RIABNI™

DOSING GUIDE

RIABNI™ is the only rituximab with up to 7 days storage when diluted in 0.9% Sodium Chloride, USP[1-4]

- Protect diluted solution from light
- Refrigerate at 2˚C to 8˚C (36˚F to 46˚F)
- Only administer RIABNI™ as an intravenous (IV) infusion

Longer storage may allow for reduced drug wastage, improved planning and resource utilization

IMPORTANT SAFETY INFORMATION

BOXED WARNINGS: FATAL INFUSION-RELATED REACTIONS, SEVERE MUCOCUTANEOUS REACTIONS, HEPATITIS B VIRUS REACTIVATION, PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

- Infusion-Related Reactions: Rituximab product administration can result in serious, including fatal, infusion-related reactions. Deaths within 24 hours of rituximab infusion have occurred. Approximately 80% of fatal infusion-related reactions occurred in association with the first infusion. Monitor patients closely. Discontinue RIABNI™ infusion for severe reactions and provide medical treatment for Grade 3 or 4 infusion-related reactions.
- Severe Mucocutaneous Reactions: Severe, including fatal, mucocutaneous reactions can occur in patients receiving rituximab products. Discontinue RIABNI™ in patients who experience a severe mucocutaneous reaction. The safety of readministration of RIABNI™ to patients with severe mucocutaneous reactions has not been determined.
- Hepatitis B Virus (HBV) Reactivation: HBV reactivation can occur in patients treated with rituximab products, in some cases resulting in fulminant hepatitis, hepatic failure, and death. Screen all patients for HBV infection before treatment initiation, and monitor patients during and after treatment with RIABNI™. Discontinue RIABNI™ and concomitant medications in the event of HBV reactivation.
- Progressive Multifocal Leukoencephalopathy (PML), including fatal PML, can occur in patients receiving rituximab products. Discontinue RIABNI™ and consider discontinuation or reduction of any concomitant chemotherapy or immunosuppressive therapy in patients who develop PML.

AMGEN®

Please see Indications on next page, additional Important Safety Information, and full Prescribing Information.

INDICATIONS

- **Non-Hodgkin's Lymphoma (NHL)**
  RIABNI (rituximab-arrx) is indicated for the treatment of adult patients with:
  - Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent.
  - Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy.
  - Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy.
  - Previously untreated diffuse large B-cell, CD20-positive NHL in combination with cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) or other anthracycline-based chemotherapy regimens.
- **Chronic Lymphocytic Leukemia (CLL)**
  RIABNI, in combination with fludarabine and cyclophosphamide (FC), is indicated for the treatment of adult patients with previously untreated and previously treated CD20-positive CLL.

RIABNI™ (rituximab-arrx) Injection 100mg/vial & 500mg/vial

Please see additional Important Safety Information, and full Prescribing Information.

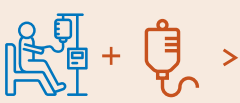
DOSING SCHEDULE[1]

RIABNI™ has an **identical dosing schedule to Rituxan®**

CD20-Positive B-Cell Non-Hodgkin's Lymphoma (NHL)—375 mg/m²

PREVIOUSLY UNTREATED, FOLLICULAR, B-CELL NHL

RIABNI™ (induction therapy)



UP TO 8 DOSES

BREAK*

RIABNI™ (maintenance therapy)

RIABNI™
1 DOSE EVERY 8 WEEKS

FOR A TOTAL OF 12 DOSES

*If patient has a complete or partial response, then maintenance doses can be started after 8 weeks.

RELAPSED OR REFRACTORY, LOW-GRADE OR FOLLICULAR, B-CELL NHL

RIABNI™ (as single-agent therapy)

RIABNI™
ONCE WEEKLY
4 OR 8 DOSES

RETREATMENT FOR RELAPSED OR REFRACTORY, LOW-GRADE OR FOLLICULAR, B-CELL NHL

RIABNI™ (as single-agent therapy)

RIABNI™
ONCE WEEKLY
4 DOSES

CD20-Positive B-Cell Non-Hodgkin's Lymphoma (NHL)—375 mg/m²

NON-PROGRESSING, LOW-GRADE, B-CELL NHL, AFTER FIRST-LINE CVP CHEMOTHERAPY

BEFORE RIABNI™

1ST-LINE CVP CHEMOTHERAPY
(Complete 6-8 cycles)

RIABNI™
(following completion of CVP chemotherapy)

RIABNI™ ONCE WEEKLY
(4 doses)

BREAK

UP TO 16 DOSES

DIFFUSE LARGE B-CELL NHL (DLBCL)

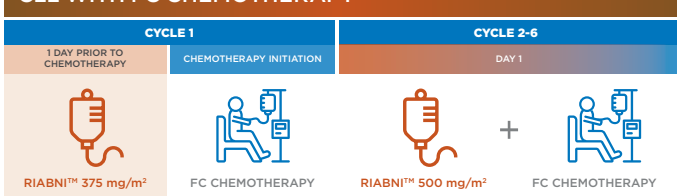
CYCLE OF CHEMOTHERAPY

RIABNI™ DAY 1 OF EACH CYCLE

UP TO 8 DOSES

Chronic Lymphocytic Leukemia (CLL)

CLL WITH FC CHEMOTHERAPY



EVERY 28 DAYS

CVP = cyclophosphamide, vincristine, prednisone;
FC = fludarabine, cyclophosphamide.

RIABNI™ (rituximab-arrx) Injection 100mg/vial & 500mg/vial

Please see additional Important Safety Information, and full Prescribing Information.

ADMINISTRATION PREPARATION[1,*]

RIABNI™ HAS THE SAME ADMINISTRATION AND INFUSION RATES AS RITUXAN®

RIABNI™ is supplied as a clear to slightly opalescent, colorless to slightly yellow liquid. Do not use vial if particulates or discoloration is present.

PREPARING RIABNI™ SOLUTION

- Use a sterile needle and syringe to prepare RIABNI™
- Withdraw the necessary amount of RIABNI™
- Dilute to a final concentration of 1 mg/mL to 4 mg/mL in an infusion bag containing either 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP

GENTLY INVERT THE BAG TO MIX THE SOLUTION

- Do not mix or dilute with other drugs
- Discard any unused portion left in the vial

ONLY ADMINISTER RIABNI™ AS AN INTRAVENOUS (IV) INFUSION

- Do not administer as an IV push or bolus

*Prior to preparation, protect vials from direct sunlight.

ADMINISTRATION GUIDELINES:

- Premedicate patient before each infusion of RIABNI™
- Interrupt the infusion or slow the infusion rate for infusion-related reactions
- See Boxed WARNINGS, Dosage and Administration, Warnings and Precautions, and Adverse Reactions sections of the full Prescribing Information

RIABNI™ (rituximab-arrx) Injection 100mg/vial & 500mg/vial

Please see additional Important Safety Information, and full Prescribing Information.

INFUSION RATES[1]

RIABNI™ HAS IDENTICAL INFUSION RATES TO RITUXAN®

FIRST INFUSION

Initial Rate	INCREASE RATE	Maximum Rate
50 mg/hr	**+ 50 mg/hr** EVERY 30 MINUTES	**400 mg/hr**

SUBSEQUENT INFUSIONS

STANDARD INFUSION

Initial Rate	INCREASE RATE	Maximum Rate
100 mg/hr	**+ 100 mg/hr** EVERY 30 MINUTES	**400 mg/hr**

90-MINUTE INFUSION*

Initial Rate	INCREASE RATE	
20% of total dose FOR 30 MINUTES	**80% of total dose** FOR 60 MINUTES	**Only for Previously Untreated Follicular NHL and DLBCL Patients who:** • Had no Grade 3 or 4 infusion-related adverse events during Cycle 1 • Are receiving a GC-containing chemotherapy regimen in Cycles 2 through 8

DLBCL = diffuse large B-cell lymphoma; GC = glucocorticoid.

*Patients who have clinically significant cardiovascular disease or who have a circulating lymphocyte count ≥ 5000/mm³ before Cycle 2 should not be administered the 90-minute infusion.

See Boxed WARNINGS, Dosage and Administration, Warnings and Precautions, and Adverse Reactions sections of the full Prescribing Information.

RIABNI™ (rituximab-arrx) Injection 100mg/vial & 500mg/vial

Please see additional Important Safety Information, and full Prescribing Information.

PREPARE PATIENTS
FOR TREATMENT WITH RIABNI™

Patients may have a better treatment experience if you help set their expectations. Some key communication points are included here and are available in the RIABNI™ Patient Brochure.

HOW THEY WILL TAKE RIABNI™[1]

Explain that RIABNI™ is given as an infusion and whether it is being given alone or with other medicines.

LET PATIENTS KNOW:[1]

- How long their first infusion will take (4 to 6 hours or longer)
- Future infusions may be shorter (3 to 4 hours or even 90 minutes), depending on how their body tolerated their last infusion

WHAT WILL HAPPEN ON THE FIRST DAY OF RIABNI™ TREATMENT

	Premedicate before each infusion
	The first infusion of RIABNI™ will be administered
	After the first treatment, the treatment team will give a checkup and make sure the patient is ready to go home

WHAT TO LOOK OUT FOR AFTER TREATMENT

Patients should alert their healthcare provider, or get medical help right away, if they notice any of these symptoms during or after their RIABNI™ infusion:

- Hives (itchy red welts) or rash
- Itching
- Swelling of your lips, tongue, throat, or face
- Sudden cough
- Shortness of breath, difficulty breathing, or wheezing
- Weakness
- Dizziness or feeling faint
- Palpitations (feeling like your heart is racing or fluttering)
- Chest pain

Direct patients to the website **www.RIABNI.com** and the RIABNI™ Medication Guide for more information about RIABNI™ treatment and potential side effects.

RIABNI™ (rituximab-arrx) Injection 100mg/vial & 500mg/vial

STORAGE

RIABNI™ IS THE ONLY RITUXIMAB WITH 1-WEEK STORAGE AFTER DILUTION IN 0.9% SODIUM CHLORIDE, USP[1-4]

	RIABNI™	RITUXAN® AND ALL OTHER RITUXIMAB DRUGS
STORAGE TIME	UP TO **7** DAYS* when diluted in 0.9% Sodium Chloride, USP	UP TO **1** DAY

*Must be refrigerated and protected from light.

ADDITIONAL STORAGE REQUIREMENTS[1]

- Store refrigerated at 2°C to 8°C (36°F to 46°F).
- Protect diluted solution from light.
- DO NOT FREEZE OR SHAKE.

1-WEEK STORAGE MAY ALLOW FOR

- REDUCED DRUG WASTE
- IMPROVED PLANNING & RESOURCE UTILIZATION

AMGEN®

RIABNI™ (rituximab-arrx) Injection 100mg/vial & 500mg/vial

Please see additional Important Safety Information, and full Prescribing Information.

IMPORTANT SAFETY INFORMATION AND INDICATIONS

BOXED WARNINGS: FATAL INFUSION-RELATED REACTIONS, SEVERE MUCOCUTANEOUS REACTIONS, HEPATITIS B VIRUS REACTIVATION, PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

- **Infusion-Related Reactions: Rituximab product administration can result in serious, including fatal, infusion-related reactions. Deaths within 24 hours of rituximab infusion have occurred. Approximately 80% of fatal infusion-related reactions occurred in association with the first infusion. Monitor patients closely. Discontinue RIABNI™ infusion for severe reactions and provide medical treatment for Grade 3 or 4 infusion-related reactions.**
- **Severe Mucocutaneous Reactions: Severe, including fatal, mucocutaneous reactions can occur in patients receiving rituximab products. Discontinue RIABNI™ in patients who experience a severe mucocutaneous reaction. The safety of readministration of RIABNI™ to patients with severe mucocutaneous reactions has not been determined.**
- **Hepatitis B Virus (HBV) Reactivation: HBV reactivation can occur in patients treated with rituximab products, in some cases resulting in fulminant hepatitis, hepatic failure, and death. Screen all patients for HBV infection before treatment initiation, and monitor patients during and after treatment with RIABNI™. Discontinue RIABNI™ and concomitant medications in the event of HBV reactivation.**
- **Progressive Multifocal Leukoencephalopathy (PML), including fatal PML, can occur in patients receiving rituximab products. Discontinue RIABNI™ and consider discontinuation or reduction of any concomitant chemotherapy or immunosuppressive therapy in patients who develop PML.**

Warnings and Precautions

Infusion-Related reactions (IRR)

- Rituximab products can cause severe, including fatal, infusion-related reactions. Severe reactions typically occurred during the first infusion with time to onset of 30-120 minutes.
- Rituximab-product-induced infusion-related reactions and sequelae include urticaria, hypotension, angioedema, hypoxia, bronchospasm, pulmonary infiltrates, acute respiratory distress syndrome, myocardial infarction, ventricular fibrillation, cardiogenic shock, anaphylactoid events, or death.
- Premedicate patients with an antihistamine and acetaminophen prior to dosing. Institute medical management (e.g., glucocorticoids, epinephrine, bronchodilators, or oxygen) for infusion-related reactions as needed. Depending on the severity of the infusion-related reaction and the required interventions, temporarily or permanently discontinue RIABNI™. Resume infusion at a minimum 50% reduction in rate after symptoms have resolved.
- Closely monitor the following patients: those with preexisting cardiac or pulmonary conditions, those who experienced prior cardiopulmonary adverse reactions, and those with high numbers of circulating malignant cells (≥25,000/mm^3).

Severe Mucocutaneous Reactions

- Mucocutaneous reactions, some with fatal outcome, can occur in patients treated with rituximab products. These reactions include paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis.
- The onset of these reactions has been variable and includes reports with onset on the first day of rituximab exposure. Discontinue RIABNI™ in patients who experience a severe mucocutaneous reaction. The safety of readministration of rituximab products to patients with severe mucocutaneous reactions has not been determined.

Hepatitis B Virus Reactivation

- Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death, can occur in patients treated with drugs classified as CD20-directed cytolytic antibodies, including rituximab products. Cases have been reported in patients who are hepatitis B surface antigen (HBsAg) positive and also in patients who are HBsAg negative but are hepatitis B core antibody (anti-HBc) positive. Reactivation also has occurred in patients who appear to have resolved hepatitis B infection (i.e., HBsAg negative, anti-HBc positive, and hepatitis B surface antibody [anti-HBs] positive).
- HBV reactivation is defined as an abrupt increase in HBV replication manifesting as a rapid increase in serum HBV DNA level or detection of HBsAg in a person who was previously HBsAg negative and anti-HBc positive. Reactivation of HBV replication is often followed by hepatitis, i.e., increase in transaminase levels. In severe cases, increase in bilirubin levels, liver failure, and death can occur.
- Screen all patients for HBV infection by measuring HBsAg and anti-HBc before initiating treatment with RIABNI™. For patients who show evidence of prior hepatitis B infection (HBsAg positive [regardless of antibody status] or HBsAg negative but anti-HBc positive), consult with physicians with expertise in managing hepatitis B regarding monitoring and consideration for HBV antiviral therapy before and/or during RIABNI™ treatment.
- Monitor patients with evidence of current or prior HBV infection for clinical and laboratory signs of hepatitis or HBV reactivation during and for several months following RIABNI™ therapy. HBV reactivation has been reported up to 24 months following completion of rituximab therapy.
- In patients who develop reactivation of HBV while on RIABNI™, immediately discontinue RIABNI™ and any concomitant chemotherapy, and institute appropriate treatment. Insufficient data exist regarding the safety of resuming rituximab product treatment in patients who develop HBV reactivation. Resumption of RIABNI™ treatment in patients whose HBV reactivation resolves should be discussed with physicians with expertise in managing HBV.

Progressive Multifocal Leukoencephalopathy (PML)

- JC virus infection resulting in multifocal leukoencephalopathy (PML) and death can occur in rituximab product-treated patients with hematologic malignancies or with autoimmune diseases. The majority of patients with hematologic malignancies diagnosed with PML received rituximab in combination with chemotherapy or as part of a hematopoietic stem cell transplant. The patients with autoimmune diseases had prior or concurrent immunosuppressive therapy. Most cases of PML were diagnosed within 12 months of their last infusion of rituximab.
- Consider the diagnosis of PML in any patient presenting with new-onset neurologic manifestations. Evaluation of PML includes, but is not limited to, consultation with a neurologist, brain MRI, and lumbar puncture. Discontinue RIABNI™ and consider discontinuation or reduction of any concomitant chemotherapy or immunosuppressive therapy in patients who develop PML.

Tumor Lysis Syndrome

- Acute renal failure, hyperkalemia, hypocalcemia, hyperuricemia, or hyperphosphatemia from tumor lysis, some fatal, can occur within 12–24 hours after the first infusion of RIABNI™ in patients with non-Hodgkin's lymphoma (NHL). A high number of circulating malignant cells (≥25,000/mm^3), or high tumor burden, confers a greater risk of TLS.
- Administer aggressive intravenous hydration and anti-hyperuricemic therapy in patients at high risk for TLS. Correct electrolyte abnormalities, monitor renal function and fluid balance, and administer supportive care, including dialysis as indicated.

Infections

- Serious, including fatal, bacterial, fungal, and new or reactivated viral infections can occur during and following the completion of rituximab product-based therapy. Infections have been reported in some patients with prolonged hypogammaglobulinemia (defined as hypogammaglobulinemia >11 months after rituximab exposure).
- New or reactivated viral infections included cytomegalovirus, herpes simplex virus, parvovirus B19, varicella zoster virus, West Nile virus, and hepatitis B and C. Discontinue RIABNI™ for serious infections and institute appropriate anti-infective therapy.
- RIABNI™ is not recommended for use in patients with severe, active infections.

Cardiovascular Adverse Reactions

- Cardiac adverse reactions, including ventricular fibrillation, myocardial infarction, and cardiogenic shock may occur in patients receiving rituximab products. Discontinue infusions for serious or life-threatening cardiac arrhythmias. Perform cardiac monitoring during and after all infusions of RIABNI™ for patients who develop clinically significant arrhythmias, or who have a history of arrhythmia or angina.

Renal Toxicity

- Severe, including fatal, renal toxicity can occur after rituximab product administration in patients with NHL. Renal toxicity has occurred in patients who experience TLS and in patients with NHL administered concomitant cisplatin therapy during clinical trials. The combination of cisplatin and RIABNI™ is not an approved treatment regimen. Monitor closely for signs of renal failure and discontinue RIABNI™ in patients with a rising serum creatinine or oliguria.

Bowel Obstruction and Perforation

- Abdominal pain, bowel obstruction and perforation, in some cases leading to death, can occur in patients receiving rituximab products in combination with chemotherapy. In postmarketing reports, the mean time to documented gastrointestinal perforation was 6 (range 1–77) days in patients with NHL. Evaluate if symptoms of obstruction such as abdominal pain or repeated vomiting occur.

Immunization

- The safety of immunization with live viral vaccines following rituximab product therapy has not been studied, and vaccination with live virus vaccines is not recommended before or during treatment.
- For patients treated with RIABNI™, physicians should review the patient's vaccination status and patients should, if possible, be brought up to date with all immunizations in agreement with current immunization guidelines prior to initiating RIABNI™; administer non-live vaccines at least 4 weeks prior to a course of RIABNI™.

Embryo-Fetal Toxicity

- Based on human data, rituximab products can cause fetal harm due to B-cell lymphocytopenia in infants exposed in utero. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception with RIABNI™ and for 12 months after the last dose.

Additional Important Safety Information

Adverse Reactions

- The most common Grade 3 or 4 adverse reactions in clinical trials of NHL and chronic lymphocytic leukemia (CLL) were infusion-related reactions, neutropenia, leukopenia, anemia, thrombocytopenia, and infections. Additionally, lymphopenia and lung disorder were seen in NHL trials; and febrile neutropenia, pancytopenia, hypotension, and hepatitis B were seen in CLL trials.
- The most common adverse reactions (incidence ≥25%) in clinical trials of NHL and CLL were infusion-related reactions. Additionally, fever, lymphopenia, chills, infection, and asthenia were seen in NHL trials; and neutropenia was seen in CLL trials.

Pregnancy and Nursing Mothers

- Based on human data, rituximab products can cause adverse developmental outcomes including B-cell lymphocytopenia in infants exposed in utero. Advise pregnant women of the risk to a fetus. There are limited data on the presence of rituximab products in human milk and the effect on the breastfed child, and there are no data on the effect on milk production. Rituximab is detected in the milk of lactating cynomolgus monkeys, and maternal IgG is present in human breast milk. Rituximab has also been reported to be excreted at low concentrations in human breast milk. Given that the clinical significance of this finding for children is not known, advise women not to breastfeed during treatment with RIABNI™ and for 6 months after the last dose due to the potential of serious adverse events in breastfed children.

Attention Healthcare Provider: Provide Medication Guide to patient prior to RIABNI™ infusion and advise patients to read guide.

You may report side effects to the FDA at (800) FDA-1088 or **www.fda.gov/medwatch**. You may also report side effects to Amgen at 1-800-772-6436.

Please see the full Prescribing Information, including BOXED WARNINGS and Medication Guide, for additional Important Safety Information.

INDICATIONS

- **Non-Hodgkin's Lymphoma (NHL)**
  RIABNI (rituximab-arrx) is indicated for the treatment of adult patients with:
  - Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent.
  - Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy.
  - Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy.
  - Previously untreated diffuse large B-cell, CD20-positive NHL in combination with cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) or other anthracycline-based chemotherapy regimens.
- **Chronic Lymphocytic Leukemia (CLL)**
  RIABNI, in combination with fludarabine and cyclophosphamide (FC), is indicated for the treatment of adult patients with previously untreated and previously treated CD20-positive CLL.

References: 1. RIABNI™ (rituximab-arrx) Prescribing Information, Amgen Inc. **2.** Rituxan® (rituximab) full Prescribing Information, Genentech, Inc. **3.** TRUXIMA® (rituximab-abbs) Prescribing Information, Teva Pharmaceuticals. **4.** RUXIENCE™ (rituximab-pvvr) Prescribing Information, Pfizer.