Important information about MabThera® to assist healthcare professionals*

KEY MESSAGES FOR HEALTH CARE PROFESSIONALS

- Use of MabThera may be associated with an increased risk of infections or Progressive Multifocal Leukoencephalopathy (PML).

KEY ACTIONS FOR HEALTH CARE PROFESSIONALS TO THEIR PATIENTS

- All patients treated with MabThera for non-oncology indications must be given the patient alert card with each infusion.
- Advise patients (or parents/legal guardians of paediatric patients) on the risk of infections and PML, including the symptoms to be aware of and the need to contact their doctor immediately if they experience any, and provide patients with the Educational Material for patients at each infusion.
- Check for infections, for immunosuppression, for prior/current medication affecting the immune system and recent history of, or planned, vaccination, prior to MabThera treatment.
- Supervise closely patients during administration in an environment where full resuscitation facilities are immediately available.
- Monitor patients for infections, especially PML, during and after MabThera treatment.

You should always consult the Summary of Products Characteristics (SmPC) before prescribing, preparing or administering MabThera.

About PML

PML is a rare, progressive, demyelinating disease of the central nervous system that can lead to severe disability or be fatal[1]. PML is caused by activation of the JC (John Cunningham) virus, a polyomavirus that is latent in up to 70% of healthy adults[1]. The JC virus usually only causes PML in immunocompromised patients[2]. The factors leading to activation of a latent infection are not fully understood.
It is not well understood how MabThera may affect the development of PML, however very rarely (<1/10'000 patients), confirmed cases of PML, some of which were fatal, have been reported worldwide in patients treated with MabThera for non-oncology diseases. Most cases of PML were diagnosed within 1 year of their last infusion of MabThera, however patients should be monitored for up to 2 years after treatment.

For additional information on PML, consult the references at the end of this brochure[2,3,4].

What to consider during and/or after treatment with MabThera

Monitor patients for any new or worsening neurological symptoms or signs suggestive of PML during treatment with MabThera and for up to 2 years following discontinuation of the treatment. To confirm diagnosis, consultation with a neurologist and further evaluation including a MRI scan (preferably with contrast), cerebrospinal fluid testing for JC viral DNA and repeat neurological assessments are recommended.

- **Suspected PML:** Suspend further dosing of MabThera until PML has been excluded.
- **Diagnosed PML:** MabThera must be permanently discontinued.

What to tell your patient

PML

- Very rarely patients treated with MabThera for RA, GPA or MPA have developed a serious brain infection called PML, which in some cases has been fatal.

- To carry the MabThera Patient Alert Card with them at all times, which contains important safety information regarding the risk of infections, including PML. The Patient Alert Card will be given to them at each infusion.

- To 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
  - loss of balance or a change in the way they walk or talk
  - decreased strength or weakness on one side of the body
  - blurred vision or loss of vision.

- Advise patient to tell their carers or relatives about the symptoms to look out for, as these might not be recognized directly by patients.

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, weight loss, pain when they have not hurt themselves, feeling generally unwell, tired or low in energy, burning pain when passing urine.

What to consider before giving Mabthera treatment

Patients should be **evaluated for any potential risk of infections** before initiating and before giving further MabThera treatment, as indicated below:

Do not give MabThera to patients who:

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

Take special care before you give MabThera 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 which 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).

Carefully follow the guidance provided in the label in these situations.

Further information

In case of any adverse events – including any possible side effects not listed in the leaflet – or product complaints associated with the use of any Roche products, please talk to the HCP or report the details in accordance with the national requirements via the national spontaneous reporting systems to:

The National Pharmacovigilance Centre (NPC)
Land Line: 19999.
Fax: +966112057662
Email: npc.drug@sfda.gov.sa

Roche Products Saudi Arabia L.L.C.
Direct Tel. +966 12211 4618
Mobile: +966 5678 44 692
Email: jeddah.drug_safety@roche.com

Company contact point

Should you have any questions regarding the use of ROCHE PRODUCT, please feel free to contact us at jeddah.medinfo@roche.com

Roche Products Saudi Arabia

This document has been reviewed and approved by The Saudi Food and Drug Authority (SFDA)

1. Calabrese LH et al. Progressive multifocal leukoencephalopathy in rheumatic diseases: evolving clinical and pathologic patterns of disease. Arthritis Rheum 2007; 56: 2116-2128.
2. Kartau M et al. Progressive Multifocal Leukoencephalopathy: Current Insights. Degener Neurol Neuromuscul Dis. 2019; 9:109-121.
3. Snopková S et al. Progressive multifocal leukoencephalopathy - epidemiology, immune response, clinical differences, treatment. Epidemiol Mikrobiol Imunol. 2019; 68 :24-31.
4. Berger JR et al., Progressive multifocal leukoencephalopathy in rituximab-treated rheumatic diseases: a rare event. J Neurovirol. 2018; 24: 323-331.