Information to assist healthcare professionals in caring for patients receiving Truxima® therapy for non-oncology indications

About this guide
This guide is intended to present important safety information including the risk of infections and progressive multifocal leukoencephalopathy (PML) associated with the use of Truxima® in non-oncology diseases, and to provide important patient counselling information to assist healthcare professionals in caring for patients receiving Truxima® therapy. It does not contain all information about this product. You should always consult the Summary of Product Characteristics before prescribing, preparing or administering Truxima®.

Truxima® in rheumatoid arthritis: indications and usage
Truxima® in combination with methotrexate (MTX) is indicated for the treatment of adult patients with severe active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to other disease-modifying anti-rheumatic drugs (DMARDs), including one or more tumor necrosis factor (TNF) inhibitor therapies.[1]
Rituximab® has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function when given in combination with MTX.[1]
The efficacy and safety of rituximab in alleviating the symptoms of RA in patients with an inadequate response to TNF inhibitors was demonstrated in a pivotal randomized, controlled, double-blind, multicenter study. Eligible patients had active RA, diagnosed according to the criteria of the American College of Rheumatology (ACR). Structural joint damage was assessed radiographically and expressed as change in modified total Sharp score and its components, the erosion score and joint space narrowing score.[1]

Truxima® in granulomatosis with polyangiitis or microscopic polyangiitis: indications and usage
Truxima®, in combination with glucocorticoids, is indicated for the induction of remission in adult patients with severe, active granulomatosis with polyangiitis (Wegener's) (GPA) and microscopic polyangiitis (MPA).[1]
The efficacy and safety of rituximab in GPA and MPA was determined in a randomized, active-comparator, double-blind study in patients with severe, active GPA or MPA. The primary objective of the study was to determine if rituximab plus glucocorticoids was non-inferior to conventional therapy in the induction of complete remission, defined as a Birmingham Vasculitis Activity Score for Wegener's granulomatosis (BVAS/WG) of 0 and off glucocorticoid therapy at 6 months.[1]

Prior to administering Truxima® therapy
Before you administer Truxima® ask and/or check if the patient:
- Is allergic to Truxima® or to any of the excipients or to murine proteins.
- Has an active, severe infection or severely decreased immune system function.
- Has had or now has viral hepatitis or any other hepatic disease.
- Is taking or has previously taken medicines which may affect the immune system, such as chemotherapy or immunosuppressive agents.
- Have an underlying condition that may further predispose them to serious infection (such as hypogammaglobulinaemia).
- Has signs of an infection, such as a fever, cough or headache, or is feeling unwell.
- Has an infection, is being treated for an infection or has a history of recurring, chronic or severe infections.
- Has recently received a vaccination or is scheduled for any vaccination.
- Is taking or has recently taken any other medicines (including those they have bought from pharmacy, supermarket or health store).
- Is pregnant or wants to become pregnant, or is breastfeeding.
- Is taking treatment for high blood pressure.
- Has a history of cardiac disease and/or cardiotoxic chemotherapy or a history of breathing problems.

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During or after administration of Truxima® therapy
- Patients should be closely monitored during administration of Truxima® in an environment where full resuscitation facilities are immediately available.
- Medicinal products for the treatment of hypersensitivity reactions, e.g., epinephrine (adrenaline), antihistamines and glucocorticoids, should be available for immediate use in the event of an allergic reaction during administration of Truxima®.
- Use of Truxima® may be associated with an increased risk of infections.
- Patients reporting signs and symptoms of infection following Truxima® therapy should be promptly evaluated and treated appropriately. Before giving a subsequent course of Truxima® treatment, patients should be reevaluated for any potential risk of infections.
- Use of Truxima® may be associated with an increased risk of progressive multifocal leukoencephalopathy (PML). Patients must be monitored regularly for any new or worsening of neurological symptoms or signs suggestive of PML.
  - Cases of PML with fatal outcome have been reported following use of Truxima® for the treatment of autoimmune diseases (see following pages).

- Inform patients of the importance of seeking medical attention immediately if they experience any of these symptoms after their Truxima® treatment:
- Symptoms of an infection, for example fever, persistent cough, weight loss or listlessness.
- 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.

Progressive multifocal leukoencephalopathy
As described in the Summary of Product Characteristics[1], use of Truxima® may be associated with an increased risk of PML.

About PML
PML is a rare, progressive, demyelinating disease of the central nervous system that can lead to death or severe disability.[2] PML is caused by activation of the JC (John Cunningham) virus, a polyomavirus that resides in latent form in up to %70 of healthy adults.[3] The JC virus typically only causes PML in immunocompromised patients.[2] The factors leading to activation of latent infection are not fully understood.

Truxima® and PML in non-oncology diseases
A small number of confirmed cases of PML have been reported worldwide in patients who have been treated with rituximab for the indications of RA and GPA/ MPA in addition to some other diseases. The patients had received prior or concurrent immunosuppressive therapy. Most cases of PML were diagnosed within 12 months of their last infusion of rituximab.
While the potential role of Truxima® in the development of PML is unclear, the information to date suggests that some patients who receive Truxima® have an increased risk of PML.

PML: patient counselling information
- Patients should be advised of the potential benefits and risks of treatment with Truxima®.
- Inform patients that very rarely, some patients taking Truxima® have had a serious brain infection, which in many cases has been fatal.
- Instruct the patient to contact their doctor or nurse immediately if they experience memory loss, trouble thinking, difficulty with walking and/or loss of vision.

All patients treated with Truxima® for RA, GPA or MPA must be given the Truxima® Patient Alert Card with each infusion. The Alert Card contains

important safety information regarding potential increased risk of infections, including PML.
Inform the patient of the importance of keeping the Alert Card with them at all times and of telling their partner or caregiver about their treatment, as they may notice symptoms that the patient is not aware of.

PML: patient monitoring
Patients must be monitored at regular intervals for any new or worsening of neurological symptoms or signs that may be suggestive of PML. The physician should be particularly alert to symptoms suggestive of PML that the patient may not notice - for example, cognitive, neurological or psychiatric symptoms.
The physician should evaluate the patient to determine if the symptoms are indicative of neurological dysfunction and if so, whether these symptoms are possibly suggestive of PML.
If PML is suspected, further dosing must be suspended until PML has been excluded.
If any doubt exists, consultation with a neurologist is recommended and further evaluation, including an MRI scan (preferably with contrast), cerebrospinal fluid testing for JC viral DNA and repeat neurological assessments, should be considered.
If a patient develops PML, the dosing of Truxima® must be permanently discontinued.
Following reconstitution of the immune system in immunocompromised patients with PML, stabilization or improved outcome has been seen. It remains unknown if early detection of PML and suspension of Truxima® therapy may lead to similar stabilization or improved outcome.

Other infections
Serious infections, including fatal infections, can occur during therapy with Truxima®. Truxima® should not be administered to patients with an active, severe infection (e.g. tuberculosis, sepsis, hepatitis or opportunistic infections) or severely immunocompromised patients (e.g. where levels of CD4 or CD8 are very low). Physicians should exercise caution when considering the use of Truxima® in patients with a history of recurring or chronic infections (e.g. hepatitis B) or with underlying conditions which may further predispose patients to serious infection (e.g. hypogammaglobulinaemia). It is recommended that immunoglobulin levels are determined prior to initiating treatment with Truxima®.

Further information
Consult the Summary of Product Characteristics before prescribing, preparing or administering Truxima®. If you have any questions, require further information please contact: Abdulkareem bin Mubarak
Mobile phone: +966550017554. Email: SAPV@hikma.com

Truxima® (rituximab)
▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information.
Healthcare professionals are encouraged to report any adverse reactions related to mentioned medications to the National Pharmacovigilance and Drug Safety Centre (NPC). Channels for reporting Adverse Drug Reactions exist, mentioned below, and it is encouraged to use them and report as soon you so experiecne or become aware of one.
The National Pharmacovigilance Center (NPC)
Fax: +966-11-205-7662
SFDA Call Center: 19999
Email: npc.drug@sfda.gov.sa
Website: https://ade.sfda.govs.sa/
And to: Company contact point: Abdulkareem bin Mubarak
Mobile: +966550017554.Telephone: 00966114173731 Ext. 1086
Email: SAPV@hikma.com

References
1. Hikma Pharmaceuticals. Truxima® concentrate for solution for infusion Summary of Product Characteristics November 2017.
2. Calabrese LH, et al. Arthritis Rheum 2007;56:2116-2128.
3. Egli A, et al. J Infect Dis 2009;199:837-846.

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Truxima®
Rituximab

Physician Information Booklet

Important information about
Truxima® (rituximab)

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