Guide for healthcare professionals

WHAT YOU SHOULD KNOW ABOUT RUXIENCE®* (rituximab)

Important information to assist healthcare professionals in:

- Communicating risk of progressive multifocal leukoencephalopathy (PML) and infections to patients receiving RUXIENCE® therapy for non-oncology indications
- Caring for patients receiving RUXIENCE® therapy

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

*This educational material is provided by Pfizer and is mandatory as a condition of the Marketing Authorisation in order to further minimise important selected risks.

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ABOUT THIS GUIDE

This guide is intended to summarise Important Safety Information about RUXIENCE® when it is used in all indications. This information is intended to assist healthcare professionals in communicating key safety messages to-and caring for-patients receiving RUXIENCE® therapy.

DURING OR AFTER ADMINISTRATION OF RUXIENCE® THERAPY

Patients should be advised of the potential benefits and risks of treatment with RUXIENCE®. Patients should be closely monitored during administration of RUXIENCE® in an environment where full resuscitation facilities are immediately available. Use of RUXIENCE® in all indications may be associated with an increased risk of infections, including PML.1

Patients with non oncology indications treated with RUXIENCE® must be given the RUXIENCE® Patient Alert Card with each infusion. The Alert Card contains Important Safety Information regarding potential increased risk of infections, including PML. Please familiarise yourself with the Patient Alert Card. Since it does not contain all of the information about this product, you should always consult the Summary of Products Characteristics (SmPC) before prescribing, preparing, or administering RUXIENCE®. RUXIENCE® SmPC is available on the European Medicines Agency website: https://www.ema.europa.eu/en/documents/product-information/ruxience-epar-product-information_en.pdf

PML

About PML

PML is a rare, progressive, demyelinating disease of the central nervous system that can lead to severe disability or death.[2] PML is caused by activation of the John Cunningham (JC) virus, a polyomavirus that is widely latent in the general population.[2] The JC virus usually only causes PML in immunocompromised patients.[3] The factors leading to activation of a latent infection are not fully understood.[2]

RUXIENCE® and PML in non-oncology indications

A small number of confirmed cases of PML, some of which were fatal, have been reported worldwide in patients who have been prescribed RUXIENCE® for non-oncology indications. These patients had received immunosuppressant therapy before or during their RUXIENCE® treatment. Most patients were diagnosed with PML within 1 year of their last infusion of RUXIENCE®. However, patients should be monitored for up to 2 years after treatment. It is not clear how RUXIENCE® affects the development of PML, but evidence suggests that some patients who receive RUXIENCE® may develop PML.

WHAT TO TELL YOUR PATIENTS

- Some patients treated with RUXIENCE® have developed a serious brain infection called PML, which, in some cases, has been fatal.
- Patients should carry the RUXIENCE® Patient Alert Card with them at all times. The Patient Alert Card will be given to them at each infusion.
- Patients should tell their partners or caregivers about the symptoms to look out for.
- Patients should contact their doctor, pharmacist, or nurse immediately if they experience any of the following signs or symptoms suggestive of PML:
  - Confusion, memory loss, or problems thinking straight.
  - Loss of balance or a change in the way they walk or talk.
  - Loss of strength or weakness on one side of the body.
  - Blurred vision or loss of vision.

PATIENT MONITORING

Monitor patients for any new or worsening neurological symptoms or signs suggestive of PML during treatment with RUXIENCE® and for up to 2 years after treatment. In particular, look out for symptoms and signs patients themselves may not notice, such as cognitive, neurological, or psychiatric symptoms. Assess patients promptly to determine if the symptoms are indicative of neurological dysfunction and if they are suggestive of PML.

SUSPECTED PML

Suspend further dosing of RUXIENCE® until PML has been excluded.
To confirm diagnosis, consultation with a neurologist and further evaluation-including an MRI scan (preferably with contrast), cerebrospinal fluid testing for JC viral DNA, and repeat neurological assessments-are recommended.

DIAGNOSED PML

RUXIENCE® must be permanently discontinued.[1]

Stabilisation or improved outcome has been seen following reconstitution of the immune system in immunocompromised patients with PML.

It is unknown if early detection of PML and suspension of RUXIENCE® therapy may lead to similar stabilisation or improved outcome in patients treated with RUXIENCE®.

RUXIENCE® should be administered as an intravenous (IV) infusion only to avoid administration route error.

INFECTIONS

Tell patients to contact their doctor, pharmacist, or nurse immediately if they experience any of the following signs of possible infection:

- Fever.
- Persistent cough.
- Pain when they have not hurt themselves.
- Feeling generally unwell, tired, or lethargic.
- Burning pain when passing urine.

Patients reporting signs of infection following RUXIENCE® therapy should be promptly evaluated and treated appropriately. Before giving further RUXIENCE® treatment, re-evaluate patients for any potential risk of infections, as indicated under "Do not give RUXIENCE® to patients who" and "Take special care before you give RUXIENCE® to patients who" headings.

DO NOT GIVE RUXIENCE® TO PATIENTS WHO:

- Are allergic to rituximab or to any of the other ingredients.
- Are allergic to murine proteins.
- Have an active severe infection, such as tuberculosis, sepsis, hepatitis, or an opportunistic infection.
- Are severely immunocompromised, eg, levels of CD4 or CD8 are very low.

TAKE SPECIAL CARE BEFORE YOU GIVE RUXIENCE® TO PATIENTS WHO:

- Have signs of an infection – signs may include fever, cough, headache, or feeling generally unwell.
- Have an active infection or are being treated for an infection.
- Have a history of recurring, chronic, or severe infections.
- Have, or have ever had, viral hepatitis or any other hepatic disease.
- Are taking, or have ever taken, medicines that may affect their immune system, such as chemotherapy or immunosuppressants.
- Are taking, or have recently taken, any other medicines (including those they have bought from a pharmacy, supermarket, or health store).
- Have recently received a vaccination or are planning to have one.
- Are taking medicines for high blood pressure.
- Are pregnant, trying to become pregnant, or are breastfeeding.
- Have heart disease or have received cardiotoxic chemotherapy.
- Have breathing problems.
- Have an underlying condition which may further predispose them to a serious infection (such as hypogammaglobulinaemia).

FURTHER INFORMATION

Consult the SmPC before prescribing, preparing, or administering RUXIENCE®.
RUXIENCE® SmPC is available on the European Medicines Agency website: https://www.ema.europa.eu/en/documents/product-information/ruxience-epar-product-information_en.pdf.

If you have any questions or problems, contact Pfizer.

REFERENCES

1. RUXIENCE® Summary of Product Characteristics. Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 Bruxelles, Belgium.

2. Calabrese LH, Molloy ES, Huang D, Ransohoff RM. Progressive multifocal leukoencephalopathy in rheumatic diseases: evolving clinical and pathologic patterns of disease. *Arthritis Rheum*. 2007;56(7):2116–2128.

3. Egli A, Infanti L, Dumoulin A, et al. Prevalence of polyomavirus BK and JC infection and replication in 400 healthy blood donors. J Infect Dis. 2009;199(6):837–846.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any Suspected Adverse Drug Reactions (side effects) or medication errors using:

ADR Reporting

The Medicines Authority ADR reporting form, which is available online at http://www.medicinesauthority.gov.mt/adrportal, and sent by post or email to;

P: Pharmacovigilance Section at Post-Licensing Directorate, Medicines Authority, Sir Temi Zammit Buildings, Malta Life Sciences Park, San Gwann SGN 3000

E: postlicensing.medicinesauthority@gov.mt

Alternatively, you may also report such events promptly to Pfizer at Pfizer Hellas S.A., 243 Messoghion Ave. N.Psychiko, Athens GR-15451, Greece. Pfizer Hellas Pharmacovigilance Department contact details: +30 210 67 85 908 and +30 210 67 85 808 (24hour line), fax: +30 210 81 99 096, or via the webportal Pfizer's Adverse Event Reporting Portal (pfizersafetyreporting.com). Healthcare professionals should report adverse events or reactions by brand name and batch number.