indicated for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy, including high-dose cisplatin (see Table for a list of chemotherapy regimens).

Aprepitant is a moderate CYP3A4 inhibitor and should not be used concurrently with pimozide, terfenadine, astemizole, or cisapride. Inhibition of cytochrome P450 isoenzyme 3A4 (CYP3A4) by aprepitant could result in elevated plasma concentrations of these drugs, potentially causing serious or life-threatening reactions. Aprepitant is contraindicated in patients who are hypersensitive to any component of the product. Aprepitant should be used with caution in patients receiving concomitant medicinal products, including chemotherapy agents that are primarily metabolized through CYP3A4.

No dosage adjustment for aprepitant is necessary in elderly patients, in patients with mild to moderate hepatic insufficiency, and no dosage adjustment is necessary for patients with renal insufficiency or for patients with ESRD undergoing hemodialysis. There are no clinical or pharmacokinetic data in patients with severe hepatic insufficiency, and the pharmacokinetics of aprepitant have not been evaluated in patients below 18 years of age.

Chronic continuous use of aprepitant for prevention of nausea and vomiting is not recommended because it has not been studied and because the drug interaction profile may change during chronic continuous use.

Coadministration of aprepitant with warfarin may result in a clinically significant decrease in International Normalized Ratio (INR) of prothrombin time. The efficacy of oral contraceptives during administration of aprepitant may be reduced.

DRUG AND FOOD INTERACTIONS

The manufacturer's prescribing information lists no food/drug interactions.

DOSAGE AND ADMINISTRATION

Aprepitant is given for 3 days as part of a regimen that includes a corticosteroid and a 5-HT₃ antagonist. The recommended dose of aprepitant is 125 mg orally 1 hour prior to chemotherapy treatment (Day 1) and 80 mg once daily in the morning on Days 2 and 3. Aprepitant has not been studied for the treatment of established nausea and vomiting.

Table: Chemotherapy Regimens and Utilization of Aprepitant

Acute Emetic Category *	Chemotherapy Agents	Approved Use of Aprepitant
High Risk: cisplatin	Cisplatin	In combination with other anti-emetic agents for the prevention of acute and delayed nausea and vomiting in patients receiving initial and repeat courses of chemotherapy
High Risk: noncisplatin	Actinomycin-D Carboplatin Carmustine Cyclophosphamide Cytarabine Dacarbazine Daunorubicin Doxorubicin Epirubicin Hexamethylmelamine Idarubicin Ifosfamide Interleukin-2 (high dose) Lomustine Mechlorethamine Streptozocin	In combination with other anti-emetic agents for the prevention of acute and delayed nausea and vomiting in patients receiving initial and repeat courses of chemotherapy
Intermediate Risk	Docetaxel Etoposide Gemcitabine Irinotecan Mitomycin Mitoxantrone Oxaliplatin Paclitaxel Teniposide Topotecan	In combination with other anti-emetic agents for the prevention of acute and delayed nausea and vomiting in patients who have previously failed other anti-emetic therapy upon receiving the same chemotherapeutic regimen
Low Risk	1-Asparaginase 2-Chlorodeoxyadenosine 6-Mecaptopurine 6-Thioguanine Bleomycin Busulfan Chlorambucil Fludarabine Fluorouracil Hydroxyurea L-Asparaginase Melphalan Methotrexate Tamoxifen Vinblastine Vincristine Vindesine Vinorelbine	Anti-emetic use not recommended

*For combination chemotherapy the patient should be administered the anti-emetics appropriate for the chemotherapeutic agent of greatest emetic risk.

Gemtuzumab ozogamicin Powder for Injection (Mylotarg®) Single-use 20 mL vial = 5 mg gemtuzumab ozogamicin

Gemtuzumab ozogamicin is a chemotherapeutic agent composed of a recombinant humanized IgG₄ kappa antibody attached to a cytotoxic antitumor antibiotic, calicheamicin. The antibody portion of gemtuzumab ozogamicin binds to the CD33 antigen expressed by hematopoietic cells. This antigen is expressed on the surface of leukemic blasts in more than 80% of patients with acute myeloid leukemia (AML). Binding of the anti-CD33 antibody portion of gemtuzumab ozogamicin with the CD33 antigen results in the formation of a complex that is internalized, which released inside the lysosomes of myeloid cells, binds to DNA in the minor groove resulting in DNA double strand breaks and cell death.

Gemtuzumab ozogamicin is indicated for the treatment of patients with CD33 positive acute myeloid leukemia in first relapse who are ≥ 60 years of age and who are not considered candidates for cytotoxic chemotherapy.

Gemtuzumab ozogamicin is contraindicated in patients with a known hypersensitivity to gemtuzumab ozogamicin or any of its components: anti-CD33 antibody (hP67.6), calicheamicin derivatives, or inactive ingredients.

DRUG AND FOOD INTERACTIONS

The manufacturer's prescribing information lists no food/drug interactions.

DOSAGE AND ADMINISTRATION

The recommended dose of gemtuzumab ozogamicin is 9 mg/m², administered as a 2-hour intravenous infusion. Physicians should consider leukoreduction with hydroxyurea or leukapheresis to reduce the peripheral white blood count to below 30,000/ μ L prior to administration of gemtuzumab ozogamicin. Appropriate measures should be taken to prevent hyperuricemia. Patients should receive the following prophylactic medications 1 hour before gemtuzumab ozogamicin administration: diphenhydramine 50 mg by mouth and acetaminophen 650-1000 mg by mouth; thereafter, 2 additional doses of acetaminophen 650-1000 mg by mouth, 1 every 4 hours as needed. Vital signs should be monitored during infusion and for 4 hours following infusion. The recommended treatment course of gemtuzumab ozogamicin is a total of 2 doses with 14 days apart.

Preparation for administration: All preparation should take place in a biologic safety hood with the fluorescent light off. Prior to reconstitution, drug vials should be allowed to come to room temperature. Reconstitute the contents of each vial with 5 mL Sterile Water for Injection, USP, using sterile syringes. Gently swirl each vial. Each vial should be inspected for complete solution and for particulate. The final concentration of drug in the vial is 1 mg/mL. Withdraw the desired volume from each vial and inject into a 100 mL IV bag of 0.9% Sodium Chloride Injection. Place the 100-mL IV bag into an UV protectant bag. The resulting drug solution in the IV bag should be used immediately.

Administration: Once the reconstituted gemtuzumab ozogamicin is diluted into the IV bag containing normal saline, the resulting solution should be infused over a 2-hour period. A separate IV line equipped with a low protein-binding 1.2-micron terminal filter must be used for administration of the drug. Gemtuzumab ozogamicin may be given peripherally or through a central line. **DO NOT ADMINISTER AS AN INTRAVENOUS PUSH OR BOLUS.**

Formulary Additions and Deletions (January 1, 2003 - Present)					
Generic Name	Trade Name	Therapeutic Class	Action	Date	Comments
Aprepitant	EMEND	Antiemetic	Added	11/22/03	See Utilization guidelines
Aripiprazole	Abilify	Antipsychotic	Added	3/25/03	Restricted to psychiatry
Aspirin/Dipyridamole	Aggrenox	Antiplatelet Agent	Added	2/25/03	
Attapulgite	Kaopectate	Antidiarrheal	Deleted	7/16/03	Removed from market
Bivalirudin	Angiomax	Anticoagulant	Added	11/27/03	
Carbamazepine	Carbatol	Anticonvulsant	Added	9/9/03	
Caspofungin	Caspofungin	Antifungal	Added	3/25/03	Order form restriction
Ciprofloxacin	Oloven	Topical Antibiotic	Deleted	9/25/03	Ophthalmic solution only
Clemastine	Tavist	Antihistamine	Deleted	8/27/03	
Clemastine/ Phenylpropandamine	Tavist-D	Antihistamine/ Decongestant	Deleted	8/27/03	
Dalteparin	Fragmin	LMWH/Heparin	Deleted	2/25/03	
Dexrazoxane	Zincard	Cardioprotectant	Added	5/27/03	
Docusate/ Casanthranol	Peri-Colace	Stool Softener	Deleted	12/16/03	Discontinued by manufacturer
Dutasteride	Avodart	BPH Agent	Added	2/25/03	
Escitalopram	Lexapro	Antidepressant	Added	3/25/03	
Ezetimibe	Zetia	Antilipemic	Added	8/28/03	
Fish Oil Concentrate		Dietary Supplement	Added	1/25/03	
Flurandrenolide	Cordran	Corticosteroid	Deleted	10/8/03	Discontinued by manufacturer
Gentuzumab Ozogamicin	Mylotarg	Antineoplastic	Added	11/22/03	
Lidocaine 5%	Lidoderm	Local Anesthetic	Added	8/28/03	
Moxifloxacin	Vigamox	Topical Antibiotic	Added	9/25/03	Ophthalmic solution
Mumps Skin Test Antigen	MSTAMumps Skin Test Antigen	Diagnostic Agent	Deleted	2/3/03	Discontinued by manufacturer
Oxybutynin	Oxytrol	Urinary Antispasmodic	Added	8/28/03	
Tegaserod maleate	Zelnorm	Irritable Bowel Agent	Added	2/25/03	