FOR MEDIA USE ONLY

About Signifor	Signifor® (pasireotide) is the first and only pituitary-directed medicine approved by the US Food and Drug Administration (FDA) for the treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative. Signifor is a multireceptor targeting somatostatin analog (SSA) that binds with high affinity to four of the five somatostatin receptor subtypes (sst 1, 2, 3 and 5).
Key data	The approval of Signifor is based on data from PASPORT-CUSHINGS (PASireotide clinical trial PORTfolio - CUSHING'S disease), the largest randomized Phase III study to evaluate a medical therapy in patients with Cushing's disease. Results from the study found that a decrease in mean urinary-free cortisol (UFC), the key measure of biochemical control of the disease, was sustained over time in most patients, with a subset of patients reaching normalized levels. The study also showed that certain clinical manifestations of Cushing's disease tended to improve. The primary endpoint, the proportion of patients who achieved normalization of UFC after six months without dose up-titration relative to randomized dose, was met in patients treated with 0.9 mg twice daily. Mean UFC levels were normalized in 26% and 15% of the patients randomized to receive Signifor 0.9 mg and 0.6 mg, respectively, at month six. The median reduction in mean UFC from baseline to month six was around 47% in both dose groups. Reductions in UFC were observed after one month of treatment with Signifor and were sustained during the treatment period in most patients. In addition, 34% and 41% of patients experienced a reduction in mean UFC from baseline ≤ upper limit of normal (ULN) or ≥50% in the 0.6 mg and 0.9 mg groups, respectively. Decreases in blood pressure, weight, body mass index and waist circumference were observed during the study. Limited conclusions can be drawn on these decreases due to variability of response across patients and the absence of a control group. The most common adverse events (AE) (≥20%) occurring in patients in either dose group receiving Signifor were diarrhea, nausea, hyperglycemia, cholelithiasis, headache, abdominal pain, fatigue and diabetes mellitus. The safety profile of Signifor was similar to that of other SSAs with the exception of the greater degree of hyperglycemia.
Dosing And Administration	Signifor is a twice-daily subcutaneous (sc) injection. The recommended initial dose is either 0.6 mg or 0.9 mg by subcutaneous injection twice a day. The dose may be titrated based on response and tolerability. For patients who are started on 0.6 mg twice a day, a dosage increase to 0.9 mg twice a day may be considered based on the response to the treatment, as long as the 0.6 mg dosage is well tolerated by the patient. The recommended initial dose for patients with moderate hepatic impairment is 0.3 mg twice a day and the maximum dose is 0.6 mg twice a day. Signifor should not be used in patients with severe hepatic impairment.
How Signifor works	Signifor binds with high affinity to four of the five somatostatin receptors (sst 1, 2, 3 and 5), which are expressed in the non-cancerous adrenocorticotropic hormone (ACTH)-secreting pituitary tumors that cause Cushing's disease, resulting in inhibition

	of ACTH secretion.
Cushing's disease	Cushing's syndrome is an endocrine disorder caused by excessive cortisol, a vital hormone that regulates metabolism, maintains cardiovascular function and helps the body respond to stress. Cushing's disease is a form of Cushing's syndrome, in which excess cortisol production is triggered by a non-cancerous ACTH-secreting pituitary adenoma. The first line and most common treatment approach for Cushing's disease is surgical removal of the tumor. Cushing's disease is a rare but serious disease that affects approximately one to two patients per million per year. It most commonly affects adults who are as young as 20 to 50 years and affects women three times more often than men. Cushing's disease may present with weight gain, central obesity, a round, red and full face, severe fatigue and weakness, striae (purple stretch marks), high blood pressure, depression and anxiety.
Signifor Important Safety Information	Treatment with Signifor leads to suppression of adrenocorticotropic hormone (ACTH) secretion in Cushing's disease patients. Suppression of ACTH may lead to a decrease in circulating levels of cortisol and potentially hypocortisolism. Patients need to be monitored and instructed how to monitor for signs and symptoms of hypocortisolism. Temporary exogenous steroid (glucocorticoid) replacement therapy and/or dose reduction or interruption of Signifor therapy may be necessary. Elevations in blood glucose levels have been frequently reported in healthy volunteers and patients treated with Signifor. Cushing's disease patients with poor glycemic control may be at higher risk of developing severe hyperglycemia and associated complications. Glycemic status should be assessed prior to starting treatment with Signifor. Patients need to be closely monitored for hyperglycemia; if hyperglycemia develops, the initiation or adjustment of antidiabetic treatment is recommended. 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. Bradycardia has been reported with use of Signifor. Patients with cardiac disease and/or risk factors for bradycardia need to be closely monitored. Signifor is associated with QT prolongation. Caution should be exercised in patients who have or may develop QT prolongation. Hypokalemia or hypomagnesemia must be corrected prior to initiating therapy and monitored thereafter. A baseline electrocardiogram (ECG) should be performed prior to the start of Signifor therapy and monitoring for an effect on QTc interval is advisable during therapy. Elevations in AST (aminotransferases) or ALT (alanine aminotransferase) were reported with the use of Signifor. Monitoring of liver function is recommended prior to starting treatment with Signifor. Liver function should be monitored again after one or two weeks on treatment, then monthly for the first three months and every six months thereafter. Therapy should be discontinued if AST or ALT increase five times the upper limit of normal (ULN) or greater. Cholelithiasis has been frequently reported with the use of Signifor. Ultrasonic evaluation of the gallbladder prior to treatment, and thereafter at six and 12 month intervals is recommended. Monitoring of pituitary hormones is recommended prior to initiating treatment and periodically thereafter as clinically appropriate. Signifor should not be used during pregnancy unless medically necessary. Breast feeding should be discontinued during treatment with Signifor. Signifor may affect the way other medicines work, and other medicines can affect

	how Signifor works. Caution should be exercised with the concomitant use of bromocriptine, cyclosporine, anti-arrhythmic medicines or drugs that may lead to QT prolongation. The most common adverse events (AE) (≥20%) occurring in patients in either dose group receiving Signifor were diarrhea, nausea, hyperglycemia, cholelithiasis, headache, abdominal pain, fatigue and diabetes mellitus.

About Signifor
Signifor® (pasireotide) is approved in the US for the treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative and in the European Union (EU) for the treatment of adult patients with Cushing's disease for whom surgery is not an option or for whom surgery has failed.

Signifor is expected to be available in the US by March 2013 and will be dispensed exclusively through a single specialty pharmacy. For more information about Signifor distribution, doctors and patients can contact Patient Assistance Now Endocrinology (PAN Endo) at 1-877-503-3377 (Press Option 3 for Signifor) or visit www.Signifor.us for more information. PAN Endo also offers quick and easy access to information about the many reimbursement and support programs available for its endocrinology medicines. Enrollment into PAN Endo will begin in January 2013.

For the treatment of Cushing's disease, Signifor has been studied as a twice-daily subcutaneous (sc) injection and is currently being evaluated as a long-acting release (LAR), once-monthly intramuscular (IM) injection as part of a global Phase III program in Cushing's disease and acromegaly. Signifor is a multireceptor targeting SSA that binds with high affinity to four of the five somatostatin receptor subtypes (sst 1, 2, 3 and 5).

There is no guarantee that Signifor will become commercially available anywhere else in the world. As an investigational compound, the safety and efficacy profile of Signifor has not yet been established in all countries for the treatment of Cushing's disease or any other indications. Access to Signifor outside of the approved indications has been carefully controlled and monitored in clinical trials designed to better understand the potential benefits and risks of the compound.

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