רופא/ה, רוקח/ת נכבד/ה

חברת טבע מודיעה על העדכונים הבאים בעלוני התכשיר:

Copaxone 20 mg/ ml Solution for injection

קופקסון 20 מ"ג /מ"ל

Contains: Glatiramer acetate 20 mg

<u>התוויה כפי שאושרה בתעודת הרישום:</u>

For reducing the frequency of relapses in patients with relapsing-remitting multiple sclerosis.

Copaxone is indicated for the treatment of patients who have experienced a well-defined first clinical episode and are determined to be at high risk of developing clinically definite multiple sclerosis (CDMS).

These patients should have MRI findings which are compatible with the diagnosis of multiple sclerosis.

<u>בפירוט שלהלן כלולים העדכונים העיקריים בלבד (תוספות מסומנות באדום והסרות מידע כטקסט מחוק):</u>

עדכונים בעלון לצרכן

2. לפני השימוש בתרופה

אזהרות מיוחדות הנוגעות לשימוש בתרופה

קופקסון יכול לגרום לתגובות אלרגיות חמורות, שבחלקן עלולות להיות מסכנות חיים.
תגובות אלה יכולות להתרחש זמן קצר לאחר המתן, אפילו חודשים ועד שנים לאחר התחלת הטיפול ואפילו אם ההזרקות הקודמות היו נטולות תגובות אלרגיות.
הסימנים והתסמינים של תגובות אלרגיות עלולים לחפוף לתגובות לאחר ההזרקה.
הרופא יתדרך אותך ביחס לסימנים של תגובה אלרגית.

הריון והנקה

עלייך להיוועץ ברופא ביחס לשימוש בקופקסון במהלך היריון. פני לרופא אם את בהיריון, אם את חושבת שאת בהיריון או אם את מתכננת היריון.

ניתן להשתמש בקופקסון במהלך ההריון לאחר התייעצות עם הרופא.

היקף מוגבל של נתונים משימוש בבני אדם הראה שלקופקסון אין השפעות שליליות על יילודים/ תינוקות שינקו. ניתן להשתמש בקופקסון במהלך הנקה.

4. תופעות לוואי

כמו בכל תרופה, קופקסון עלול לגרום לתופעות לוואי בחלק מהמטופלים. אל תיבהל למקרא רשימת תופעות הלוואי. ייתכן ולא תסבול מאף אחת מהן.

תגובות אלרגיות (רגישות יתר, תגובה אנפילקטית)

לעיתים ~~נדירות~~ עלולה להתפתח תגובה אלרגית חמורה לתכשיר זה זמן קצר לאחר ההזרקה.

זוהי תופעת לוואי שאינה שכיחה. תגובות אלה יכולות להתרחש חודשים ועד שנים לאחר התחלת הטיפול בקופקסון, גם אם הזרקות קודמות היו נטולות תגובות אלרגיות .

אם הינך חש באופן פתאומי באחת מתופעות הלוואי הבאות הפסק את השימוש בתרופה וספר לרופא מיד, או פנה לחדר המיון בבית החולים הקרוב:

- נפיחות בעפעפיים, בפנים, ~~או~~ בשפתיים, בפה, בגרון או בלשון
- פריחה מפושטת (כתמים אדומים או סרפדת)
- ~~•~~ פירכוסים
- קוצר נשימה פתאומי, קשיי נשימה או ציפצופים
- קשיים בבליעה או בדיבור
- עילפון, הרגשת סחרחורת או הרגשת עילפון
- קריסה/ התמוטטות

עדכונים בעלון לרופא

4.4 Special warnings and precautions for use

Copaxone should only be administered subcutaneously. Copaxone should not be administered by intravenous or intramuscular routes.

Glatiramer acetate can cause post-injection reactions as well as anaphylactic reactions (see section 4.8):

...

Anaphylactic reactions

~~Convulsions and/or anaphylactoid or allergic reactions have been reported rarely. Serious hypersensitivity reactions (e.g. bronchospasm, anaphylaxis or urticaria) may rarely occur . If reactions are severe, appropriate treatment should be instituted and Copaxone should be discontinued~~

Anaphylactic reactions may occur shortly following administration of glatiramer acetate, even months up to years after initiation of treatment (see section 4.8). Cases with fatal outcome have been reported. Some signs and symptoms of anaphylactic reactions may overlap with post-injection reactions.

All patients receiving treatment with Copaxone and caregivers should be informed about the signs and symptoms specific for anaphylactic reactions and that they should seek immediate emergency medical care in case of experiencing such symptoms (see section 4.8).

If an anaphylactic reaction occurs, treatment with Copaxone must be discontinued (see section 4.3).

4.6 Fertility, pregnancy and lactation

Pregnancy

A moderate amount of data on pregnant women (between 300-1 000 pregnancy outcomes) indicate no malformative or feto/neonatal toxicity.
Animal studies do not indicate reproductive toxicity ~~Studies in animals have not shown reproductive toxicity~~ (see section 5.3).
~~Current data on the use of Copaxone 20 mg/ml in pregnant women indicate no malformative or feto/neonatal toxicity. Data on The use of Copaxone 40 mg/ml are consistent with these findings. To date, no relevant epidemiological data are available. As a precautionary measure, it is preferable to avoid the use of Copaxone during pregnancy unless the benefit to the mother outweighs the risk to the foetus.~~

The use of Copaxone may be considered during pregnancy, if necessary.

4.8 Undesirable effects

Most Copaxone safety data were accumulated for Copaxone 20 mg/ml administered as a subcutaneous injection once daily. This section presents accumulated safety data from four placebo-controlled trials with Copaxone 20 mg/ml administered once daily, and from one placebo-controlled trial with Copaxone 40 mg/ml administered three times a week.

A direct comparison of the safety between Copaxone 20 mg/ml (administered daily) and 40 mg/ml (administered three times per week) in the same study has not been performed.

Copaxone 20 mg/ml (administered once daily)

In all clinical trials with Copaxone 20 mg/ml, injection-site reactions were seen to be the most frequent adverse reactions and were reported by the majority of patients receiving

Copaxone. In controlled studies, the proportion of patients reporting these reactions, at least once, was higher following treatment with Copaxone 20 mg/ml (70%) than placebo injections (37%). The most commonly reported injection-site reactions, which were more frequently reported in Copaxone 20 mg/ml vs. placebo-treated patients, ~~in clinical trials and in post marketing experience,~~ were erythema, pain, mass, pruritus, oedema, inflammation and hypersensitivity ~~and rare occurrence of lipoatrophy and skin necrosis~~.

A reaction, associated with at least one or more of the following symptoms, has been described as the Immediate post-injection reaction: vasodilatation (flushing), chest pain, dyspnoea, palpitation or tachycardia. This reaction may occur within minutes of a Copaxone injection. At least one component of this Immediate post-injection reaction was reported at least once by 31% of patients receiving Copaxone 20 mg/ml compared to 13% of patients receiving placebo.

Adverse reactions identified from clinical trials and post marketing experience are presented in the table below. ~~All adverse reactions, which were more frequently reported in Copaxone vs. placebo-treated patients, are presented in the table below. This data~~ Data from clinical trials was derived from four pivotal, double-blind, placebo-controlled clinical trials with a total of 512 patients treated with Copaxone 20 mg/day and 509 patients treated with placebo for up to 36 months. Three trials in relapsing-remitting MS (RRMS) included a total of 269 patients treated with Copaxone 20 mg/day and 271 patients treated with placebo for up to 35 months. The fourth trial in patients who have experienced a first clinical episode and were determined to be at high risk of developing clinically definite MS included 243 patients treated with Copaxone 20 mg/day and 238 patients treated with placebo for up to 36 months.

System Organ Class (SOC)	**Very Common (≥1/10)**	**Common (≥1/100 to <1/10)**	**Uncommon (≥1/1,000 to <1/1,00)**	**Rare (≥1/10,000 to <1/1,000)**	**Not known (cannot be estimated from the available data)**
Immune system disorders		Hypersensitivity	Anaphylactic reaction		
~~Pregnancy, puerperium and perinatal Conditions~~			~~Abortion~~		

In the fourth trial noted above, an open-label treatment phase followed the placebo-controlled period. No change in the known risk profile of Copaxone 20 mg/ml was observed during the open-label follow-up period of up to 5 years.

Copaxone 40 mg/ml (administered three times per week)

The safety of Copaxone 40 mg/ml was assessed based on a double-blind, placebo controlled

clinical trial in RRMS patients with a total of 943 patients treated with Copaxone 40 mg/ml three times per week, and 461 patients treated with placebo for 12 months.

In general, the kind of adverse drug reactions seen in patients treated with Copaxone 40 mg/ml administered three times per week were those already known and labelled for Copaxone 20 mg/ml administered daily. In particular, adverse injection site reactions (ISR) and immediate post-injection reactions (IPIR) were reported at lower frequency for Copaxone 40 mg/ml administered three times per week than for Copaxone 20 mg/ml administered daily (35.5 % vs. 70 % for ISRs and 7.8 % vs. 31 % for IPIRs, respectively).

Injection site reactions were reported by 36% of the patients on Copaxone 40 mg/ml compared to 5% on placebo. Immediate post-injection reaction was reported by 8% of the patients on Copaxone 40 mg/ml compared to 2% on placebo.

A few specific adverse reactions are noted:
• Anaphylactic reactions may occur shortly following administration of glatiramer acetate, even months up to years after initiation of treatment (see section 4.4).
• No injection site necrosis was reported.
• Skin erythema and pain in extremity, not labelled for Copaxone 20 mg/ml, were reported each by 2.1% of the patients on Copaxone 40 mg/ml (Common: ≥ 1/100 to < 1/10).
• Drug-induced liver injury and toxic hepatitis, were each reported by one patient (0.1%) on Copaxone 40 mg/ml (Uncommon: ≥ 1/1,000 to < 1/100).

~~The following adverse reaction reports were collected from MS patients treated with Copaxone in uncontrolled clinical trials and from post-marketing experience with Copaxone: hypersensitivity reactions (including rare occurrence of anaphylaxis, >1/10000, < 1/1000).~~