for the treatment of rheumatoid arthritis, an indication that was expanded in 2002 to include improvement of physical function in patients without an adequate response to methotrexate therapy.

This MAb binds and neutralizes TNF-a, one of the primary cytokines that propagate the inflammatory response in patients with Crohn disease and rheumatoid arthritis. Thus, infliximab reduces the intestinal inflammation indicative of this disease process. Administration of single induction doses of infliximab when patients with Crohn disease are not receiving immunosuppressive drugs can lead to the development of antibodies to the chronic MAb itself. When antibodies to infliximab are present in high concentrations, patients demonstrate shortened duration of benefit, complete loss of response, and/or infusion reactions to the drug itself.

Infliximab is supplied in single-use 20-mL vials containing 100 mg of the drug. It has been associated with hypersensitivity reactions, including urticaria, dyspnea, and hypotension, and should be discontinued in case of a severe reaction. Additionally, anti-TNF therapy may result in the formation of autoimmune antibodies and rarely in the development of a lupus-like syndrome. If a patient develops symptoms suggestive of a lupus-like syndrome and is positive for antibodies against double-stranded DNA, infliximab therapy should be discontinued.

Muromonab-CD3 (Orthoclone OKT3)

Muromonab-CD3 is a murine MAb that reacts with a T3 (CD3) molecule linked to an antigen receptor on the surface membrane of human T lymphocytes. It blocks both generation and functions of the T cells in response to antigenic challenge and is indicated for the treatment of organ transplant rejection. Usually, it is combined with azathioprine, cyclosporine, and/or corticosteroids to prevent acute rejection of renal transplants. Simultaneously, the amount of immunosuppressive drugs a patient must receive has been reduced, effecting better outcomes.

Muromonab-CD3 injection is administered by IV push over a period not less than 1 minute. For acute renal allograft rejection, it is given IV at 5 mg per day for 10 to 14 days. To decrease the incidence of reactions resulting from the first injection of muromonab, methylprednisolone sodium succinate 8 mg/kg should be administered intravenously 1 to 4 hours beforehand. The patient's temperature should not exceed 37.8°C at the time of administration.

Muromonab-CD3 injection should be drawn into the syringe through a low–protein-binding 0.2- to 0.22-mm filter. The filter should be discarded and the needle for the intravenous bolus injection attached. Because the drug is a protein solution, it may develop a few fine translucent particles that do not affect its potency. This solution has no preservative and so must be used immediately upon opening and the unused portion discarded. As with other protein products, it must not be shaken.

Omalizumab (Xolair)

Omalizumab is the first humanized therapeutic antibody for the treatment of asthma and the first approved therapy designed to target immunoglobulin E (IgE) in the management of asthma. It was approved by the FDA in 2003 for subcutaneous treatment of moderate to severe persistent asthma in patients more than 12 years of age who demonstrate a positive skin test or in vitro reaction to a perennial aeroallergen (Fig. 19.15). Another requisite for its use is that the patient is inadequately controlled with inhaled corticosteroids.

Omalizumab is administered subcutaneously every 2 to 4 weeks. Dosing is based on

FIGURE 19.15 The product package of Xolair. (Courtesy of Genentech, Inc.)