אוגוסט 2026

רופא/ה, רוקח/ת נכבד/ה,

חברת פאדאגיס ישראל סוכנויות בע"מ מבקשת להודיע על שינוי התוויה ומשטר מינון בהתאם, כפי שאושרו ע"י משרד הבריאות עבור התכשיר מטה וכן על עדכון העלון לרופא של התכשיר:

שם התכשיר: **TRUXIMA / טרוקסימה**

החומר הפעיל בתכשיר וחוזקו: Rituximab 10 mg/ml

צורת מינון ודרך מתן: Concentrate for solution for infusion , Intravenous (I.V.)

פרזנטציות: 1 vial x 50 ml, 2 vials x 10 ml

ההתוויה הרשומה לתכשיר בישראל:
Truxima is indicated in adults for the following indications:

Non-Hodgkin's lymphoma (NHL)
Truxima is indicated for the treatment of patients with relapsed or refractory low-grade or follicular, B-cell non-Hodgkin's lymphoma. Truxima is indicated for the treatment of previously untreated patients with low-grade or follicular lymphoma in combination with chemotherapy. Truxima is indicated for the treatment of patients with CD20 positive diffuse large B-cell non-Hodgkin's lymphoma in combination with CHOP chemotherapy. Truxima maintenance therapy is indicated for the treatment of follicular lymphoma patients responding to induction therapy.

Chronic lymphocytic leukaemia (CLL)
Truxima in combination with chemotherapy is indicated for the treatment of patients with previously untreated and relapsed/refractory CLL. Only limited data are available on efficacy and safety for patients previously treated with monoclonal antibodies including rituximab or patients refractory to previous rituximab plus chemotherapy.

Rheumatoid arthritis
Truxima is indicated, in combination with methotrexate, to reduce signs and symptoms in adult patients with moderately to severely active rheumatoid arthritis who had an inadequate response or intolerance to one or more TNF antagonist therapies.

Granulomatosis with polyangiitis and microscopic polyangiitis
Truxima, in combination with glucocorticoids, is indicated for the treatment of adult patients with granulomatosis with polyangiitis (GPA) (Wegener’s Granulomatosis (WG)) and microscopic polyangiitis (MPA).

Pemphigus vulgaris
Truxima is indicated for the treatment of adult patients with moderate to severe pemphigus vulgaris (PV).

בהודעה זו מצוינים השינויים המהותיים בלבד ברקע צהוב הנוגעים לשינוי ההתוויה ומשטר המינון שאושרו ע"י משרד הבריאות וכן עדכוני בטיחות ועדכוני נוסח בהתאם לעלון האסמכתא של תכשיר הייחוס כפי שעודכן בישראל במאי 2026. ישנם עדכונים נוספים שלא מופיעים בהודעה זו. עדכונים ספציפיים לתכשיר טרוקסימה עפ"י עלון EMA סומנו ברקע אפור.

העלון המעודכן לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות:
https://israeldrugs.health.gov.il/#!/byDrug

בברכה,
פאדאגיס ישראל סוכנויות בע"מ

Padagis®

עלון לרופא

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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Pemphigus vulgaris

Truxima is indicated for the treatment of adult patients with moderate to severe pemphigus vulgaris (PV).

4.2 Posology and method of administration

[…]

Rheumatoid arthritis, granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), and pemphigus vulgaris

In patients with rheumatoid arthritis or pemphigus vulgaris, premedication with 100 mg intravenous methylprednisolone should be completed 30 minutes prior to Truxima infusions to decrease the incidence and severity of infusion related reactions (IRRs).

[…]

Posology

[…]

Rheumatoid arthritis

A course of Truxima consists of two 1000 mg intravenous infusions. The recommended dosage of Truxima is 1000 mg by intravenous infusion followed by a second 1000 mg intravenous infusion two weeks later.

Subsequent courses should be administrated every 24 weeks or based on clinical evaluation, but not sooner than every 16 weeks.

Available data suggest that clinical response is usually achieved within 16 - 24 weeks of an initial treatment course. Continued therapy should be carefully reconsidered in patients who show no evidence of therapeutic benefit within this time period.

[…]

Method of administration

[…]

Non-Hodgkin's lymphoma, chronic lymphocytic leukaemia, rheumatoid arthritis, pemphigus vulgaris, granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA)

[…]

Rheumatoid arthritis

Alternative subsequent, faster, infusion schedule

If patients did not experience a serious infusion related reaction with their first or subsequent infusions

of a dose of 1000 mg Truxima administered over the standard infusion schedule, a more rapid infusion can be administered for second and subsequent infusions using the same concentration as in previous infusions (4 mg/mL in a 250 mL volume). Initiate at a rate of 250mg/hour for the first 30 minutes and then 600 mg/hour for the next 90 minutes. If the more rapid infusion is tolerated, this infusion schedule can be used when administering subsequent infusions.

Patients who have clinically significant cardiovascular disease, including arrhythmias, or previous serious infusion reactions to any prior biologic therapy or to rituximab, should not be administered the more rapid infusion.
[…]

4.3 Contraindications
[…]
Severe heart failure (New York Heart Association Class IV) or severe, uncontrolled cardiac disease for use in rheumatoid arthritis, granulomatosis with polyangiitis, microscopic polyangiitis and pemphigus vulgaris only (see section 4.4 regarding other cardiovascular diseases).

4.4 Special warnings and precautions for use
[…]
Progressive multifocal leukoencephalopathy (PML)
Very rare cases of fatal PML have been reported following use of rituximab for the treatment of rheumatoid arthritis and autoimmune diseases [including Systemic Lupus Erythematosus (SLE) and vasculitis] and during post-marketing use of rituximab in NHL and CLL (where the majority of patients had received rituximab in combination with chemotherapy or as part of haematopoietic stem cell transplant).
[…]
Immunisations
[…]
Rheumatoid arthritis, granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), and pemphigus vulgaris
Methotrexate (MTX) naïve populations with rheumatoid arthritis
The use of Truxima is not recommended in MTX-naïve patients since a favourable benefit risk relationship has not been established.

Infusion related reactions
[…]
Severe IRRs with fatal outcome have been reported in rheumatoid arthritis patients in the post-marketing setting. In rheumatoid arthritis most infusion-related events reported in clinical trials were mild to moderate in severity.
[…]
IRRs in patients with GPA, MPA and pemphigus vulgaris were consistent with those seen for rheumatoid arthritis patients in clinical trials and in the post-marketing setting (see section 4.8).
[…]

Immunisation
[…]
Patients treated with rituximab may receive non-live vaccinations; however, response rates to non-live vaccines may be reduced. In a randomised trial, patients with rheumatoid arthritis treated with rituximab and methotrexate had comparable response rates to tetanus recall antigen (39% vs. 42%), reduced rates to pneumococcal polysaccharide vaccine (43% vs. 82% to at least 2 pneumococcal antibody serotypes), and KLH neoantigen (47% vs. 93%), when given 6 months after rituximab as compared to patients only receiving methotrexate. Should non-live vaccinations be required whilst receiving rituximab therapy, these should be completed at least 4 weeks prior to commencing the next course of rituximab.

In the overall experience of rituximab repeat treatment over one year in rheumatoid arthritis, the proportions of patients with positive antibody titres against S. pneumoniae, influenza, mumps, rubella, varicella and tetanus toxoid were generally similar to the proportions at baseline.

Concomitant/sequential use of other DMARDs in rheumatoid arthritis

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The concomitant use of Truxima and anti-rheumatic therapies other than those specified under the rheumatoid arthritis indication and posology is not recommended.

There are limited data from clinical trials to fully assess the safety of the sequential use of other DMARDs (including TNF inhibitors and other biologics) following rituximab (see section 4.5). The available data indicate that the rate of clinically relevant infection is unchanged when such therapies are used in patients previously treated with rituximab, however patients should be closely observed for signs of infection if biologic agents and/or DMARDs are used following Truxima therapy.

[…]

Excipients

[…]

This medicine contains 7~~.0~~ mg of polysorbate 80 (E433) in ~~each~~ 10 mL vial~~, which is equivalent to 0.7 mg/mL~~ and 35~~.0~~ mg of polysorbate 80 (E433) in ~~each~~ 50 mL vial, which is equivalent to 0.7 mg/mL (for 10 mL vial) and 3.5 mg/mL (for 50 mL/vial).

Polysorbates may cause allergic reactions.

[…]

4.5 Interaction with other medicinal products and other forms of interaction

[…]

Co-administration with methotrexate had no effect on the pharmacokinetics of rituximab in rheumatoid arthritis patients.

[…]

In patients with rheumatoid arthritis, 283 patients received subsequent therapy with a biologic DMARD following rituximab. In these patients the rate of clinically relevant infection while on rituximab was 6.01 per 100 patient years compared to 4.97 per 100 patient years following treatment with the biologic DMARD.

4.8 Undesirable effects

[…]

Table 1 Adverse reactions reported in clinical trials or during post-marketing surveillance in patients with NHL and CLL disease treated with rituximab monotherapy/maintenance or in combination with chemotherapy

MedDRA System Organ Class	Very Common	Common	Uncommon	Rare	Very Rare	Not known
Infections and infestations	bacterial infections, viral infections, [+]bronchitis	sepsis, [+]pneumonia, [+]febrile infection, [+]herpes zoster, [+]respiratory tract infection, fungal infections, infections of unknown aetiology, [+]acute bronchitis, [+]sinusitis, hepatitis B[1]		serious viral infection[2], Pneumocystis jirovecii pneumonia	progressive multifocal leukoencephalopathy	enteroviral meningoencephalitis[2,3]

[…]

Experience from rheumatoid arthritis

Summary of the safety profile

The overall safety profile of rituximab in rheumatoid arthritis is based on data from patients from clinical trials and from post-marketing surveillance.

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The safety profile of rituximab in patients with moderate to severe rheumatoid arthritis (RA) is summarised in the sections below. In clinical trials more than 3100 patients received at least one treatment course and were followed for periods ranging from 6 months to over 5 years; approximately 2400 patients received two or more courses of treatment with over 1000 having received 5 or more courses. The safety information collected during post marketing experience reflects the expected adverse reaction profile as seen in clinical trials for rituximab (see section 4.4).

Patients received 2 x 1000 mg of rituximab separated by an interval of two weeks; in addition to methotrexate (10-25 mg/week). Rituximab infusions were administered after an intravenous infusion of 100 mg methylprednisolone; patients also received treatment with oral prednisone for 15 days.

Tabulated list of adverse reactions

Adverse reactions are listed in Table 2. Frequencies are defined as very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥ 1/10,000 to < 1/1000), very rare (<1/10,000) and not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

The adverse reactions identified only during post marketing surveillance, and for which a frequency could not be estimated, are listed under "not known", see footnotes.

The most frequent adverse reactions considered due to receipt of rituximab were IRRs. The overall incidence of IRRs in clinical trials was 23% with the first infusion and decreased with subsequent infusions. Serious IRRs were uncommon (0.5% of patients) and were predominantly seen during the initial course. In addition to adverse reactions seen in RA clinical trials for rituximab, progressive multifocal leukoencephalopathy (PML) (see section 4.4) and serum sickness-like reaction have been reported during post marketing experience.

Table 2 Summary of adverse reactions reported in clinical trials or during post-marketing surveillance occurring in patients with rheumatoid arthritis receiving rituximab

MedDRA System Organ Class	Very Common	Common	Uncommon	Rare	Very rare	Not known
Infections and infestations	upper respiratory tract infection, urinary tract infections	bronchitis, sinusitis, gastroenteritis, tinea pedis			progressive multifocal leukoencephalopathy, reactivation of hepatitis B	serious viral infection[1,2], enteroviral meningoencephalitis[2]
Blood and lymphatic system disorders		neutropenia[3]		late neutropenia[4]	serum sickness-like reaction	
Immune system disorders	[5]infusion related reactions (hypertension, nausea, rash, pyrexia, pruritus, urticaria, throat irritation, hot flush, hypotension, rhinitis, rigors,		[5]infusion related reactions (generalised oedema, bronchospasm, wheezing, laryngeal oedema, angioneurotic oedema, generalised pruritus, anaphylaxis, anaphylactoi			
General disorders and administration site conditions						

MedDRA System Organ Class	Very Common	Common	Uncommon	Rare	Very rare	Not known
	tachycardia, fatigue, oropharyngeal pain, oedema peripheral, erythema)		d reaction)			
Metabolism and nutrition disorders		hypercholesterolemia				
Psychiatric disorders		depression, anxiety				
Nervous system disorders	headache	paraesthesia, migraine, dizziness, sciatica				
Cardiac disorders				angina pectoris, atrial fibrillation, heart failure, myocardial infarction	atrial flutter	
Gastrointestinal disorders		dyspepsia, diarrhoea, gastro-oesophageal reflux, mouth ulceration, upper abdominal pain				
Skin and subcutaneous tissue disorders		alopecia			toxic epidermal necrolysis (Lyell's syndrome), Stevens-Johnson syndrome[7]	
Musculoskeletal disorders and connective tissue disorders		arthralgia / musculoskeletal pain, osteoarthritis, bursitis				
Investigations	decreased IgM levels[6]	decreased IgG levels[6]				

MedDRA System Organ Class	Very Common	Common	Uncommon	Rare	Very rare	Not known

[1] See also section infections below.
[2] Observed during post-marketing surveillance
[3] Frequency category derived from laboratory values collected as part of routine laboratory monitoring in clinical trials
[4] Frequency category derived from post-marketing data.
[5] Reactions occurring during or within 24 hours of infusion. See also infusion-related reactions below. IRRs may occur as a result of hypersensitivity and/or to the mechanism of action.
[6] Includes observations collected as part of routine laboratory monitoring.
[7] Includes fatal cases

Multiple courses
Multiple courses of treatment are associated with a similar adverse reaction profile to that observed following first exposure. The rate of all adverse reactions following first rituximab exposure was highest during the first 6 months and declined thereafter. This is mostly accounted for by IRRs (most frequent during the first treatment course), RA exacerbation and infections, all of which were more frequent in the first 6 months of treatment.

Description of selected adverse reactions
Infusion-related reactions
The most frequent adverse reactions following receipt of rituximab in clinical studies were IRRs (refer to Table 2). Among the 3189 patients treated with rituximab, 1135 (36%) experienced at least one IRR with 733/3189 (23%) of patients experiencing an IRR following first infusion of the first exposure to rituximab. The incidence of IRRs declined with subsequent infusions. In clinical trials fewer than 1% (17/3189) of patients experienced a serious IRR. There were no CTC Grade 4 IRRs and no deaths due to IRRs in the clinical trials. The proportion of CTC Grade 3 events and of IRRs leading to withdrawal decreased by course and were rare from course 3 onwards. Premedication with intravenous glucocorticoid significantly reduced the incidence and severity of IRRs (see sections 4.2 and 4.4). Severe IRRs with fatal outcome have been reported in the post-marketing setting.

In a trial designed to evaluate the safety of a more rapid rituximab infusion in patients with rheumatoid arthritis, patients with moderate-to-severe active RA who did not experience a serious IRR during or within 24 hours of their first studied infusion were allowed to receive a 2-hour intravenous infusion of rituximab. Patients with a history of a serious infusion reaction to a biologic therapy for RA were excluded from entry. The incidence, types and severity of IRRs were consistent with that observed historically. No serious IRRs were observed.

Infections
The overall rate of infection reported from clinical trials was approximately 94 per 100 patient years in rituximab treated patients. The infections were predominately mild to moderate and consisted mostly of upper respiratory tract infections and urinary tract infections. The incidence of infections that were serious or required IV antibiotics was approximately 4 per 100 patient years. The rate of serious infections did not show any significant increase following multiple courses of rituximab. Lower respiratory tract infections (including pneumonia) have been reported during clinical trials, at a similar incidence in the rituximab arms compared to control arms.

In the post marketing setting, serious viral infections have been reported in RA patients treated with rituximab. Cases of progressive multifocal leukoencephalopathy with fatal outcome have been reported following use of rituximab for the treatment of autoimmune diseases. This includes rheumatoid arthritis and off-label autoimmune diseases, including Systemic Lupus Erythematosus (SLE) and vasculitis.
In patients with non-Hodgkin's lymphoma receiving rituximab in combination with cytotoxic chemotherapy, cases of hepatitis B reactivation have been reported (see non-Hodgkin's lymphoma). Reactivation of hepatitis B infection has also been very rarely reported in RA patients receiving rituximab (see Section 4.4).

Cardiovascular adverse reactions
Serious cardiac reactions were reported at a rate of 1.3 per 100 patient years in the rituximab treated patients compared to 1.3 per 100 patient years in placebo treated patients. The proportions of patients experiencing cardiac reactions (all or serious) did not increase over multiple courses.

Neurologic events
Cases of posterior reversible encephalopathy syndrome (PRES) / reversible posterior leukoencephalopathy syndrome (RPLS) have been reported. Signs and symptoms included visual disturbance, headache, seizures and altered mental status, with or without associated hypertension. A diagnosis of PRES/RPLS requires confirmation by brain imaging. The reported cases had recognised risk factors for PRES/RPLS, including the patients' underlying disease, hypertension, immunosuppressive therapy and/or chemotherapy.

Neutropenia
Events of neutropenia were observed with rituximab treatment, the majority of which were transient and mild or moderate in severity. Neutropenia can occur several months after the administration of Truxima (see section 4.4).

In placebo-controlled periods of clinical trials, 0.94% (13/1382) of rituximab treated patients and 0.27% (2/731) of placebo patients developed severe neutropenia.

Neutropenic events, including severe late onset and persistent neutropenia, have been rarely reported in the post-marketing setting, some of which were associated with fatal infections.

Skin and subcutaneous tissue disorders
Toxic Epidermal Necrolysis (Lyell's syndrome) and Stevens-Johnson syndrome, some with fatal outcome, have been reported very rarely.

Laboratory abnormalities
Hypogammaglobulinaemia (IgG or IgM below the lower limit of normal) has been observed in RA patients treated with rituximab. There was no increased rate in overall infections or serious infections after the development of low IgG or IgM (see section 4.4).

A small number of spontaneous and literature cases of hypogammaglobulinaemia have been observed in paediatric patients treated with rituximab, in some cases severe and requiring long-term immunoglobulin substitution therapy. The consequences of long term B cell depletion in paediatric patients are unknown.
[…]
Description of selected adverse reactions
Infusion-related reactions
In PV Study 1, infusion-related reactions were common (58%). Nearly all infusion-related reactions were mild to moderate. The proportion of patients experiencing an infusion-related reaction was 29% (11 patients), 40% (15 patients), 13% (5 patients), and 10% (4 patients) following the first, second, third, and fourth infusions, respectively. No patients were withdrawn from treatment due to infusion-related reactions. Symptoms of infusion-related reactions were similar in type and severity to those seen in RA and GPA/MPA patients.
[…]