CD20 is a B-cell-restricted antigen that, for the most part, is expressed from the pre-B-cell to the mature B-cell stage of B-cell differentiation. Several transcription factors regulate CD20 expression during B-cell differentiation, the most important of which appear to be PU.1 and Pip (PU.1 interacting protein). As B cells differentiate to plasma cells, CD20 expression is down-regulated, which coincides with PU.1 downregulation in plasma cells. Analogous to their normal B-cell counterparts, CD20 is expressed on malignant lymphoplasmacytic cells from most patients with Waldenstrom's macroglobulinemia and on malignant plasma cells from a fraction (20%) of multiple myeloma patients. CD20 also is expressed on subpopulations of normal donor plasma cells, which may include autoantibody-secreting plasmacytes. In view of these findings, the anti-CD20 chimeric monoclonal antibody, rituximab (Rituxan; Genentech, Inc, South San Francisco, CA and IDEC Pharmaceutical Corporation, San Diego, CA), has been evaluated in the treatment of Waldenstrom's macroglobulinemia and multiple myeloma, as well as in nonmalignant plasma cell disorders including IgM polyneuropathies, immune thrombocytopenias, and autoimmune hemolytic anemias, with reported activity in these entities. An update of these clinical efforts is presented in this report.