Pharmacotherapeutic report on rituximab (Mabthera®) for the indication 'maintenance therapy for patients with follicular lymphoma who respond to a first-line induction therapy'.

Medicine. Rituximab. Concentrate for solution for intravenous infusion, 10 mg per ml, vials containing 10 ml or 50 ml.

Therapeutic indication (among others):
"Non-Hodgkin's lymphoma (NHL): for the treatment of previously untreated patients with stage III-IV follicular lymphoma in combination with chemotherapy; **for the maintenance treatment of follicular lymphoma patients responding to induction therapy (this assessment);** for the treatment (as monotherapy) of patients with stage III-IV follicular lymphoma who are chemoresistant or are in their second or subsequent relapse after chemotherapy; for the treatment of patients with CD20-positive diffuse large B-cell non-Hodgkin's lymphoma in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone) chemotherapy."
Dose. Maintenance treatment for follicular lymphoma patients who respond to induction therapy: 375 mg/m^2 body surface area once every 2 months by intravenous infusion; starting 2 months after the last dose of induction therapy; treatment until disease progression or for a maximum period of two years.
Mechanism of action. Rituximab is a chimeric mouse/human monoclonal antibody. It binds specifically to the CD20 antigen on the surface of normal and malignant B-lymphocytes. Possible mechanisms of effector-mediated cell lysis include complement-dependent cytotoxicity (CDC) and antibody-dependent cellular cytotoxicity (ADCC). Binding to CD20 antigen on B-lymphocytes has also been demonstrated to induce cell death via apoptosis.

Summary of therapeutic value
Intended effects. When treating patients with follicular lymphoma who respond to first-line induction therapy, maintenance treatment with rituximab prolongs the progression-free survival (PFS) significantly in comparison with watchful waiting (observation). After a median follow-up of 36 months, 75% of the rituximab group is still free of progression in comparison with 58% of the observation group. Furthermore, the *time to next anti-lymphoma treatment* as well as the *time to next chemotherapy treatment* were both extended after maintenance therapy with rituximab. There is no evidence that rituximab maintenance therapy increases the overall survival. There is no significant difference in quality of life between the rituximab maintenance group and the observation group.
Unintended effects. Maintenance treatment with rituximab is associated with more severe undesirable effects in comparison with the observation group. The most frequent adverse drug reactions in patients receiving rituximab were infusion-related reactions, infections and cardiovascular events. One case of hepatitis B reactivation with fatal outcome has been reported.
Experience. Ample experience has been obtained with rituximab.

Applicability. To avoid serious infusion reactions, rituximab should be administered under the close supervision of an experienced physician in an environment where full resuscitation facilities are at hand. Caution is required in cases involving patients who are hypersensitive to murine proteins, active infections, immunocompromised state, severe heart failure (New York Heart Association Class IV) or uncontrolled cardiac diseases.
Ease of use. Rituximab is administered as an intravenous infusion.

Final conclusion. For the maintenance treatment of follicular lymphoma patients who respond to first-line induction therapy, rituximab has an added therapeutic value in comparison with observation.