הודעה על החמרה (מידע בטיחות) בעלון לרופא
(מעודכן 05.2013)

תאריך: 03 בינואר 2016

שם תכשיר באנגלית ומספר הרישום:

Signifor 0.3mg / 1 mL [33762], Signifor 0.6mg / 1 mL [33767], Signifor 0.9mg / 1 mL [33768]

שם בעל הרישום: נוברטיס ישראל בע"מ

טופס זה מיועד לפירוט ההחמרות בלבד!

טקסט שחור – טקסט מאושר
טקסט עם קו תחתי – הוספת טקסט לעלון המאושר
~~טקסט עם קו חוצה~~ – מחיקת טקסט מהעלון המאושר
טקסט המסומן בצהוב – החמרה

ההחמרות המבוקשות		
פרק בעלון	**טקסט נוכחי**	**טקסט חדש**

….. Patients who develop increased transaminase levels should be monitored with a second liver function evaluation to confirm the finding. If the finding is confirmed, the patient should be followed with frequent liver function monitoring until values return to pre-treatment levels. Therapy with pasireotide should be discontinued if the patient develops jaundice or other signs suggestive of clinically significant liver dysfunction, in the event of a sustained increase in AST (aspartate aminotransferase) or ALT of 5 x ULN or greater, or if ALT or AST elevations greater than 3 x ULN occur concurrently with bilirubin elevations greater than 2 x ULN. Following discontinuation of treatment with pasireotide, patients should be monitored until resolution. Treatment should not be restarted ~~if the liver function abnormalities are suspected to be related to Signifor~~. ….. Monitoring for an effect on the QTc interval is advisable and ~~A baseline~~ ECG should be performed prior to the start of Signifor therapy, one week after the beginning of the treatment and as clinically indicated thereafter. Hypokalaemia and/or hypomagnesaemia must be corrected prior to administration of Signifor and ~~electrolytes~~ should be monitored periodically during therapy.	….. Patients who develop increased transaminase levels should be monitored with a second liver function evaluation to confirm the finding. If the finding is confirmed, the patient should be followed with frequent liver function monitoring until values return to pre-treatment levels. Therapy with pasireotide should be discontinued if the patient develops jaundice or other signs suggestive of clinically significant liver dysfunction, in the event of a sustained increase in AST (aspartate aminotransferase) or ALT of 5 x ULN or greater, or if ALT or AST elevations greater than 3 x ULN occur concurrently with bilirubin elevations greater than 2 x ULN. Following discontinuation of treatment with pasireotide, patients should be monitored until resolution. Treatment should not be restarted if the liver function abnormalities are suspected to be related to Signifor. ….. A baseline ECG should be performed prior to the start of Signifor therapy, one week after the beginning of the treatment and as clinically indicated thereafter. Hypokalaemia and/or hypomagnesaemia must be corrected prior to administration of Signifor and electrolytes should be monitored periodically during therapy.	**4.4 Special warnings and precautions for use**

מעוצב:לא הורחב ב / נדחס ב

מעוצב:שמאל, משמאל לימין, כניסה: לפני: 0 ס"מ, תלויה: 1 ס"מ, אחרי: 0 ס"מ, רווח לפני: 0 נק', ללא בקרת שורות מיותמות, מנע הפרדת פיסקאות, עצירות טאב: לא ב 2.1 ס"מ

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מעוצב:לא הורחב ב / נדחס ב

מעוצב:גופן: מודגש

מעוצב:סמן

מעוצב:גופן: 11 נק', גופן עבור עברית ושפות אחרות: 11 נק', אנגלית (ארה"ב), סמן

מעוצב:לא הורחב ב / נדחס ב

מעוצב:לא הורחב ב / נדחס ב

מעוצב:לא הורחב ב / נדחס ב

מעוצב:לא הורחב ב / נדחס ב

מעוצב:שמאל, רמה 1, משמאל לימין, כניסה: לפני: 0 ס"מ, תלויה: 1 ס"מ, אחרי: 0 ס"מ, ללא בקרת שורות מיותמות, מנע הפרדת פיסקאות, עצירות טאב: לא ב 2.1 ס"מ

מעוצב:לא הורחב ב / נדחס ב

מעוצב:לא הורחב ב / נדחס ב

מעוצב:גופן: מודגש

מעוצב:סמן

Description of selected adverse reactions	Description of selected adverse reactions	**4.8 Undesirable effects**
Glucose metabolism disorders Elevated ~~fasting plasma~~ glucose ~~levels~~ was the most frequently reported Grade 3 laboratory abnormality (23.2% of patients) in the phase III study in Cushing's disease patients. Mean HbA_{1c} increases were less pronounced in patients with normal glycaemia (n=62 overall) at study entry (i.e. 5.29% and 5.22% at baseline and 6.50% and 6.75% at month 6 for the 0.6 and 0.9 mg twice daily dose groups, respectively) relative to pre-diabetic patients (i.e. n=38 overall; 5.77% and 5.71% at baseline and 7.45% and 7.13% at month 6) or diabetic patients (i.e. n=54 overall; 6.50% and 6.42% at baseline and 7.95% and 8.30% at month 6). Mean fasting plasma glucose levels commonly increased within the first month of treatment, with decreases and stabilisation observed in subsequent months. Fasting plasma glucose and HbA_{1c} values generally decreased over the 28 days following pasireotide discontinuation but remained above baseline values. Long-term follow-up data are not available. Patients with baseline HbA_{1c} ≥7% or who were taking antidiabetic medicinal products prior to randomisation tended to have higher mean changes in fasting plasma glucose and HbA_{1c} relative to other patients. Adverse reactions of hyperglycaemia and diabetes mellitus led to study discontinuation in 5 (3.1%) and 4 (2.5%) patients, respectively. One case of ketosis and one case of ketoacidosis have been reported during compassionate use of Signifor.	*Glucose metabolism disorders* Elevated fasting plasma glucose levels was the most frequently reported Grade 3 laboratory abnormality (23.2% of patients) in the phase III study in Cushing's disease patients. Mean HbA_{1c} increases were less pronounced in patients with normal glycaemia (n=62 overall) at study entry (i.e. 5.29% and 5.22% at baseline and 6.50% and 6.75% at month 6 for the 0.6 and 0.9 mg twice daily dose groups, respectively) relative to pre-diabetic patients (i.e. n=38 overall; 5.77% and 5.71% at baseline and 7.45% and 7.13% at month 6) or diabetic patients (i.e. n=54 overall; 6.50% and 6.42% at baseline and 7.95% and 8.30% at month 6). Mean fasting plasma glucose levels commonly increased within the first month of treatment, with decreases and stabilisation observed in subsequent months. Fasting plasma glucose and HbA_{1c} values generally decreased over the 28 days following pasireotide discontinuation but remained above baseline values. Long-term follow-up data are not available. Patients with baseline HbA_{1c} ≥7% or who were taking antidiabetic medicinal products prior to randomisation tended to have higher mean changes in fasting plasma glucose and HbA_{1c} relative to other patients. Adverse reactions of hyperglycaemia and diabetes mellitus led to study discontinuation in 5 (3.1%) and 4 (2.5%) patients, respectively. One case of ketosis and one case of ketoacidosis have been reported during compassionate use of Signifor.	

מעוצב:רווח לפני: 1.0 נק'