Pfizer enCompass® Overview and Frequently Asked Questions (FAQs)

Pfizer enCompass Overview

Pfizer enCompass offers reimbursement and patient support intended to help eligible patients prescribed INFLECTRA® (infliximab-dyyb) for Injection and RUXIENCE® (rituximab-pvvr) for rheumatoid arthritis (RA) navigate the reimbursement process, including verifying and confirming patient insurance benefits, prior authorization (PA) assistance and following up with claims submission and co-pay assistance for eligible commercially insured patients.

Pfizer offers programs that provide financial assistance to eligible patients if they need help getting access to their Pfizer medicine. Assistance may include help with out-of-pocket costs for INFLECTRA and RUXIENCE for eligible patients through the Pfizer enCompass Co-Pay Assistance Program.

To request support through Pfizer enCompass or learn more about eligibility requirements for available financial assistance options, please call Pfizer enCompass to speak to an Access Counselor at 1-844-722-6672, Monday through Friday, 8 AM to 8 PM ET, or visit www.pfizerencompass.com.

HCPs can also enroll into the Pfizer enCompass Provider Portal at www.pfizerencompassonline.com and initiate an electronic benefit verification (eBV) or enroll into the Pfizer enCompass Co-Pay Assistance Program. HCPs can download an editable PDF of the Pfizer enCompass Enrollment Form for INFLECTRA and RUXIENCE from www.pfizerencompass.com or from the provider portal and fax or mail the completed form.

HCPs can enroll patients directly into the Pfizer enCompass Co-Pay Assistance Program using the co-pay portal at www.pfizercopay.com. This option is best for patients who do not require additional patient support, such as a BV.

To learn more, select from the following to navigate to frequently asked questions:

Pfizer enCompass Co-Pay Assistance Program

Pfizer enCompass Provider Portal

Please see Important Safety Information and Indications on pages 6-11, and full Prescribing Information, including BOXED WARNING and Medication Guide, available at RUXIENCEhcp.com.

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Pfizer enCompass® FAQs

Pfizer enCompass Co-Pay Assistance Program

Q. What support is available through the Pfizer enCompass Co-Pay Assistance Program?

A. The Pfizer enCompass Co-Pay Assistance Program for INFLECTRA provides eligible, commercially insured patients assistance of up to $20,000 per calendar year for claims received by the program. Eligible enrolled patients may pay as little as $0 for each INFLECTRA treatment. Federal and state healthcare beneficiaries not eligible. Private insurance only. The co-pay program covers only drug costs, not procedures, administration fees, or office visits. Please see full Terms and Conditions on page 4.

The Pfizer enCompass Co-Pay Assistance Program for RUXIENCE provides eligible, commercially insured patients assistance of up to $25,000 per calendar year for claims received by the program. Eligible enrolled patients may pay as little as $0 for each RUXIENCE treatment. Federal and state healthcare program beneficiaries not eligible. Private insurance only. The co-pay program covers only drug costs, not procedures, administration fees, or office visits. Please see full Terms and Conditions on page 4.

Q. How can I receive additional information about the Pfizer enCompass Co-Pay Assistance Program?

A. Please contact Pfizer enCompass at 1-844-722-6672. Pfizer enCompass Access Counselors are available from 8 AM to 8 PM ET, Monday through Friday, to answer HCP and patient questions. You may also access program resources, including digital brochures and forms, at www.pfizerencompass.com.

Q. What are the patient eligibility criteria for the Pfizer enCompass Co-Pay Assistance Program?

A. For patients to be eligible for this program, they must have commercial insurance that covers INFLECTRA and RUXIENCE, and they cannot be enrolled in a state or federally funded health care insurance program. This program offer is not valid for cash-paying patients. Please see full Terms and Conditions on page 4.

Q. What is the Pfizer Co-Pay Portal?

A. The Pfizer enCompass Co-Pay Assistance Program is powered by www.PfizerCopay.com. The co-pay portal allows HCPs to register their practice; enroll eligible patients in the Pfizer enCompass Co-Pay Program; submit claims; select preferences, including payment method and payment address; and view a patient's status in the co-pay program as well as claim/payment status and history. By navigating to Claims > Payment History, the HCP will be able to search either by check number or date range of payments made to the practice. Using this feature, they will be able to see the amount paid, date of service, patient name, patient date of birth, co-pay card group number, and co-pay card ID number associated with their checks from the co-pay program.

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Pfizer enCompass® FAQs

Pfizer enCompass Co-Pay Assistance Program (continued)

Q. Who can use the Pfizer Co-Pay Portal?

A. The Pfizer Co-Pay Portal allows HCPs, specialty pharmacies, and/or patients to register and enroll in Pfizer's co-pay assistance programs.

Q. How can I get started in the Pfizer Co-Pay Portal?

A. You can get started by visiting www.PfizerCopay.com.

Q. How do I submit co-pay claims using the Pfizer Co-Pay Portal?

A. HCPs have 3 ways to submit co-pay claims. You can submit claims directly at www.PfizerCopay.com or fax claims to 1-877-847-FAX1 (1-877-847-3291). To mail claims, please contact Pfizer enCompass at 1-844-722-6672. Claims must be submitted within 180 days of each treatment date and complete claims require a copy of the Explanation of Benefits (EOB) document for the treatment date, available from the patient's insurance company.

Q. How do I receive payment for co-pay claims submitted using the Pfizer Co-Pay Portal?

A. HCPs can receive payment via electronic funds transfer (EFT) or check. Patients who choose not to assign benefits to their HCP can get payments by check (if the patient has already paid the co-pay) or have the funds loaded onto the Smartcard (if the patient has not paid the co-pay).

Q. What is the Smartcard and how does it work?

A. The Pfizer enCompass Co-Pay Assistance Program for INFLECTRA and RUXIENCE includes a Smartcard option for HCPs to receive payment. The Smartcard may be used as both a debit and co-pay card. Patients use this card to pay their co-pays to HCPs using the debit card feature.

A co-pay claim must be submitted and approved prior to funds being loaded onto the Smartcard.

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Pfizer enCompass Co-Pay Assistance Program (continued)

Terms and Conditions

By using this program, you acknowledge that you currently meet the eligibility criteria and will comply with the terms and conditions below:

The Pfizer enCompass Co-Pay Assistance Program for INFLECTRA® and RUXIENCE® is not valid for patients that are enrolled in a state or federally funded insurance program, including but not limited to Medicare, Medicaid, TRICARE, Veterans Affairs health care, a state prescription drug assistance program, or the Government Health Insurance Plan available in Puerto Rico (formerly known as "La Reforma de Salud"). Program offer is not valid for cash-paying patients. Patients prescribed RUXIENCE for pemphigus vulgaris are not eligible for this co-pay savings program. With this program, eligible patients may pay as little as $0 co-pay per INFLECTRA or RUXIENCE treatment. There are specific maximum annual patient savings for each product, which range from $20,000 (INFLECTRA) to $25,000 (RUXIENCE) for out-of-pocket expenses for the respective product including co-pays or coinsurances. The amount of any benefit is the difference between your co-pay and $0. After the maximum benefit, you will be responsible for the remaining monthly out-of-pocket costs. Patient must have private insurance with coverage of INFLECTRA or RUXIENCE. This offer is not valid when the entire cost of your prescription drug is eligible to be reimbursed by your private insurance plans or other private health or pharmacy benefit programs. You must deduct the value of this assistance from any reimbursement request submitted to your private insurance plan, either directly by you or on your behalf. You are responsible for reporting use of the program to any private insurer, health plan, or other third party who pays for or reimburses any part of the prescription filled using the program, as may be required. You should not use the program if your insurer or health plan prohibits use of manufacturer co-pay assistance programs. This program is not valid where prohibited by law. This program cannot be combined with any other savings, free trial or similar offer for the specified prescription. **Co-pay card will be accepted only at participating pharmacies. This program is not health insurance**. This program is good only in the U.S. and Puerto Rico. This program is limited to 1 per person during this offering period and is not transferable. No other purchase is necessary. Data related to your redemption of the program assistance may be collected, analyzed, and shared with Pfizer, for market research and other purposes related to assessing Pfizer's programs. Data shared with Pfizer will be aggregated and de-identified; it will be combined with data related to other assistance redemptions and will not identify you. Pfizer reserves the right to rescind, revoke or amend this program without notice. This program may not be available to patients in all states. For more information about Pfizer, visit www.pfizer.com. For more information about the Pfizer enCompass Co-Pay Assistance Program, call Pfizer enCompass at 1-844-722-6672. Program terms and offer will expire at the end of each calendar year. Before the calendar year ends, you will receive information and eligibility requirements for continued participation.

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Pfizer enCompass® FAQs

Pfizer enCompass Provider Portal

Q. What is the Pfizer enCompass Provider Portal, and who can use it?

A. Pfizer enCompass has a Provider Portal for HCPs and their staff. The portal allows the convenience of online, real-time access to Pfizer enCompass support and resources through electronic submission of requests for a variety of support, including patient insurance BVs and patient support. BVs may also be completed through the portal using electronic features such as eBV.

Q. How do I access the Pfizer enCompass Provider Portal?

A. The Pfizer enCompass Provider Portal is available at www.pfizerencompassonline.com. For more information, please contact Pfizer enCompass at 1-844-722-6672. Pfizer enCompass Access Counselors are available from 8 AM to 8 PM ET, Monday through Friday, to answer HCP and patient questions.

Q. Is the Pfizer enCompass Provider Portal HIPAA-compliant?

A. Yes, Pfizer has established and approved procedures and protocols that comply with HIPAA privacy and security regulations. Pfizer enCompass understands the impact of HIPAA and has taken the following steps to demonstrate our commitment to compliance:

- Appointment of a Privacy and Security Officer
- Implementation of a process to monitor changes to HIPAA regulations
- Use of procedures and protocols that comply with HIPAA privacy and security regulations

Q. What type of information is accessible once logged into the Pfizer enCompass Provider Portal?

A. In addition to access to the same Pfizer enCompass support that is available by phone and fax, Provider Portal users have access to billing, coding, and claim submission information, and resources to support the reimbursement process, including digital brochures and forms.

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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 RUXIENCE 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 RUXIENCE in patients who experience a severe mucocutaneous reaction. The safety of readministration of RUXIENCE 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 RUXIENCE. Discontinue RUXIENCE and concomitant medications in the event of HBV reactivation

Progressive Multifocal Leukoencephalopathy (PML), including fatal PML, can occur in patients receiving rituximab products. Discontinue RUXIENCE and consider discontinuation or reduction of any concomitant chemotherapy or immunosuppressive therapy in patients who develop PML

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. For patients with rheumatoid arthritis (RA), granulomatosis with polyangiitis (GPA) (Wegener's granulomatosis), and microscopic polyangiitis (MPA), methylprednisolone 100 mg intravenously or its equivalent is recommended 30 minutes prior to each infusion. Institute medical management (eg, 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 RUXIENCE. 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 RUXIENCE 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 (HBV) Reactivation

- 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 has also occurred in patients who appear to have resolved hepatitis B infection (ie, 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, ie, increase in transaminase levels. In severe cases, increase in bilirubin levels, liver failure, and death can occur

Continued on the next page

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IMPORTANT SAFETY INFORMATION (Continued)

Hepatitis B Virus (HBV) Reactivation (Continued)

- Screen all patients for HBV infection by measuring HBsAg and anti-HBc before initiating treatment with RUXIENCE. 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 RUXIENCE 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 RUXIENCE therapy. HBV reactivation has been reported up to 24 months following completion of rituximab therapy
- In patients who develop reactivation of HBV while on RUXIENCE, immediately discontinue RUXIENCE 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 RUXIENCE 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 progressive 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 RUXIENCE and consider discontinuation or reduction of any concomitant chemotherapy or immunosuppressive therapy in patients who develop PML

Tumor Lysis Syndrome (TLS)

- Acute renal failure, hyperkalemia, hypocalcemia, hyperuricemia, or hyperphosphatemia from tumor lysis, some fatal, can occur within 12–24 hours after the first infusion of RUXIENCE 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 antihyperuricemic 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 RUXIENCE for serious infections and institute appropriate anti-infective therapy
- RUXIENCE 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 RUXIENCE 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 RUXIENCE is not an approved treatment regimen. Monitor closely for signs of renal failure and discontinue RUXIENCE in patients with a rising serum creatinine or oliguria

Continued on the next page

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IMPORTANT SAFETY INFORMATION (Continued)

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 RUXIENCE, 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 RUXIENCE; administer nonlive vaccines at least 4 weeks prior to a course of RUXIENCE
- The effect of rituximab on immune responses was assessed in a randomized, controlled study in patients with RA treated with rituximab and methotrexate (MTX) compared to patients treated with MTX alone
- A response to pneumococcal vaccination (a T-cell–independent antigen) as measured by an increase in antibody titers to at least 6 of 12 serotypes was lower in patients treated with rituximab plus MTX as compared to patients treated with MTX alone (19% vs 61%). A lower proportion of patients in the rituximab plus MTX group developed detectable levels of anti-keyhole limpet hemocyanin antibodies (a novel protein antigen) after vaccination compared to patients on MTX alone (47% vs 93%)
- A positive response to tetanus toxoid vaccine (a T-cell–dependent antigen with existing immunity) was similar in patients treated with rituximab plus MTX compared to patients on MTX alone (39% vs 42%). The proportion of patients maintaining a positive Candida skin test (to evaluate delayed type hypersensitivity) was also similar (77% of patients on rituximab plus MTX vs 70% of patients on MTX alone)
- Most patients in the rituximab-treated group had B-cell counts below the lower limit of normal at the time of immunization. The clinical implications of these findings are not known

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. Verify pregnancy status in females of reproductive potential prior to initiating RUXIENCE. Advise females of reproductive potential to use effective contraception during treatment with RUXIENCE and for 12 months after the last dose

Concomitant Use With Other Biologic Agents and Disease Modifying Antirheumatic Drugs (DMARDs), Other Than MTX, in RA, GPA, and MPA

- Limited data are available on the safety of the use of biologic agents or DMARDs, other than MTX, in RA patients exhibiting peripheral B-cell depletion following treatment with rituximab products. Observe patients closely for signs of infection if biologic agents and/or DMARDs are used concomitantly. Use of concomitant immunosuppressants other than corticosteroids has not been studied in GPA or MPA patients exhibiting peripheral B-cell depletion following treatment with rituximab products

Use in RA Patients Who Have Not Had Prior Inadequate Response to Tumor Necrosis Factor (TNF) Antagonists

- While the efficacy of rituximab was supported in 4 controlled trials in patients with RA with prior inadequate responses to non-biologic DMARDs, and in a controlled trial in MTX-naïve patients, a favorable risk-benefit relationship has not been established in these populations. The use of RUXIENCE in patients with RA who have not had prior inadequate response to one or more TNF antagonists is not recommended

Lactation

- Rituximab has 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 RUXIENCE and for 6 months after the last dose due to the potential for serious adverse reactions in breastfed children

Continued on the next page

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IMPORTANT SAFETY INFORMATION (Continued)

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
- In RA clinical trials, among all exposed patients, adverse reactions reported in greater than 10% of patients include infusion-related reactions, upper respiratory tract infection, nasopharyngitis, urinary tract infection, and bronchitis
- In RA placebo-controlled studies, adverse reactions reported in ≥5% of patients were hypertension (8% vs 5%), nausea (8% vs 5%), upper respiratory tract infection (7% vs 6%), arthralgia (6% vs 4%), pyrexia (5% vs 2%), and pruritus (5% vs 1%), rituximab-treated vs placebo, respectively

Clinical Trials Experience in RA Infusion-Related Reactions

- In the rituximab RA pooled placebo-controlled studies, 32% of rituximab-treated patients experienced an adverse reaction during or within 24 hours following their first infusion, compared to 23% of placebo-treated patients receiving their first infusion. The incidence of adverse reactions during the 24-hour period following the second infusion, rituximab or placebo, decreased to 11% and 13%, respectively. Acute infusion-related reactions (manifested by fever, chills, rigors, pruritus, urticaria/rash, angioedema, sneezing, throat irritation, cough, and/or bronchospasm, with or without associated hypotension or hypertension) were experienced by 27% of rituximab-treated patients following their first infusion, compared to 19% of placebo-treated patients receiving their first placebo infusion. The incidence of these acute infusion-related reactions following the second infusion of rituximab or placebo decreased to 9% and 11%, respectively. Serious acute infusion-related reactions were experienced by <1% of patients in either treatment group. Acute infusion-related reactions required dose modification (stopping, slowing, or interruption of the infusion) in 10% and 2% of patients receiving rituximab or placebo, respectively, after the first course

Infections

- In the pooled, placebo-controlled studies, 39% of patients in the rituximab group experienced an infection of any type compared to 34% of patients in the placebo group. The most common infections were nasopharyngitis, upper respiratory tract infections, urinary tract infections, bronchitis, and sinusitis
- The incidence of serious infections was 2% in the rituximab-treated patients and 1% in the placebo group
- In the experience with rituximab in 2578 RA patients, the rate of serious infections was 4.31 per 100 patient-years. The most common serious infections (≥ 0.5%) were pneumonia or lower respiratory tract infections, cellulitis, and urinary tract infections. Fatal serious infections included pneumonia, sepsis, and colitis. Rates of serious infection remained stable in patients receiving subsequent courses. In 185 rituximab-treated RA patients with active disease, subsequent treatment with a biologic DMARD, the majority of which were TNF antagonists, did not appear to increase the rate of serious infection

Cardiovascular Adverse Reactions

- In the pooled, placebo-controlled studies, the proportion of patients with serious cardiovascular reactions was 1.7% and 1.3% in the rituximab and placebo treatment groups, respectively. Three cardiovascular deaths occurred during the double-blind period of the RA studies including all rituximab regimens (3/769=0.4%) as compared to none in the placebo treatment group (0/389)
- In the experience with rituximab in 2578 RA patients, the rate of serious cardiac reactions was 1.93 per 100 patient-years. The rate of myocardial infarction (MI) was 0.56 per 100 patient-years (28 events in 26 patients), which is consistent with MI rates in the general RA population. These rates did not increase over 3 courses of rituximab
- Since patients with RA are at increased risk for cardiovascular events compared with the general population, patients with RA should be monitored throughout the infusion and RUXIENCE should be discontinued in the event of a serious or life-threatening cardiac event

Continued on the next page

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IMPORTANT SAFETY INFORMATION (Continued)

Hypophosphatemia and Hyperuricemia

- In the pooled, placebo-controlled studies, newly occurring hypophosphatemia (<2.0 mg/dL) was observed in 12% (67/540) of patients on rituximab vs 10% (39/398) of patients on placebo. Hypophosphatemia was more common in patients who received corticosteroids. Newly occurring hyperuricemia (>10 mg/dL) was observed in 1.5% (8/540) of patients on rituximab vs 0.3% (1/398) of patients on placebo

Retreatment in Patients With RA

- In the experience with rituximab in RA patients, 2578 patients have been exposed to rituximab and have received up to 10 courses of rituximab in RA clinical trials, with 1890, 1043, and 425 patients having received at least 2, 3, and 4 courses, respectively. Most of the patients who received additional courses did so 24 weeks or more after the previous course and none were retreated sooner than 16 weeks. The rates and types of adverse reactions reported for subsequent courses of rituximab were similar to rates and types seen for a single course of rituximab
- In RA Study 2, where all patients initially received rituximab, the safety profile of patients who were retreated with rituximab was similar to those who were retreated with placebo

Immunogenicity

- A total of 273/2578 (11%) patients with RA tested positive for antirituximab antibodies at any time after receiving rituximab. Antirituximab antibody positivity was not associated with increased rates of infusion-related reactions or other adverse events. Upon further treatment, the proportions of patients with infusion-related reactions were similar between antirituximab antibody–positive and –negative patients, and most reactions were mild to moderate. Four antirituximab antibody–positive patients had serious infusion-related reactions, and the temporal relationship between antirituximab antibody positivity and infusion-related reaction was variable

Clinical Trials Experience in GPA and MPA

- Adverse reactions reported in ≥15% of rituximab-treated patients were infections, nausea, diarrhea, headache, muscle spasms, anemia, and peripheral edema (other important adverse reactions include infusion-related reactions)

Induction Treatment of Patients With Active GPA/MPA (GPA/MPA Study 1) Infusion-Related Reactions

- In GPA/MPA Study 1, 12% vs 11% (rituximab-treated vs cyclophosphamide-treated, respectively) of patients experienced at least one infusion-related reaction. Infusion-related reactions included cytokine release syndrome, flushing, throat irritation, and tremor. In the rituximab group, the proportion of patients experiencing an infusion reaction was 12%, 5%, 4%, and 1% following the first, second, third, and fourth infusions, respectively. Patients were premedicated with antihistamine and acetaminophen before each rituximab infusion and were on background oral corticosteroids, which may have mitigated or masked an infusion-related reaction; however, there is insufficient evidence to determine whether premedication diminishes the frequency or severity of infusion-related reactions

Infections

- In GPA/MPA Study 1, 62% vs 47% (rituximab-treated vs cyclophosphamide-treated, respectively) of patients experienced an infection by month 6. The most common infections in the rituximab group were upper respiratory tract infections, urinary tract infections, and herpes zoster. The incidence of serious infections was 11% vs 10% (rituximab-treated vs cyclophosphamide-treated, respectively), with rates of approximately 25 and 28 per 100 patient-years, respectively. The most common serious infection was pneumonia

Hypogammaglobulinemia

- Hypogammaglobulinemia (IgA, IgG, or IgM below the lower limit of normal) has been observed in patients with GPA and MPA treated with rituximab in GPA/MPA Study 1. At 6 months, in the rituximab group, 27%, 58%, and 51% of patients with normal immunoglobulin levels at baseline had low IgA, IgG, and IgM levels, respectively, compared to 25%, 50%, and 46% in the cyclophosphamide group

Immunogenicity

- A total of 23/99 (23%) rituximab-treated adult patients with GPA or MPA tested positive for antirituximab antibodies by 18 months in GPA/MPA Study 1. The clinical relevance of antirituximab antibody formation in rituximab-treated adult patients is unclear

Continued on the next page

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You may also visit www.pfizerencompass.com.

IMPORTANT SAFETY INFORMATION (Continued)

Treatment of Patients With GPA/MPA Who Have Achieved Disease Control With Induction Treatment (GPA/MPA Study 2)

- In GPA/MPA Study 2, the safety profile was consistent with the known safety profile of rituximab in immunologic indications

Infusion-Related Reactions (IRR)

- In GPA/MPA Study 2, 7/57 (12%) patients in the non-US-licensed approved rituximab arm reported infusion-related reactions. The incidence of IRR symptoms was highest during or after the first infusion (9%) and decreased with subsequent infusions (<4%). One patient had 2 serious IRRs; 2 IRRs led to a dose modification; and no IRRs were severe, fatal, or led to withdrawal from the study

Infections

- In GPA/MPA Study 2, 30/57 (53%) patients in the non-US-licensed approved rituximab arm and 33/58 (57%) in the azathioprine arm reported infections. The incidence of all-grade infections was similar between the arms. The incidence of serious infections was similar in both arms (12%). The most commonly reported serious infection in the group was mild or moderate bronchitis

INDICATIONS

- Non-Hodgkin's Lymphoma (NHL)
  RUXIENCE® (rituximab-pvvr) 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)
  - In combination with fludarabine and cyclophosphamide (FC), for the treatment of adult patients with previously untreated and previously treated CD20-positive CLL
- Rheumatoid Arthritis (RA)
  - In combination with methotrexate (MTX), for the treatment of adult patients with moderately to severely active RA who have had an inadequate response to one or more tumor necrosis factor (TNF) antagonist therapies
- Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA) in adult patients in combination with glucocorticoids

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