muromonab-CD3 (myo-roe-moe-nab CD3)

Classification
Therapeutic: immunosuppressants
Pharmacologic: monoclonal antibodies

Pregnancy Category: C

Indications
Acute renal allograft rejection reactions in transplant patients that have occurred despite conventional antirejection therapy. Acute corticosteroid-resistant hepatic or cardiac allograft rejection reactions.

Action
Cytotoxic immunoglobulin antibody that acts as an immunosuppressant by interfering with normal T-cell function. Therapeutic Effects: Reversal of graft rejection in transplant patients.

Pharmacokinetics
Absorption: Administered IV only, resulting in complete bioavailability.
Distribution: Unknown.
Metabolism and Excretion: Eliminated by binding to T lymphocytes.
Half-life: 18 hr.

TIME/ACTION PROFILE (noted as levels of circulating CD3-positive T cells)

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
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<tbody>
<tr>
<td>IV</td>
<td>mins</td>
<td>2–7 days</td>
<td>1 wk</td>
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</tbody>
</table>

Contraindications/Precautions
Contraindicated in: Hypersensitivity to muromonab-CD3, murine (mouse) proteins, or polysorbate; Previous muromonab therapy; Fluid overload; Fever or 100 F; Chickenpox or recent exposure to chickenpox; Herpes zoster.

Use Cautiously in: Active infections; Depressed bone marrow reserve; Chronic debilitating illnesses; HF; OB, Lactation, Pedi: Pregnancy, lactation, or children <2 yr (safety not established).

Adverse Reactions/Side Effects
CNS: tremor, aseptic meningitis, dizziness, headache.
Resp: PULMONARY EDEMA, dyspnea, shortness of breath, wheezing.
CV: chest pain.
GI: diarrhea, nausea, vomiting.
Misc: CYTOKINE RELEASE SYNDROME, infections, chills, fever, hypersensitivity reactions, Q risk of lymphoma.

Interactions
Drug-Drug: Additive immunosuppression with other immunosuppressives. Concurrent prednisone and azathioprine dosages should be reduced during muromonab therapy (Q risk of infection and lymphoproliferative disorders). Cyclosporine should be reduced or discontinued during muromonab (Q risk of infection and lymphoproliferative disorders). Q risk of adverse CNS reactions with live-virus vaccines.
Drug-Natural Products: Concomitant use with astragalus, echinacea, and melatonin may interfere with immunosuppression.

Route/Dosage
IV (Adults): 5 mg/day for 10–14 days (pretreatment with corticosteroids, acetaminophen, and/or antihistamines recommended).

NURSING IMPLICATIONS
Assessment
● Assess for fluid overload (monitor weight and intake and output, assess for edema and rales/crackles). Notify health care professional if patient has experienced 3% or more weight gain in the previous week. Chest x-ray examination should be obtained within 24 hr before beginning therapy. Fluid-overloaded patients are at high risk of developing pulmonary edema. Monitor vital signs and breath sounds closely.
● Assess for cytokine release syndrome (CRS), usually manifested by high fever and chills, headache, tremor, nausea and vomiting, chest pain, muscle and joint pain, generalized weakness, shortness of breath, dizziness, abdominal pain, malaise, diarrhea, and trembling of hands, but may occasionally cause a severe, life-threatening, shock-like reaction. The severity of this reaction is greatest with initial dose. Reaction occurs within 50–180 hr and may persist for up to 6 hr. Acetaminophen and anti-inflammatory agents may alleviate symptoms.

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Histamines may be used to treat early reactions. Patient temperature should be maintained below 37.8°C (100°F) at administration of each dose. Manifestations of CRS may be prevented or minimized by pretreatment with methylprednisolone sodium succinate 8 mg/kg IV given 1–4 hr before 1st dose of muromonab-CD3. Hydrocortisone 100 mg IV may also be given 30 min after the 1st and possibly 2nd dose to control respiratory side effects. Serious symptoms of CRS may require oxygen, IV fluids, corticosteroids, vasopressors, antihistamines, and intubation.

- Monitor for signs of anaphylactic or hypersensitivity reactions at each dose. Resuscitation equipment should be readily available.
- Monitor for infections (fever, chills, rash, sore throat, purulent discharge, dysuria). Notify physician immediately if these symptoms occur; then maintain discontinuation of therapy.
- Monitor for development of septic meningitis. Start to watch for 1 day after each dose. Assess for fever, headache, nuchal rigidity, and photophobia.

**Lab Test Considerations:**
- Monitor CBC with differential and platelet count before and periodically throughout therapy.
- Monitor assays of T cells (CD3, CD4, CD8); target CD3 is 25 cells/mm³ or plasma levels as determined by ELISA daily; target levels should be 800 ng/mL.
- Monitor BUN, serum creatinine, and hepatic enzymes (AST, ALT, alkaline phosphatase, bilirubin), especially during the first 1–3 days of therapy. May cause transient.

**Potential Nursing Diagnoses**
- Risk for infection (Side Effects)
- Excess fluid volume (Side Effects)

**Implementation**
- Physician will reduce dose of corticosteroids and azathioprine and discontinue cyclosporine during 10–14-day course of muromonab-CD3. Cyclosporine may be resumed 5 days before end of therapy.
- Initial dose is administered during hospitalization; patient should be monitored closely for 48 hr. Subsequent doses may be administered on outpatient basis.
- Keep medication refrigerated at 2–8°C. Do not freeze or shake vial. Solution may contain a few fine translucent particles that do not affect potency. Discard unused portion.

**IV Administration**
- **pH:** 6.5–7.5
- **Direct IV:** Draw solution into syringe via low-protein-binding 0.2- or 0.22-micrometer filter to ensure removal of translucent protein particles that may be present. Discard filter and attach 20-gauge needle for IV administration.
- **Concentration:** 1 mg/mL (undiluted). **Rate:** Administer IV push over 1 min. Do not administer as IV infusion.

**Y-Site Incompatibility:** Do not admix; do not administer in IV line containing other medications. If line must be used for other medications, flush with 0.9% NaCl before and after muromonab-CD3.

**Patient/Family Teaching**
- Explain purpose of medication to patient. Inform patient of possible initial-dose side effects, which are markedly reduced in subsequent doses. Explain that patient will need to resume lifelong therapy with other immunosuppressive drugs after completion of muromonab-CD3 course.
- Inform patient of potential for CRS. Describe reportable symptoms.
- Instruct patient to continue to avoid crowds and persons with known infections, as this drug also suppresses the immune system.
- Instruct patient to notify health care professional at first sign of rash, urticaria, tachycardia, dyspnea, or difficulty swallowing.
- Explain that patient will need to avoid driving or other activities requiring alertness until response is known.
- Instruct patient not to receive any vaccinations and to avoid contact with persons receiving oral polio vaccine without advice of health care professional.

**Evaluation/Desired Outcomes**
- Reversal of the symptoms of acute organ rejection.

Why was this drug prescribed for your patient?