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Section:	Prescription Drugs	**Effective Date:**	July 1, 2022
Subsection:	Endocrine and Metabolic Drugs	**Original Policy Date:**	May 6, 2013
Subject:	Signifor	**Page:**	1 of 4

Last Review Date: June 16, 2022

Signifor

Description

Signifor (pasireotide)

Background
Signifor (pasireotide diaspartate) is an injection for the treatment of Cushing's disease patients who cannot be helped through surgery. Cushing's disease is caused by over-production of cortisol, a hormone made by the adrenal glands. Signifor exerts its pharmacological activity via binding to somatostatin receptors (SSTRs). Pasireotide binds and activates the SSTRs resulting in inhibition of ACTH (adrenocorticotropic hormone) secretion, which leads to decreased cortisol secretion (1).

Regulatory Status
FDA-approved indication: Signifor is a somatostatin analog indicated for the treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative (1).

Elevations in blood glucose levels have been seen in healthy volunteers and patients treated with Signifor. The glycemic status [fasting plasma glucose (FPG) or hemoglobin A1c (HbA1c)] should be assessed prior to starting treatment with Signifor. (1).

Signifor is associated with QT prolongation and liver test elevations. It is recommended to obtain a baseline electrocardiogram and liver tests and monitor during treatment. Hypokalemia and hypomagnesemia must be corrected prior to Signifor administration and should be monitored periodically during therapy (1).

Bradycardia has been reported with the use of Signifor. Patients with cardiac disease and/or risk factors for bradycardia, such as history of clinically significant bradycardia, high-grade heart block, or concomitant use of drugs associated with bradycardia, should be carefully monitored (1).

As the pharmacological activity of Signifor mimics that of somatostatin, inhibition of pituitary hormones, other than ACTH, may occur. Monitoring of pituitary function (e.g., TSH/free T4) should occur prior to initiation of therapy with Signifor and should be repeated periodically during treatment. If hypocortisolism occurs, consider a temporary dose reduction or interruption of treatment with Signifor, as well as temporary, exogenous glucocorticoid replacement therapy (1).

Cholelithiasis has been frequently reported. Ultrasonic examination of the gallbladder before, and at 6- to 12-month intervals during Signifor therapy is recommended (1).

The safety and efficacy of Signifor in pediatric patients have not been studied (1).

Related policies
Isturisa, Korlym, Signifor LAR

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Signifor may be considered **medically necessary** in patients 18 years and older with Cushing's disease and if the conditions indicated below are met.

Signifor may be considered **investigational** in patient's less than 18 years old and for all other indications.

Prior-Approval Requirements

Age 18 years of age and older

Diagnosis

Patient must have the following:

Cushing's disease

AND ALL of the following**:**

a. Pituitary surgery was not curative, or patient is not a candidate for surgery
b. Baseline fasting plasma glucose and/or hemoglobin A1c levels have been or will be obtained, and prescriber agrees to monitor blood glucose levels during treatment
c. Baseline liver function tests (LFTs) have been or will be obtained, and prescriber agrees to monitor LFTs during treatment
d. Gallbladder ultrasound examination has been or will be obtained prior to initiation of therapy, and prescriber agrees to perform gallbladder ultrasounds at 6 month intervals during treatment

Prior – Approval *Renewal* Requirements

Age 18 years of age and older

Diagnosis

Patient must have the following:

Cushing's disease

AND ALL of the following:

a. Prescriber agrees to monitor blood glucose levels during treatment
b. Prescriber agrees to monitor LFTs during treatment
c. Prescriber agrees to perform gallbladder ultrasounds at 6 month intervals during treatment

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary
Signifor is a somatostatin analog indicated for the treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative. Elevations in blood glucose levels have been seen in healthy volunteers and patients treated with Signifor. Signifor is associated with QT prolongation, elevated liver tests, and cholelithiasis. The safety and efficacy of Signifor in pediatric patients have not been studied (1).

Prior approval is required to ensure the safe, clinically appropriate and cost-effective use of Signifor while maintaining optimal therapeutic outcomes.

References

1. Signifor [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2020.

Policy History

Date	Action
June 2013	Addition to PA
September 2014	Annual editorial review and reference update Removal of EKG and pituitary testing
September 2015	Annual editorial review and reference update
June 2016	Annual editorial review and reference update Policy number change from 5.08.26 to 5.30.26
December 2017	Annual review
November 2018	Annual editorial review and reference update
December 2019	Annual review and reference update
September 2020	Annual review and reference update
December 2020	Annual review
September 2021	Annual review and reference update
June 2021	Annual review. Revised requirements for clarity

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 16, 2022 and is effective on July 1, 2022.