ינואר 2024

רופא/ה רוקח/ת נכבד/ה,

חברת פאדאגיס ישראל סוכנויות בע"מ מבקשת להודיע על העדכונים הבאים בעלון לרופא עבור התכשיר:

טרוקסימה / TRUXIMA

החומר הפעיל בתכשיר וחוזקו: Rituximab 10 mg/ml

<u>התוויות רשומות לתכשיר בישראל:</u>

Truxima is indicated in adults for the following indications:

* <u>Non-Hodgkin's lymphoma (NHL)</u>
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.

* <u>Chronic lymphocytic leukaemia (CLL)</u>
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.

* <u>Granulomatosis with polyangiitis and microscopic polyangiitis</u>
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).

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

<u>מהות העדכון</u>:
בהודעה זו מצוינים ומסומנים ברקע צהוב השינויים המהותיים המתייחסים לעדכוני בטיחות.
העלונים כוללים גם עדכונים נוספים (כגון שינויי נוסח).

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

בברכה,
פאדאגיס ישראל סוכנויות בע"מ

עלון לרופא

4.4 Special warnings and precautions for use

[…]

Non-Hodgkin's lymphoma and chronic lymphocytic leukaemia
[…]

Cases of enteroviral meningoencephalitis including fatalities have been reported following use of rituximab.

False negative serologic testing of infections
Due to the risk of false negative serologic testing of infections, alternative diagnostic tools should be considered in case of patients presenting with symptoms indicative of rare infectious disease e.g. West Nile virus and neuroborreliosis.
[…]

Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), and pemphigus vulgaris

[…]

Cases of enteroviral meningoencephalitis including fatalities have been reported following use of rituximab.

False negative serologic testing of infections
Due to the risk of false negative serologic testing of infections, alternative diagnostic tools should be considered in case of patients presenting with symptoms indicative of rare infectious disease e.g. West Nile virus and neuroborreliosis.

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4.8 Undesirable effects

[…]

Table 1 ADRs 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		serious viral infection[2] Pneumocystis jirovecii	PML	enteroviral meningoencephalitis[2, 3]

MedDRA System Organ Class	Very Common	Common	Uncommon	Rare	Very Rare	Not known
		bronchitis, +sinusitis, hepatitis B[1]				
[…]						

[…]

[3] observed during post-marketing surveillance

[…]

Description of selected adverse reactions

Infections

Rituximab induces B-cell depletion in about 70-80% of patients, but was associated with decreased serum immunoglobulins only in a minority of patients.

Localised candida infections as well as Herpes zoster were reported at a higher incidence in the rituximab-containing arm of randomised studies. Severe infections were reported in about 4% of patients treated with rituximab monotherapy. Higher frequencies of infections overall, including grade 3 or 4 infections, were observed during rituximab maintenance treatment up to 2 years when compared to observation. There was no cumulative toxicity in terms of infections reported over a 2-year treatment period. In addition, other serious viral infections either new, reactivated or exacerbated, some of which were fatal, have been reported with rituximab treatment. The majority of patients had received rituximab in combination with chemotherapy or as part of a haematopoetic stem cell transplant. Examples of these serious viral infections are infections caused by the herpes viruses (Cytomegalovirus, Varicella Zoster Virus and Herpes Simplex Virus), JC virus (progressive multifocal leukoencephalopathy (PML)), enterovirus (meningoencephalitis) and hepatitis C virus (see section 4.4). Cases of fatal PML that occurred after disease progression and retreatment have also been reported in clinical trials. Cases of hepatitis B reactivation, have been reported, the majority of which were in patients receiving rituximab in combination with cytotoxic chemotherapy. In patients with relapsed/refractory CLL, the incidence of grade 3/4 hepatitis B infection (reactivation and primary infection) was 2% in R-FC vs 0% FC. Progression of Kaposi's sarcoma has been observed in rituximab-exposed patients with pre-existing Kaposi's sarcoma. These cases occurred in non-approved indications and the majority of patients were HIV positive.

[…]

Table 2 Adverse reactions occurring at 6-months in ≥ 5% of adult patients receiving rituximab in GPA/MPA Study (Rituximab n=99, and at a higher frequency than the comparator group), or during postmarketing surveillance.

MedDRA System organ class Adverse reaction	Frequency
Infections and infestations	
[…]	[…]
Serious viral infection[1,2]	not known
Enteroviral meningoencephalitis[1]	not known
[…]	[…]

[…]

Table 3 Adverse reactions in rituximab-treated pemphigus vulgaris patients in PV Study 1 (up to month 24) and PV Study 2 (up to Week 52), or during postmarketing surveillance

MedDRA System Organ Class	Very Common	Common	Not known
Infections and infestations	Upper respiratory tract infection	Herpes virus infection Herpes zoster Oral herpes Conjunctivitis Nasopharyngitis Oral candidiasis Urinary tract infection	serious viral infection[1,2] Enteroviral meningoencephalitis[1]
[…]	[…]	[…]	[…]

[…]