Rituximab Therapeutic Cheat Sheet

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TRADE NAME

- Rituxan

MECHANISM OF ACTION

- Binds B cell surface antigen CD20 to trigger B cell depletion via 3 mechanisms:[1]
  - Natural killer cells bind CD20+ cells with bound rituximab and secrete cytotoxic granules to destroy B cells.
  - Binding of rituximab activates the classical complement pathway, leading to induction of cell death via membrane attack complexes.
  - Rituximab promotes cell death via multiple proposed signaling pathways, including MAPK, NFκB, ERK, and AKT.
- C20 is expressed almost exclusively on B cells so rituximab is specific to these cells, sparing plasma cells and protecting acquired immunity and antibody levels.[1]
- Beyond B cell depletion, rituximab has also been shown to decrease desmoglein reactive CD4+ T cells and increase interleukin-10 producing regulatory B cells, which may lead to disease remission after rituximab administration.[1]

FDA-APPROVED USE[1]

- Pemphigus vulgaris (primary dermatologic use) in adult patients[2]
- Other approved uses: CD20+ non-Hodgkin B cell lymphoma, CD20+ chronic lymphocytic leukemia, rheumatoid arthritis, granulomatous with polyangiitis, microscopic polyangiitis.

OFF-LABEL DERMATOLOGIC USES[1]

- Autoimmune blistering diseases (pemphigus foliaceous, bullous pemphigoid, mucous membrane pemphigoid, epidermolysis bullosa acquisita)
- Dermatomyositis
- Cutaneous lupus erythematosus
- Graft-versus-host disease

DOSING (INTRAVENOUS)[1]

- Initial dose of 1000 mg IV every 2 weeks for 2 doses (in combination with tapering doses of systemic steroids).
- Maintenance dose of 500 mg IV at 12 months and then every 6 months after as needed.

ADMINISTRATION CONSIDERATIONS

- Provide immunizations at least 4 weeks before treatment to allow development of appropriate immunity.[1]
- Initiation early in disease has been shown to more effective for treatment of pemphigus vulgaris.[1]
- Depletion of B cells starts 2-3 weeks after treatment and lasts for about 6 months.[1]
- Pre-medication with acetaminophen 650 mg, diphenhydramine 50 mg, and methylprednisolone 100 mg can reduce the risk of infusion reactions.[1]
- If combining rituximab with other immunosuppressants, antibiotic prophylaxis against Pneumocystis jirovecii pneumonia should be considered.

SIDE EFFECTS[1,3]

- Boxed warnings: hepatitis B reactivation, severe mucocutaneous reactions, infusion reactions, progressive multifocal leukoencephalopathy.
- Other than hepatitis B reactivation, these boxed warnings are predominantly seen in lymphoma treatment.
- Hypersensitivity reactions:
  - Infusion reactions (most common, occurs in 60% of pemphigus vulgaris patients)
  - Mild: headache, chills, nausea, pain, altered blood pressure
  - Severe: hypotension, angioedema, bronchospasm, urticaria
  - Mucocutaneous reactions (SJS/TEN, lichenoid, paraneoplastic pemphigus)
- Infections:
  - Hepatitis B reactivation
  - Bacterial, viral, and fungal infections
- Cardiovascular effects (arrhythmias, angina)
  - More likely in patients with a history of heart disease.
- Hematologic effects (cytopenia, including leukopenia, anemia, and thrombocytopenia)
  - Typically late onset, most often 3-4 months post-treatment.
- Gastrointestinal effects (bowel obstruction and perforation)
  - Only observed with co-administration of chemotherapy

DRUG INTERACTIONS[1]

- No formal studies.
- Combination other myelosuppressive medications may increase the risk of cytopenia.
- Combination with other immunosuppressive therapies may amplify immunosuppression.
- Renal toxicity can occur when administered with chemotherapy.

CONTRAINDICATIONS[1]

- Type I hypersensitivity to rituximab components.
- Progressive multifocal leukoencephalopathy.
- Active, severe infections.

PREGNANCY AND BREASTFEEDING[1]

- Rituximab can cause B cell lymphopenia in infants exposed in utero, so use should be avoided in pregnancy.
- IgG passes into breast milk, so women should avoid breastfeeding while on treatment and for at least 6 months after.

MONITORING[1]

- Baseline labs:
  - CBC with differential
  - Complete metabolic panel
  - Peripheral CD20 and CD3 counts via flow cytometry
  - Anti-desmoglein 1 and 3 titers via ELISA
  - Infection screening (hepatitis B and C, HIV, tuberculosis)
  - Screen for pregnancy and breastfeeding; effective birth control should be used during and for 12 months after treatment.
- Periodic monitoring:
  - CBC with differential every 2-3 months
  - Complete metabolic panel periodically
  - Yearly tuberculosis screening
- Anti-desmoglein 1 and 3 titers can be used to monitor response.