Signifor (pasireotide)

Background
Signifor (pasireotide diaspertate) 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**

Korlym

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**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 is 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. Surgery was not curative or patient is not a candidate for surgery
   b. Baseline fasting plasma glucose and/or hemoglobin A1c levels obtained and will monitor glucose values during treatment
   c. Baseline liver function tests obtained and will be monitored during treatment
   d. Gallbladder ultrasound examination obtained prior to initiation of therapy and will be repeated at 6 month intervals during therapy

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. Continue to monitor and control blood glucose levels
   b. Continue to monitor liver function
   c. Continue to perform gallbladder ultrasounds at 6 month intervals

**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

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>June 2013</td>
<td>Addition to PA</td>
</tr>
<tr>
<td>September 2014</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td></td>
<td>Removal of EKG and pituitary testing</td>
</tr>
<tr>
<td>September 2015</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>June 2016</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td></td>
<td>Policy number change from 5.08.26 to 5.30.26</td>
</tr>
<tr>
<td>December 2017</td>
<td>Annual review</td>
</tr>
<tr>
<td>November 2018</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>December 2019</td>
<td>Annual review and reference update</td>
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</tbody>
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Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 6, 2019 and is effective on January 1, 2020.