

רופא/ה רוקח/ת נכבד/ה,

חברת נוברטיס ישראל בע"מ מבקשת להודיעכם על עדכון העלון של התכשיר:

שם תכשיר	מספר רישום
Erelzi 25	163-20-36011-00
Erelzi 50	163-21-36037-00

מרכיב פעיל: ETANERCEPT

ההתוויות המאושרות לתכשירים:**Rheumatoid arthritis**

Erelzi is indicated for the treatment of active rheumatoid arthritis in adults when the response to disease-modifying antirheumatic drugs (DMARDs) including methotrexate (unless contraindicated) has been inadequate. Erelzi can be used in combination with methotrexate in patients who do not respond adequately to methotrexate alone. Reducing signs and symptoms and inhibiting the progression of structural damage in patients with moderately to severely active rheumatoid arthritis. Etanercept, alone or in combination with methotrexate, has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function.

Juvenile idiopathic arthritis

Treatment of polyarthritis (rheumatoid factor positive or negative) and extended oligoarthritis in children and adolescents from the age of 2 years who have had an inadequate response to, or who have proved intolerant of, methotrexate.

Treatment of psoriatic arthritis in adolescents from the age of 12 years who have had an inadequate response to, or who have proved intolerant of, methotrexate.

Treatment of enthesitis-related arthritis in adolescents from the age of 12 years who have had an inadequate response to, or who have proved intolerant of, conventional therapy.

Psoriatic arthritis

Treatment of active and progressive psoriatic arthritis in adults when the response to previous disease-modifying antirheumatic drug therapy has been inadequate. Etanercept 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.

Axial spondyloarthritis**Ankylosing spondylitis (AS)**

Treatment of adults with severe active ankylosing spondylitis who have had an inadequate response to conventional therapy.

Non-radiographic axial spondyloarthritis

Treatment of adults with severe non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) evidence, who have had an inadequate response to non-steroidal anti-inflammatory drugs (NSAIDs).

Plaque psoriasis

Treatment of adults patients (18 years or older) with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

Paediatric plaque psoriasis

Treatment of chronic severe plaque psoriasis in children and adolescents from the age of 6 years who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies.

מצ"ב פירוט העדכונים:

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4.7 Effects on ability to drive and use machines

Erelzi has no or negligible influence on the ability to drive and use machines.

~~No studies on the effects on the ability to drive and use machines have been performed.~~

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5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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Study 2

This multi-center, open-label, phase 4, 3-period study evaluated the withdrawal and retreatment of etanercept in patients with active nr-AxSpa who achieved an adequate response (inactive disease defined as Ankylosing Spondylitis Disease Activity Score (ASDAS) C-reactive protein (CRP) less than 1.3) following 24 weeks of treatment.

209 adult patients with active nr-AxSpa (18 to 49 years of age), defined as those patients meeting the Assessment of SpondyloArthritis International Society (ASAS) classification criteria of axial spondyloarthritis (but not meeting the modified New York criteria for AS),

having positive MRI findings (active inflammation on MRI highly suggestive of sacroiliitis associated with SpA) and/or positive hsCRP (defined as high sensitivity C-reactive protein [hsCRP] >3 mg/l), and active symptoms defined by an ASDAS CRP greater than or equal to 2.1 at the screening visit received open-label etanercept 50 mg weekly plus stable background NSAID at the optimal tolerated anti inflammatory dosage for 24 weeks in Period 1. Patients were also required to have an inadequate response or intolerance to two or more NSAIDs. At week 24, 119 (57%) patients achieved inactive disease and entered into the Period 2 40-week withdrawal phase where subjects discontinued etanercept, yet maintained the background NSAID. The primary measure of efficacy was the occurrence of flare (defined as an ASDAS erythrocyte sedimentation rate (ESR) greater than or equal to 2.1) within 40 weeks following withdrawal of etanercept. Patients who flared were retreated with etanercept 50 mg weekly for 12 weeks (Period 3).

In Period 2, the proportion of patients experiencing ≥ 1 flare increased from 22% (25/112) at week 4 to 67% (77/115) at week 40. Overall, 75% (86/115) patients experienced a flare at any time point within 40 weeks following withdrawal of etanercept.

The key secondary objective of Study 2 was to estimate time to flare after withdrawal of etanercept and additionally compare the time to flare to patients from Study 1 who met the Study 2 withdrawal phase entry requirements and continued etanercept therapy.

The median time to flare following withdrawal of etanercept was 16 weeks (95% CI: 13-24 weeks). Less than 25% of patients in Study 1 who did not have treatment withdrawn experienced a flare over the equivalent 40-weeks as in Period 2 Study 2. The time to flare was statistically significantly shorter in subjects who discontinued etanercept treatment (Study 2) compared to subjects who received continuous etanercept treatment (Study 1), $p < 0.0001$.

Of the 87 patients who entered Period 3 and were retreated with etanercept 50 mg weekly for 12 weeks, 62% (54/87) re-achieved inactive disease, with 50% of them re-achieving it within 5 weeks (95% CI: 4-8 weeks).

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Paediatric patients with juvenile idiopathic arthritis

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Of the 127 patients in the parent study, 109 participated in the open-label extension study and were followed for 8 years. At the end of the extension study, 84/109 (77%) patients had completed the study; 27 (25%) while actively taking etanercept, 7 (6%) had withdrawn from treatment due to low/inactive disease; 5 (5%) had re-started etanercept following an earlier withdrawal from treatment; and 45 (41%) had stopped etanercept (but remained under observation); 25/109 (23%) patients permanently discontinued from the study. Improvements in clinical status achieved in the parent study were generally maintained for all efficacy endpoints during the entire follow-up

period. Patients actively taking etanercept could enter an optional withdrawal-retreatment period once during the extension study based on investigator's judgement of clinical response. 30 patients entered the withdrawal period. 17 patients were reported to have a flare (defined as $\geq 30\%$ worsening in at least 3 of the 6 ACR Pedi components with $\geq 30\%$ improvement in not more than 1 of the remaining 6 components and a minimum of 2 active joints); median time to flare after etanercept withdrawal was 190 days. 13 patients were re-treated and the median time to re-treatment from withdrawal was estimated as 274 days. Due to the small number of data points, these results should be interpreted with caution.

The safety profile was consistent with that observed in the parent study.

Studies have not been done in patients with juvenile idiopathic arthritis to assess the effects of continued etanercept therapy in patients who do not respond within 3 months of initiating etanercept therapy. Additionally, studies have not been conducted to assess ~~the effects of discontinuing or reducing the recommended dose of etanercept following its long-term use in patients with JIA.~~

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בהודעה זו מצויינים רק הסעיפים בהם בוצעו שינויים מהותיים בלבד בעלון לרופא .

העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות:

<https://israeldrugs.health.gov.il/#!/byDrug>

כמו כן ניתן לקבל את העלון המודפס על ידי פניה לבעל הרישום – נוברטיס ישראל בע"מ.

לעדכוןכם בברכה,

מגר' דפנה סנדובסקי,

רוקחת ממונה חטיבת סנדוז,

נוברטיס ישראל בע"מ