הודעה על החמרה (מידע בטיחות) בעלון לצרכן

אושר – 8.16

תאריך _____19/07/2016_____

שם תכשיר באנגלית Kineret 100mg solution for injection

מספר רישום_____145-79-33059-00_____

שם בעל הרישום:___מגאפארם בע"מ_____

פרטים על השינוי/ים המבוקש/ים		
פרק בעלון	**טקסט נוכחי**	**טקסט חדש**
תופעות לוואי	כמו לכל תרופה, השימוש ב**קינרט** עלול לגרום לתופעות לוואי בחלק מהמשתמשים. אל תיבהל למקרא רשימת תופעות הלוואי. יתכן ולא תסבול מאף אחת מהן. **התייעץ עם הרופא מיד, במידה ומופיעה אצלך אחת מן התופעות לוואי הבאות:** • **זיהומים חמורים** - כגון דלקת ריאות (זיהום בדרכי הנשימה) או זיהומים בעור יכולים להופיע בזמן הטיפול ב**קינרט**. התסמינים עלולים לכלול הופעה של חום, שיעול או אדמומיות ורגישות בעור (שכיחות – לעתים קרובות). • **תופעות אלרגיה חמורות** אינן נפוצות, אולם כל אחד מהתסמינים הבאים עלול להצביע על תופעה אלרגית ל**קינרט**, ולכן יש לפנות באופן מיידי לקבלת עזרה רפואית ולא להמשיך בהזרקת **קינרט**, במידה ומופיעים: – נפיחות בפנים, בלשון או בגרון. – בעיות בבליעה או בנשימה.	כמו לכל תרופה, השימוש ב**קינרט** עלול לגרום לתופעות לוואי בחלק מהמשתמשים. אל תיבהל למקרא רשימת תופעות הלוואי. יתכן ולא תסבול מאף אחת מהן. **התייעץ עם הרופא מיד, במידה ומופיעה אצלך אחת מן התופעות לוואי הבאות:** • **זיהומים חמורים** - כגון דלקת ריאות (זיהום בדרכי הנשימה) או זיהומים בעור יכולים להופיע בזמן הטיפול ב**קינרט**. התסמינים עלולים לכלול הופעה של חום, שיעול או אדמומיות ורגישות בעור (שכיחות – לעתים קרובות). • **תופעות אלרגיה חמורות** אינן נפוצות, אולם כל אחד מהתסמינים הבאים עלול להצביע על תופעה אלרגית ל**קינרט**, ולכן יש לפנות באופן מיידי לקבלת עזרה רפואית ולא להמשיך בהזרקת **קינרט**, במידה ומופיעים: – נפיחות בפנים, בלשון או בגרון. – בעיות בבליעה או בנשימה.

	– הופעה פתאומית של דופק מהיר או הזעה. – גרד בעור או פריחה. <u>מופיעות לעיתים מאוד קרובות:</u> • אדמומיות, נפיחות, חבלות או גרד באתר ההזרקה. תסמינים אלו בדרך כלל מופיעים בצורה מתונה או בינונית ונפוצים יותר בתחילת הטיפול. • כאבי ראש <u>מופיעות לעיתים קרובות:</u> • נויטרופניה (ספירה נמוכה של תאי דם לבנים) המאובחנת באמצעות בדיקת דם, מצב רפואי זה עלול להגדיל את הסיכון ללקות בזיהום. תסמינים של זיהום עלולים לכלול חום וכאב גרון. <u>מופיעות לעיתים רחוקות:</u> • עלייה ברמות אנזימי הכבד בדם. <u>מופיעות בתדירות שאינה ידועה:</u> • סימנים להפרעות בכבד כמו עור ועיניים צהובות, בחילות, אובדן תיאבון, שתן כהה וצואה בהירה. אם אחת מתופעות הלוואי מחמירה, או כאשר אתה סובל מתופעת לוואי שלא הוזכרה בעלון, עליך להתייעץ עם הרופא.	– הופעה פתאומית של דופק מהיר או הזעה. – גרד בעור או פריחה. <u>מופיעות לעיתים מאוד קרובות:</u> • אדמומיות, נפיחות, חבלות או גרד באתר ההזרקה. תסמינים אלו בדרך כלל מופיעים בצורה מתונה או בינונית ונפוצים יותר בתחילת הטיפול. • כאבי ראש • עליה ברמות הכולסטרול בדם. <u>מופיעות לעיתים קרובות:</u> • נויטרופניה (ספירה נמוכה של תאי דם לבנים) המאובחנת באמצעות בדיקת דם, מצב רפואי זה עלול להגדיל את הסיכון ללקות בזיהום. תסמינים של זיהום עלולים לכלול חום וכאב גרון. • זיהומים חמורים כגון דלקת ריאות (זיהום בדרכי הנשימה) או זיהומים בעור • טרומבוציטופניה (ערכים נמוכים בדם של טסיות דם) <u>מופיעות לעיתים רחוקות:</u> • עלייה ברמות אנזימי הכבד בדם. <u>מופיעות בתדירות שאינה ידועה:</u> • סימנים להפרעות בכבד כמו עור ועיניים צהובות, בחילות, אובדן תיאבון, שתן כהה וצואה בהירה. אם אחת מתופעות הלוואי מחמירה, או כאשר אתה סובל מתופעת לוואי שלא הוזכרה בעלון, עליך להתייעץ עם הרופא.

הודעה על החמרה (מידע בטיחות) בעלון לרופא

פרטים על השינוי/ים המבוקש/ים

טקסט חדש

MedDRA Organ System	Frequency	Undesirable Effect
Infections and infestations	Common (≥ 1/100 to < 1/10)	Serious infections
Blood and lymphatic system disorders	Common (≥ 1/100 to < 1/10)	Neutropenia Thrombocytopenia
Immune system disorders	Uncommon (≥ 1/1,000 to < 1/100)	Allergic reactions including anaphylactic reactions, angioedema, urticaria and pruritus
Nervous system disorders	Very common (≥ 1/10)	Headache
Hepatobiliary system	Uncommon (≥ 1/1,000 to < 1/100)	Hepatic enzyme increased
	Not known (cannot be estimated from the available data)	Non-infectious hepatitis
Skin and subcutaneous tissue disorders	Very common (≥ 1/10)	Injection site reaction
	Uncommon (≥ 1/1,000 to < 1/100)	Rash
Investigations	Very common (≥1/10)	Blood cholesterol increased

Serious infections

The incidence of serious infections in RA studies conducted at the recommended dose (100 mg/day) was 1.8% in Kineret treated patients and 0.7% in placebo-treated patients. In observations up to 3 years, the serious infection rate remained stable over time.

טקסט נוכחי

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פרק בעלון

Undesirable effects

The infections observed consisted primarily of bacterial events such as cellulitis, pneumonia, and bone and joint infections. Most patients continued on study medicinal product after the infection resolved. In 43 CAPS patients followed for up to 5 years the frequency of serious infections was 0.1/year, the most common being pneumonia and gastroenteritis. Kineret was temporarily stopped in one patient, all other patients continued Kineret treatment during the infections. There were no deaths due to serious infections in RA or CAPS studies. In clinical RA studies and post-marketing experience, rare cases of opportunistic infections have been observed and included fungal, mycobacterial, bacterial, and viral pathogens. Infections have been noted in all organ systems and have been reported in patients receiving Kineret alone or in combination with immunosuppressive agents. <u>Neutropenia</u> In placebo-controlled RA studies with Kineret, treatment was associated with small reductions in the mean values for total white blood count and absolute neutrophil count (ANC). Neutropenia (ANC < 1.5 x 10^9/l) was reported in 2.4% patients receiving Kineret compared with 0.4% of placebo patients. None of these patients had serious infections associated with the neutropenia. In 43 CAPS patients followed for up to 5 years neutropenia was reported in 2 patients. Both episodes of neutropenia resolved	treated patients. In observations up to 3 years, the serious infection rate remained stable over time. The infections observed consisted primarily of bacterial events such as cellulitis, pneumonia, and bone and joint infections. Most patients continued on study medicinal product after the infection resolved. In 43 CAPS patients followed for up to 5 years the frequency of serious infections was 0.1/year, the most common being pneumonia and gastroenteritis. Kineret was temporarily stopped in one patient, all other patients continued Kineret treatment during the infections. There were no deaths due to serious infections in RA or CAPS studies. In clinical RA studies and post-marketing experience, rare cases of opportunistic infections have been observed and included fungal, mycobacterial, bacterial, and viral pathogens. Infections have been noted in all organ systems and have been reported in patients receiving Kineret alone or in combination with immunosuppressive agents. <u>Neutropenia</u> In placebo-controlled RA studies with Kineret, treatment was associated with small reductions in the mean values for total white blood count and absolute neutrophil count (ANC). Neutropenia (ANC < 1.5 x 10^9/l) was reported in 2.4% patients receiving Kineret compared with 0.4% of placebo patients. None of these patients had serious infections associated with the neutropenia.	

over time with continued Kineret treatment. Thrombocytopenia In clinical studies in RA patients, thrombocytopenia has been reported in 1.9% of treated patients compared to 0.3% in the placebo group. The thrombocytopenias have been mild, i.e. platelet counts have been >75 x10^9/L. Mild thrombocytopenia has also been observed in CAPS patients. During post-marketing use of Kineret, thrombocytopenia has been reported, including occasional case reports indicating severe thrombocytopenia (i.e. platelet counts <10 x10^9/L). Malignancies RA patients may be at a higher risk (on average 2-3 fold) for the development of lymphoma. In clinical trials, whilst patients treated with Kineret had a higher incidence of lymphoma than the expected rate in the general population, this rate is consistent with rates reported in general for RA patients. In clinical trials, the crude incidence rate of malignancy was the same in the Kineret-treated patients and the placebo-treated patients and did not differ from that in the general population. Furthermore, the overall incidence of malignancies was not increased during 3 years of patient exposure to Kineret. Allergic reactions Allergic reactions including anaphylactic reactions, angioedema, urticaria, rash, and pruritus have been reported uncommonly with Kineret. The majority of these reactions were maculopapular or urticarial rashes. In 43 CAPS patients followed for up to 5 years, no allergic event was serious and no event required discontinuation of Kineret treatment.	In 43 CAPS patients followed for up to 5 years neutropenia was reported in 2 patients. Both episodes of neutropenia resolved over time with continued Kineret treatment. Malignancies RA patients may be at a higher risk (on average 2-3 fold) for the development of lymphoma. In clinical trials, whilst patients treated with Kineret had a higher incidence of lymphoma than the expected rate in the general population, this rate is consistent with rates reported in general for RA patients. In clinical trials, the crude incidence rate of malignancy was the same in the Kineret-treated patients and the placebo-treated patients and did not differ from that in the general population. Furthermore, the overall incidence of malignancies was not increased during 3 years of patient exposure to Kineret. Allergic reactions Allergic reactions including anaphylactic reactions, angioedema, urticaria, rash, and pruritus have been reported uncommonly with Kineret. The majority of these reactions were maculopapular or urticarial rashes. In 43 CAPS patients followed for up to 5 years, no allergic event was serious and no event required discontinuation of Kineret treatment.	

Immunogenicity In clinical trials in RA, up to 3% of adult patients tested seropositive at least once during the study for antibodies capable of neutralising the biologic effects of anakinra. The occurrence of antibodies was typically transient and not associated with clinical adverse reactions or diminished efficacy. In addition, in a clinical trial 6% of paediatric patients tested seropositive at least once during the study for antibodies capable of neutralising the biologic effects of anakinra. The majority of CAPS patients in Study 03-AR-0298 developed anakinra anti-drug antibodies. This was not associated with any clinically significant effects on pharmacokinetics, efficacy, or safety. Hepatic Events In clinical studies in RA and CAPS patients, transient elevations of liver enzymes have been seen uncommonly. These elevations have not been associated with signs or symptoms of hepatocellular damage. During post-marketing use isolated case reports indicating non-infectious hepatitis have been received. Hepatic events during post marketing use have mainly been reported in patients with predisposing factors, e.g a history of transaminase elevations before start of Kineret treatment. Injection site reactions In RA patients the most common and consistently reported treatment-related adverse reactions associated with Kineret were ISRs. The majority (95%) of ISRs were reported as mild to moderate. These were typically characterised by 1 or more of the following: erythaema, ecchymosis, inflammation, and pain. At a dose of 100 mg/day, 71% of RA patients developed an ISR compared to 28% of the placebo treated patients. In 43 CAPS patients followed for up to 5 years no patient permanently or temporarily discontinued Kineret treatment due to injection site	Immunogenicity In clinical trials in RA, up to 3% of adult patients tested seropositive at least once during the study for antibodies capable of neutralising the biologic effects of anakinra. The occurrence of antibodies was typically transient and not associated with clinical adverse reactions or diminished efficacy. In addition, in a clinical trial 6% of paediatric patients tested seropositive at least once during the study for antibodies capable of neutralising the biologic effects of anakinra. The majority of CAPS patients in Study 03-AR-0298 developed anakinra anti-drug antibodies. This was not associated with any clinically significant effects on pharmacokinetics, efficacy, or safety. Hepatic Events In clinical studies in RA and CAPS patients, transient elevations of liver enzymes have been seen uncommonly. These elevations have not been associated with signs or symptoms of hepatocellular damage. During post-marketing use isolated case reports indicating non-infectious hepatitis have been received. Hepatic events during post marketing use have mainly been reported in patients with predisposing factors, e.g a history of transaminase elevations before start of Kineret treatment. Injection site reactions In RA patients the most common and consistently reported treatment-related adverse reactions associated with Kineret were ISRs. The majority (95%) of ISRs were reported as mild to moderate. These were typically characterised by 1 or more of the following: erythaema, ecchymosis, inflammation, and pain. At a dose of 100 mg/day, 71% of RA patients developed an ISR	

reactions. ISRs typically appear within 2 weeks' therapy and disappear within 4-6 weeks. The development of ISRs in patients who had not previously experienced ISRs was uncommon after the first month of therapy. Blood cholesterol increase In clinical studies of RA, 775 patients treated with daily Kineret doses of 30mg, 75mg, 150mg, 1mg/kg or 2mg/kg, there was an increase of 2.4% to 5.3% in total cholesterol levels 2 weeks after start of Kineret treatment, without a dose-response relationship. A similar pattern was seen after 24 weeks Kineret treatment. Placebo treatment (n=213) resulted in a decrease of approximately 2.2% in total cholesterol levels at week 2 and 2.3% at week 24. No data are available on LDL or HDL cholesterol. *Paediatric population* Kineret has been studied in 36 CAPS patients aged 8 months to < 18 years, for up to 5 years. With the exception of infections and related symptoms that were more frequently reported in patients <2 years of age, the safety profile was similar in all paediatric age groups. The safety profile in paediatric patients was similar to that seen in adult populations and no clinically relevant new adverse reactions were seen.	compared to 28% of the placebo treated patients. In 43 CAPS patients followed for up to 5 years no patient permanently or temporarily discontinued Kineret treatment due to injection site reactions. ISRs typically appear within 2 weeks' therapy and disappear within 4-6 weeks. The development of ISRs in patients who had not previously experienced ISRs was uncommon after the first month of therapy. *Paediatric population* Kineret has been studied in 36 CAPS patients aged 8 months to < 18 years, for up to 5 years. With the exception of infections and related symptoms that were more frequently reported in patients <2 years of age, the safety profile was similar in all paediatric age groups. The safety profile in paediatric patients was similar to that seen in adult populations and no clinically relevant new adverse reactions were seen.	

מצ"ב העלון ,שבו מסומנות ההחמרות המבוקשות על רקע צהוב.
שינויים שאינם בגדר החמרות סומנו(בעלון) בצבע טורקיז

הועבר בדואר אלקטרוני בתאריך: 19/07/2016