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EPAR summary for the public

Signifor

pasireotide

This is a summary of the European public assessment report (EPAR) for Signifor. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Signifor.

For practical information about using Signifor, patients should read the package leaflet or contact their doctor or pharmacist.

What is Signifor and what is it used for?

Signifor is a medicine for treating adults with Cushing's disease (a condition caused by too much of a hormone called cortisol) and acromegaly (excessive growth, particularly of bones in the hands, feet and face caused by too much growth hormone).

Signifor is used for these conditions when surgery has failed or is not possible and, in the case of acromegaly, when the condition is also not adequately controlled with other medicines similar to Signifor known as 'somatostatin analogues'.

Because the numbers of patients with these diseases are low, the diseases are considered 'rare', and Signifor was designated an 'orphan medicine' (a medicine used in rare diseases).

It contains the active substance pasireotide.

How is Signifor used?

Signifor is available as a solution for injection under the skin and as a powder and liquid used for injection into the muscle.

In patients with Cushing's disease, Signifor is given as an injection either under the skin (preferably at the top of the thigh and the belly) twice a day or into the buttock muscle every 4 weeks. After 2 to 4

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months, the patient's response to treatment should be evaluated, and the dose adjusted as appropriate or treatment stopped if no benefit is seen. If side effects develop the dose may need to be temporarily reduced.

For acromegaly, Signifor is given as an injection into the buttock muscle every 4 weeks. The dose may need to be adjusted according to response, or if side effects develop.

Patients can inject themselves Signifor under the skin after they have been trained. The medicine can only be obtained with a prescription. For further information, see the package leaflet.

How does Signifor work?

The active substance in Signifor, pasireotide is a somatostatin analogue. This means that it works in the same way as the natural hormone, somatostatin, to block the release of growth hormone from the pituitary glands located at the base of the brain and indirectly block the release of cortisol from the adrenal gland found above the kidneys. (To reduce cortisol, pasireotide first reduces the production of another hormone ACTH, which controls cortisol production.)

By reducing levels of cortisol and growth hormone, the medicine can help alleviate symptoms of Cushing's disease and acromegaly.

What benefits of Signifor have been shown in studies?

Cushing's disease

Signifor is effective at normalising cortisol levels in some patients with Cushing's disease. In a main study in 165 adult patients who were given the injection under the skin, 15% of patients receiving 0.6 mg Signifor and 26% of patients receiving 0.9 mg Signifor had normal urine cortisol levels within 6 months. 34% of patients receiving 0.6 mg Signifor and 41% of patients receiving 0.9 mg Signifor partially responded to treatment, with their urine cortisol levels halved within 6 months.

In a second study in 150 adult patients which used the muscle injection, around 41% of patients responded to treatment within 7 months.

Acromegaly

Signifor is effective in reducing levels of growth hormone and IGF-1 (another hormone that is elevated in acromegaly patients). In a main study in 358 previously untreated adults, 31% of patients receiving Signifor had their growth hormone and IGF-1 levels reduced to pre-defined low levels after 1 year, compared with 19% of patients receiving octreotide, another somatostatin analogue. Pre-defined levels were less than 2.5 micrograms/liter for growth hormone or within normal limits for IGF-1.

In the second study in 198 patients whose disease had not been adequately controlled with surgery or other medical treatment, 15% of patients receiving Signifor 40 mg and 20% of patients receiving Signifor 60 mg achieved pre-defined reductions in hormone levels after 24 weeks, compared with none of the 68 patients given the somatostatin analogues octreotide or lanreotide.

Continuation of both studies confirmed the long-term benefit of Signifor in patients with acromegaly.

What are the risks associated with Signifor?

The most common side effects with Signifor (seen in more than 1 patient in 10) are hyperglycaemia (high blood sugar levels), diabetes, diarrhoea, abdominal pain (stomach ache), nausea (feeling sick),

cholelithiasis (gallstones), injection site reactions, and tiredness. For the full list of all side effects reported with Signifor, see the package leaflet.

Signifor must not be used in patients with severe liver problems. For the full list of restrictions with Signifor, see the package leaflet.

Why is Signifor approved?

Signifor is effective at reducing elevated cortisol levels patients with Cushing's disease. Although the number of patients whose cortisol levels returns to normal is small, Signifor is expected tp help patients whose surgical treatments have failed or who cannot have surgery. Those patients who do not experience clinical benefit can stop treatment.

Signifor is also effective in reducing levels of growth hormone in patients with acromegaly. Although its side effects are similar to those of other somatostatin analogues, high blood sugar occurred more frequently and was more severe with Signifor. For this reason, Signifor should be used for acromegaly only when the condition is not controlled by other medicines of its class.

The European Medicines Agency concluded that the benefits of Signifor are greater than its risk and recommended that it approved in the EU.

What measures are being taken to ensure the safe and effective use of Signifor?

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Signifor have been included in the summary of product characteristics and the package leaflet.

Other information about Signifor

The European Commission granted a marketing authorisation valid throughout the European Union for Signifor on 24 April 2012.

The full EPAR for Signifor can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports. For more information about treatment with Signifor, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

The summaries of the opinions of the Committee for Orphan Medicinal Products for Signifor can be found on the Agency's website:

- Cushing's disease
- Acromegaly

This summary was last updated in 09-2017.