NOVARTIS

SIGNIFOR® (pasireotide)

0.3 mg, 0.6 mg and 0.9 mg solution for injection

Basic Succinct Statement

Version 4.0

CODE: BSS RD 13 Jan 20; APPR 08 Sep 20

This material is only meant for Healthcare Professionals

SIGNIFOR®

Important note: Before prescribing, consult full prescribing information.

Presentation: Pasireotide solution in 1 mL glass ampules containing 0.3 mg, 0.6 mg or 0.9 mg pasireotide (as pasireotide diaspartate).

Indications: Signifor is indicated for the treatment of adult patients with Cushing's disease for whom surgery is not an option or for whom surgery has failed.

Dosage and administration:

Adults*:* ♦ The recommended initial dose of Signifor is 0.6 mg by subcutaneous injection twice a day. ♦ **Children:** Signifor is not recommended for use in pediatric Cushing's disease patients. ♦ Titrate dosage based on treatment response and tolerability. ♦ Management of suspected adverse reactions may require temporary dose reduction by 0.3 mg b.i.d. decrements. ♦ Patients who have not experienced clinical benefit with Signifor® should be considered for discontinuation.

Special patient populations: ♦ No dosage adjustment required for patients with renal impairment, mild hepatic impairment or for elderly patients. ♦ The recommended initial dose for patients with moderate hepatic impairment (Child Pugh B) is 0.3 mg twice a day and the maximum dose is 0.6 mg twice a day.

Contraindications: Severe hepatic impairment (Child Pugh C).

Warnings/Precautions: ♦ **Hypocortisolism**: Monitoring and instructing patients on signs and symptoms of hypocortisolism is necessary. Temporary exogenous steroid replacement therapy and/or dose reduction or interruption of treatment with Signifor® may be necessary. ♦ **Glucose metabolism**: Self-monitoring of blood glucose and/or FPG assessments should be done weekly for the first two to three months and periodically thereafter, as clinically appropriate prior to and during the treatment, as well as over the first two to four weeks after any dose increase. Initiation or adjustment of anti-diabetics may be necessary. There have been post-marketing cases of ketoacidosis with and without diabetic history. In some cases, predisposing factors for ketoacidosis were present. Patients who present with signs and symptoms consistent with severe metabolic acidosis should be assessed for ketoacidosis regardless of diabetes history. In patients with poor glycemic control (HbA1c values >8% while receiving anti-diabetic therapy), diabetes management and monitoring should be intensified prior to initiation and during pasireotide therapy. Dose reduction or treatment discontinuation should be considered, if uncontrolled hyperglycemia persists. After treatment discontinuation, glycemic monitoring (e.g. FPG or HbA1c) should be done according to clinical practice. ♦ **Cardiovascular related events**: Careful monitoring of patients with cardiac disease and/or risk factors for bradycardia recommended. Dose adjustments of drugs such as beta-blockers, calcium channel blockers or agents to control electrolyte balance may be necessary. Caution in patients who have or may develop QT prolongation (e.g. patients with hypokalemia, hypomagnesemia, congenital long QT syndrome; with uncontrolled or significant cardiac disease including recent myocardial infarction, congestive heart failure, unstable angina or clinically significant bradycardia; patients taking anti-arrhythmic medicines or other drugs that may lead to QT prolongation). Hypokalemia or hypomagnesemia must be corrected prior to initiating therapy and periodically monitored thereafter. Baseline ECG recommended prior to initiating therapy and thereafter as clinically indicated. ♦ **Liver tests**: Monitoring of liver function is recommended prior to starting treatment with Signifor, after the first 1-2 weeks and then monthly for 3 months on treatment. Thereafter, liver function should be monitored as

clinically indicated. 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. ♦**Gallbladder and related events/ Pituitary hormones**: Monitoring of gallbladder and pituitary hormones is recommended prior to initiating and periodically during Signifor treatment. ♦**Drug-drug interactions**: Dose adjustments of cyclosporine may be required if co-administered with Signifor.

Adverse reactions: ♦**Very common (>10**%): Hyperglycemia, diabetes mellitus, diarrhea, nausea, abdominal pain, cholelithiasis, injection site reactions, fatigue, glycosylated hemoglobin increased. ♦**Common (1 to 10%)**: Adrenal insufficiency, type 2 diabetes mellitus, decreased appetite, glucose tolerance impaired, headache, dizziness, vomiting, abdominal pain upper, cholecystitis, cholestasis, alopecia, pruritus, myalgia, arthralgia, gamma-glutamyltransferase increased, alanine aminotransferase increased, aspartate aminotransferase increased, lipase increased, blood glucose increased, sinus bradycardia, QT prolongation, hypotension, blood amylase increased, prothrombin time prolonged. ♦**Uncommon (0.1 to 1%)**: Anemia. ♦**Frequency not known:** Diabetic ketoacidosis