J-C Health Care Ltd.

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01/2024

רופא/ה נכבד/ה
רוקח/ת נכבד/ה

הנדון: Remicade - רמיקד

חברת J-C Health Care Ltd מבקשת להודיעכם כי העלונים לרופא ולצרכן של התכשיר שבנדון התעדנו **בינואר 2024.**

פרטי העדכון העיקריים מופיעים בהמשך (טקסט שנוסף מסומן באדום, טקסט שהושמט מסומן בטקסט ~~כחול עם קו חוצה~~, טקסט המהווה החמרה מודגש ברקע צהוב),אך קיימים עדכונים נוספים.

ההתוויות המאושרות לתכשיר בישראל:

Adult:
- Crohn's disease:
Treatment of moderate to severe active Crohn's disease in patients who have not responded despite of a full and adequate course of therapy with a corticosteroid and/or an immunosuppressant.
Treatment of fistulising Crohn's disease in patients who have not responded despite of a full and adequate course of therapy with conventional treatment.
- Paediatric Crohn's disease:
Remicade is indicated for: Treatment of severe active crohn's disease in paediatric patients aged 6 to 17 years who have not responded to conventional therapy including a corticosteroid an immunomodulator and primary nutrition therapy or who are intolerant to or have contraindications for such therapies.
Remicade has been studied only in combination with conventional immunosuppressive therapy
- Ankylosing spondylitis:
Remicade is indicated for: treatment of ankylosing spondylitis in patients who have severe axial symptoms elevated serological markers of inflammatory activity and who have responded inadequately to conventional therapy.
- Psoriatic arthritis:
Remicade is indicated for: Treatment of active and progressive psoriatic arthritis in adults when the response to previous DMARD therapy has been inadequate.
Remicade should be administered: either in combination with methotrexate or alone in patients who show intolerance to methotrexate or for whom methotrexate is contraindicated.
- Remicade has been shown to improve physical function in patients with psoriatic arthritis and to reduce the rate of progression of peripheral joint damage as measured by X-ray in patients with polyarticular symmetrical subtypes of the disease.
- Rheumatoid arthritis:
Remicade in combination with methotrexate is indicated for the reduction of signs and symptoms as well as the improvement in physical function in: Patients with active disease when the response to disease-modifying drugs including methotrexate has been inadequate.
Patients with severe active and progressive disease not previously treated with methotrexate or other DMARDs. In this these patient populations a reduction in the rate of the progression of joint damage as measured by x-ray has been demonstrated
- **Psoriasis**:
Remicade is indicated for: Treatment of moderate to severe plaque psoriasis in adults who failed to respond to or who have a contraindication to or are intolerant to other systemic therapy including cyclosporine methotrexate or PUVA.
- Ulcerative colitis:
Remicade is indicated for: Treatment of moderately to severely active ulcerative colitis in patients who have had an inadequate response to convential therapy including corticosteroids and 6-MP or AZA or who are intolerant to or have medical contraindications for such therapies.
- Paediatric ulcerative colitis:
Remicade is indicated for treatment of severely active ulcerative colitis, in paediatric patients aged 6 to 17 years, who have had an inadequate response to conventional therapy including corticosteroids and 6 MP or AZA, or who are intolerant to or have medical contraindications for such therapies

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מרכיב פעיל: Infliximab

העלונים המעודכנים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות:
https://israeldrugs.health.gov.il/#!/byDrug.

כמו כן, מצורפים לפרסום זה וניתן לקבל העתק מודפס שלהם באמצעות פנייה לבעל הרישום: J-C Health Care Ltd, קיבוץ שפיים, 6099000, טל': 09-9591111.

בברכה,

יעל לפידות מללי
רוקחת ממונה
J-C Health Care Ltd

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העדכון בעלון לרופא הינו:

4.8 Undesirable effects

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Table 1
Undesirable effects in clinical studies and from post-marketing experience

Infections and infestations	
Very Common:	Viral infection (e.g. influenza, herpes virus infection).
Common:	Bacterial infections (e.g. sepsis, cellulitis, abscess).
Uncommon:	Tuberculosis, fungal infections (e.g. candidiasis, onychomycosis,).
Rare:	Meningitis, opportunistic infections (such as invasive fungal infections [pneumocystosis, histoplasmosis, aspergillosis, coccidioidomycosis, cryptococcosis, blastomycosis], bacterial infections [atypical mycobacterial, listeriosis, salmonellosis], and viral infections [cytomegalovirus]), parasitic infections, hepatitis B reactivation.
Not known	Vaccine breakthrough infection (after *in utero* exposure to infliximab)*.
Neoplasms benign, malignant and unspecified (including cysts and polyps)	
Rare:	Lymphoma, non-Hodgkin's lymphoma, Hodgkin's disease, leukaemia, melanoma, cervical cancer
Not known:	Hepatosplenic T-cell lymphoma (primarily in adolescents and young adult males with Crohn's disease or ulcerative colitis) , Merkel cell carcinoma, Kaposi's sarcoma.
Blood and lymphatic system disorders	
Common:	Neutropenia, leucopenia, anaemia, lymphadenopathy.
Uncommon:	Thrombocytopenia, lymphopenia, lymphocytosis.
Rare:	Agranulocytosis (including infants exposed *in utero* to infliximab), thrombotic thrombocytopenic purpura, pancytopenia, haemolytic anaemia, idiopathic thrombocytopenic purpura.
Immune system disorders	
Common:	Allergic respiratory symptom.
Uncommon:	Anaphylactic reaction, lupus-like syndrome, serum sickness or serum sickness-like reaction.
Rare:	Anaphylactic shock, vasculitis, sarcoid-like reaction.
Metabolism and nutrition disorders	
Uncommon:	Dyslipidaemia
Psychiatric disorders	
Common:	Depression, insomnia.
Uncommon:	Amnesia, agitation, confusion, somnolence, nervousness.
Rare:	Apathy.
Nervous system disorders	
Very common:	Headache.
Common:	Vertigo, dizziness, hypoaesthesia, paraesthesia.
Uncommon:	Seizure, neuropathy.

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Rare:	Transverse myelitis, central nervous system demyelinating disorders (multiple sclerosis-like disease and optic neuritis), peripheral demyelinating disorders (such as Guillain-Barré syndrome, chronic inflammatory demyelinating polyneuropathy and multifocal motor neuropathy).
Not known:	Cerebrovascular accidents in close temporal association with infusion.
Eye disorders	
Common:	Conjunctivitis.
Uncommon:	Keratitis, periorbital oedema, hordeolum.
Rare:	Endophthalmitis.
Not known	Transient visual loss occurring during or within 2 hours of infusion.
Cardiac disorders	
Common:	Tachycardia, palpitation.
Uncommon:	Cardiac failure (new onset or worsening), arrhythmia, syncope, bradycardia.
Rare:	Cyanosis, pericardial effusion.
Not known:	Myocardial ischaemia/myocardial infarction
Vascular disorders	
Common:	Hypotension, hypertension, ecchymosis, hot flush, flushing.
Uncommon:	Peripheral ischaemia, thrombophlebitis, haematoma.
Rare:	Circulatory failure, petechia, vasospasm.
Respiratory, thoracic and mediastinal disorders	
Very common:	Upper respiratory tract infection, sinusitis.
Common:	Lower respiratory tract infection (e.g. bronchitis, pneumonia), dyspnoea, epistaxis.
Uncommon:	Pulmonary oedema, bronchospasm, pleurisy, pleural effusion.
Rare:	Interstitial lung disease (including rapidly progressive disease, lung fibrosis and pneumonitis).
Gastrointestinal disorders	
Very common:	Abdominal pain, nausea.
Common:	Gastrointestinal haemorrhage, diarrhoea, dyspepsia, gastroesophageal reflux, constipation.
Uncommon:	Intestinal perforation, intestinal stenosis, diverticulitis, pancreatitis, cheilitis.
Hepatobiliary disorders	
Common:	Hepatic function abnormal, transaminases increased.
Uncommon:	Hepatitis, hepatocellular damage, cholecystitis.
Rare:	Autoimmune hepatitis, jaundice.
Not known:	Liver failure.
Skin and subcutaneous tissue disorders	
Common:	New onset or worsening psoriasis including pustular psoriasis (primarily palm & soles), urticaria, rash, pruritus, hyperhidrosis, dry skin, fungal dermatitis, eczema, alopecia.
Uncommon:	Bullous eruption, seborrhoea, rosacea, skin papilloma, hyperkeratosis, abnormal skin pigmentation.

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Rare:	Toxic epidermal necrolysis, Stevens-Johnson Syndrome, erythema multiforme, furunculosis, linear IgA bullous dermatosis (LABD), acute generalised exanthematous pustulosis (AGEP), lichenoid reactions.
Not known:	worsening of symptoms of dermatomyositis
Musculoskeletal and connective tissue disorders	
Common:	Arthralgia, myalgia, back pain.
Renal and urinary disorders	
Common:	Urinary tract infection.
Uncommon:	Pyelonephritis.
Reproductive system and breast disorders	
Uncommon:	Vaginitis.
General disorders and administration site conditions	
Very common:	Infusion-related reaction, pain.
Common:	Chest pain, fatigue, fever, injection site reaction, chills, oedema.
Uncommon:	Impaired healing.
Rare:	Granulomatous lesion.
Investigations	
Uncommon:	Autoantibody positive, weight increased[1].
Rare:	Complement factor abnormal.

* including bovine tuberculosis (disseminated BCG infection), see section 4.4

[1] At month 12 of the controlled period for adult clinical trials across all indications, the median weight increase was 3.50 kg for infliximab-treated subjects vs. 3.00 kg for placebo-treated subjects. The median weight increase for inflammatory bowel disease indications was 4.14 kg for infliximab-treated subjects vs. 3.00 kg for placebo-treated subjects, and the median weight increase for rheumatology indications was 3.40 kg for infliximab-treated subjects vs. 3.00 kg for placebo-treated subjects.

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<u>העדכון בעלון לצרכן הינו:</u>

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4. תופעות לוואי

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תופעות לוואי שאינן שכיחות (uncommon) - יכולות להופיע אצל עד אחד מתוך 100 משתמשים:

- מחסור באספקת דם, נפיחות ורידים
- הצטברות דם מחוץ לכלי הדם (המטומה) או חבורות
- בעיות בעור כמו שלפוחיות, יבלות, צבע עור חריג או פיגמנטציה, או נפיחות בשפתיים או התעבות של העור, או עור אדום עם קשקשת וקילופים
- תגובות אלרגיות חמורות (אנפילקסיס), הפרעה במערכת החיסונית הנקראת זאבת (לופוס), תגובה אלרגית לחלבונים זרים
- זמן ריפוי ממושך יותר של פצעים
- התנפחות של הכבד (הפטיטיס) או כיס המרה, נזק לכבד
- פיזור דעת, רגזנות, בלבול, עצבנות
- בעיות עיניים הכוללות טשטוש ראייה או ירידה בראייה, נפיחות בעיניים או שעורה
- אי ספיקת לב חדשה או החמרה של אי ספיקת לב קיימת, קצב לב איטי
- התעלפות
- פרכוסים, בעיות עצביות
- חור במעיים או חסימת מעיים, כאב בטן או התכווציות בבטן
- התנפחות של הלבלב (דלקת הלבלב)
- זיהומים פטרייתיים, כגון קנדידה או זיהום פטרייתי של הציפורניים
- בעיות בריאה (כגון בצקת)
- הצטברות נוזלים סביב הריאה (תפליט קרום ריאה)
- היצרות נתיב האוויר בריאות הגורם לקושי בנשימה
- רירית מודלקת של הריאה, הגורמת לכאבים חדים בחזה המורגשים יותר עם הנשימה (דלקת קרום הראות)
- שחפת
- זיהומים בכליות
- ספירת טסיות נמוכה, ריבוי כדוריות דם לבנות
- זיהומים בנרתיק
- תוצאות בדיקות דם המראות נוגדנים עצמיים
- שינויים ברמות כולסטרול ושומנים בדם
- עלייה במשקל (עבור רוב החולים, העלייה במשקל היתה קטנה)

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Instructions for use and handling – reconstitution, dilution and administration

1. Calculate the dose and the number of Remicade vials needed. Each Remicade vial contains 100 mg infliximab. Calculate the total volume of reconstituted Remicade solution required.

2. Under aseptic conditions, reconstitute each Remicade vial with 10 ml of water for injections, using a syringe equipped with a 21-gauge (0.8 mm) or smaller needle. Remove flip-top from the vial and wipe the top with a 70% alcohol swab. Insert the syringe needle into the vial through the centre of the rubber stopper and direct the stream of water for injections to the glass wall of the vial. Gently swirl the solution by rotating the vial to dissolve the lyophilised powder. Avoid prolonged or vigorous agitation. DO NOT SHAKE. Foaming of the solution on reconstitution is not unusual. Allow the reconstituted solution to stand for 5 minutes. Check that the solution is colourless to light yellow and opalescent. The solution may develop a few fine translucent particles, as infliximab is a protein. Do not use if opaque particles, discolouration, or other foreign particles are present.

3. Dilute the total volume of the reconstituted Remicade solution dose to 250 ml with sodium chloride 9 mg/ml (0.9%) solution for infusion. Do not dilute the reconstituted Remicade solution with any other diluent. The dilution can be accomplished by withdrawing a volume of the sodium chloride 9 mg/ml (0.9%) solution for infusion from the 250 ml glass bottle or infusion bag equal to the volume of reconstituted Remicade. Slowly add the total volume of reconstituted Remicade solution

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to the 250 ml infusion bottle or bag. Gently mix. For volumes greater than 250 ml, either use a larger infusion bag (e.g., 500 ml, 1000 ml) or use multiple 250 ml infusion bags to ensure that the concentration of the infusion solution does not exceed 4 mg/ml. ~~If stored refrigerated after reconstitution and dilution, the infusion solution must be allowed to equilibrate at room temperature to 25°C for 3 hours prior to Step 4 (infusion)~~.

4. Administer the infusion solution over a period of not less than the infusion time recommended (see section 4.2). Use only an infusion set with an in-line, sterile, non-pyrogenic, low protein-binding filter (pore size 1.2 micrometere ~~e~~ or less). Since no preservative is present, it is recommended that the administration of the solution for infusion is to be started as soon as possible and within 3 hours of reconstitution and dilution. When reconstitution and dilution are performed under aseptic conditions, Remicade infusion solution can be used within 24 hours if stored at 2°C to 8°C. ~~If not used immediately, in use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C-8°C, unless reconstitution/dilution has been taken place in controlled and validated aseptic conditions.~~ Do not store any unused portion of the infusion solution for reuse.
5. No physical biochemical compatibility studies have been conducted to evaluate the co-administration of Remicade with other agents. Do not infuse Remicade concomitantly in the same intravenous line with other agents.
6. Visually inspect Remicade for particulate matter or discolouration prior to administration. Do not use if visibly opaque particles, discolouration or foreign particles are observed.
7. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.