אוקטובר 2023

MabThera (rituximab) 10mg/ml IV

Concentrate for solution for intravenous infusion

רופא/ה יקר/ה, רוקח/ת יקר/ה,

חברת רוש פרמצבטיקה (ישראל) בע"מ מבקשת להודיעכם על עדכון בעלון לרופא של התכשיר מבטרה 10מ"ג/מ"ל IV. בהודעה זו מצוינים רק עדכונים מהותיים ועדכונים אשר מהווים החמרה.

ההתוויות הרשומות לתכשיר בישראל:

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

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

Rheumatoid arthritis
MabThera 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
MabThera, 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
MabThera is indicated for the treatment of adult patients with moderate to severe pemphigus vulgaris (PV).

הסבר:

טקסט עם קו תחתי בצבע כחול מציין טקסט שהוסף לעלון.
~~טקסט עם קו חוצה~~ מציין טקסט שהוסר מן העלון.

למידע נוסף יש לעיין בעלון לרופא כפי שאושר ע"י משרד הבריאות.

העלון המעודכן נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על-ידי פנייה לבעל הרישום: רוש פרמצבטיקה (ישראל) בע"מ, ת.ד 6391 , הוד השרון 4524079 טלפון 09-9737777. כתובתנו באינטרנט: www.roche.co.il.

ב ב ר כ ה,

בתאור צפרי-חגג
מחלקת רישום

לילי אדר
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4.4 Special warnings and precautions for use

Non-Hodgkin's lymphoma and chronic lymphocytic leukaemia

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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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Rheumatoid arthritis, 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

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ADRs reported in clinical trials or during postmarketing surveillance in patients with NHL and CLL disease treated with MabThera monotherapy/maintenance or in combination with chemotherapy **Table 1**

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	PML	enteroviral meningoencephalitis[2, 3]
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Description of selected adverse reactions

Infections
MabThera 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 MabThera-containing arm of randomised studies. Severe infections were reported in about 4% of patients treated with MabThera monotherapy. Higher frequencies of infections overall, including grade 3 or 4 infections, were observed during MabThera 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 MabThera treatment. The majority of patients had received MabThera 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 MabThera 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 MabThera-exposed patients with pre-existing Kaposi's sarcoma. These cases occurred in non-approved indications and the majority of patients were HIV positive.

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Table 2 Summary of adverse reactions reported in clinical trials or during postmarketing surveillance occurring in patients with rheumatoid arthritis receiving MabThera

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			PML, reactivation of hepatitis B	Serious viral infection[1], enteroviral meningoencephalitis[2]
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Table 3 Adverse reactions occurring at 6-months in ≥ 5% of adult patients receiving MabThera 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	
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Enteroviral meningoencephalitis[1]	not known
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Table 4 Adverse reactions in MabThera-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]
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