reference no: 2331
Publication date: 16 July 2026

Clinical Commissioning Policy:

Osilodrostat phosphate for adult patients with endogenous Cushing's syndrome [URN:2331]

Summary

Osilodrostat phosphate is not recommended to be available as a routinely commissioned treatment for adult patients with endogenous Cushing's Syndrome.

Committee discussion

Clinical Panel considered the evidence base and the recommendation was made to progress the policy. Please see Clinical Panel reports for full details of Clinical Panel's discussion.

The Clinical Priorities Advisory Group committee papers can be accessed here: Clinical Commissioning Policy: Osilodrostat phosphate for adult patients with endogenous Cushing's syndrome

What we have decided

NHS England has carefully reviewed the evidence to treat adult patients with endogenous Cushing's Syndrome. NHS England recognises that the published evidence identifies that, at present, there is sufficient evidence to commission this treatment. However, following the relative prioritisation process undertaken in May 2026, NHS England has concluded that, balanced against other relative priorities that were also considered during this process, Osilodrostat phosphate for adult patients with endogenous Cushing's syndrome will not be funded at this time within the resources available.

The evidence review which informs this commissioning position can be accessed here: Clinical Commissioning Policy: Osilodrostat phosphate for adult patients with endogenous Cushing's syndrome

Links and updates to other policies

NHS England has an existing clinical commissioning policy for pasireotide as an injective medical therapy for the treatment of Cushing's disease. This treatment is given as second line, and therefore will still apply in patients with Cushing's disease who have been unable to tolerate first-line treatment (including osilodrostat phosphate).

NHS England » Clinical Commissioning Policy: Pasireotide diaspartate: an injectable medical therapy for the treatment of Cushings' Disease

Plain language summary

About endogenous Cushing's Syndrome

Cushing's syndrome is an endocrine disorder caused by prolonged exposure to excessive levels of glucocorticoids, a class of hormones that play a crucial role in regulating various bodily functions including controlling the immune system, managing the use of sugars, fats, and proteins, and the stress response. The causes of Cushing's syndrome are either endogenous or exogenous.

Exogenous Cushing's syndrome is caused by exposure to glucocorticoids produced outside of the body, for example in patients prescribed steroids as part of treatment for another medical condition. Exogenous Cushing's syndrome is managed differently and is beyond the scope of this policy.

Endogenous Cushing's syndrome is due to the body excessively producing the main glucocorticoid cortisol. Cortisol is a hormone produced by the adrenal glands, which are walnut-sized endocrine glands that sit on top of the kidneys. Approximately 70% of endogenous Cushing's syndrome cases are caused by an adrenocorticotrophic hormone (ACTH)-secreting adenoma of the pituitary, a pea-sized endocrine gland at the bottom of the brain. This condition is called Cushing's disease and the excessive ACTH production by the pituitary adenoma stimulates the adrenal glands to produce too much cortisol. More rarely, ACTH can be produced by benign or cancerous tumours outside of the pituitary gland, leading to a condition of cortisol excess known as ectopic Cushing's syndrome. Other causes of endogenous Cushing's syndrome are termed ACTH-independent and include overproduction of cortisol by benign tumours (adrenal adenomas), cancerous tumours (adrenal cancer), or hyperplasia of the adrenal glands. All causes of endogenous Cushing's syndrome are within the scope of this policy.

Cushing's syndrome leads to a broad spectrum of clinical signs and symptoms. Patients can experience accumulation of fat mostly around the waist (central obesity), facial changes (moon face), proximal muscle wasting and weakness, menstrual irregularity and reduced fertility, neuropsychiatric symptoms including depression and insomnia, skin thinning, purple stretchmarks, easy bruising, as well as metabolic and cardiovascular complications including high blood pressure, type 2 diabetes, high cholesterol, blood clots, and brittle bones. Patients with Cushing's syndrome also carry an increased risk of infections due to a compromised immune system. Untreated Cushing's syndrome carries a very poor prognosis, with a relative risk of death for those with persistent disease 10-fold greater than those who have been treated successfully.

About current standard treatment

The management of Cushing's syndrome involves rapidly controlling the high cortisol levels, reversing the clinical features, and reducing long-term complications such as high blood pressure and diabetes.

The first-line treatment for most patients, if possible, is surgery to the source of their Cushing's syndrome. This involves pituitary gland surgery in cases of Cushing's disease, surgery to remove ACTH-producing tumours elsewhere in the body in cases of ectopic Cushing's syndrome, or surgery to remove the adrenal tumour/hyperplasia in cases of ACTH-independent Cushing's syndrome. Before surgery, patients will often need treatment with medications to reduce cortisol levels as this mitigates the risk of complications such as blood clots and infections.

A significant proportion of patients will have persistent or recurrent Cushing's syndrome after surgery (approximately 20%). Some patients may be considered not good candidates for surgery based on the risk of peri- and post- operative complications. Rarely, patients may decline surgery due to concerns about vision loss, pituitary hormone deficiency, or in rare cases of Cushing's induced psychosis, where consent is not feasible until their mental state improves with medical treatment. For patients who are not good candidates for, or decline surgery, possible treatment options include (alone or in combination): medical therapies to reduce cortisol levels, radiation therapy, repeat or reconsidering surgery. In cases of recurrent or severe Cushing's syndrome then surgical removal of both adrenal glands (bilateral adrenalectomy) is considered. Currently, licensed oral therapies for endogenous Cushing's syndrome include metyrapone and ketoconazole. These are both first-line therapies, and are usually used as single agents, although more rarely in combination. For those with Cushing's disease, injectable pasireotide can be used as a second-line treatment option. Limitations of these treatments include limited clinical effectiveness and risk of adverse events.

About osilodrostat phosphate treatment

Osilodrostat phosphate is an oral tablet that blocks 11β-hydroxylase, the enzyme involved in the last step of the production of cortisol in the adrenal glands.

Osilodrostat phosphate is licensed for the treatment of adults with endogenous Cushing's syndrome, however it has not been reviewed by NICE.

Epidemiology and needs assessment

Endogenous Cushing's syndrome is a rare condition with an estimated incidence between 1.8 and 3.2 per million per year and an estimated prevalence of 5.9/100,000 people in England per year (Lacroix et al, 2015). Based on the assumption of a 2.5% mortality rate, and a 95% surgical rate with 20% recurrence after any appropriate surgery, it is estimated that approximately 542 patients are suitable for this treatment per year.

- Absent treatment response is defined as neither a complete nor partial response is achieved within 3 months of pharmacological treatment at the maximum tolerated dose

mUFC levels should be interpreted with caution in patients with moderate to severe renal impairment, due to reduced urinary free cortisol excretion. Alternative methods for cortisol monitoring should be considered in these patients (e.g. serum/plasma cortisol, salivary cortisol).

An ECG should be performed prior to the start of osilodrostat phosphate treatment, within one week after treatment initiation, and as clinically indicated thereafter. If the QTc interval exceeds 480ms prior to or during treatment, cardiology consultation is recommended. Temporary dose reduction or interruption may be required.

Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. If a review is needed due to new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment, and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

Definitions

Absent response	Neither complete or partial response is achieved within 3 months of pharmacological treatment at the maximum tolerated dose.
Adrenal glands	These are endocrine (hormone-producing) glands that produce various hormones including adrenaline, androgen precursors, aldosterone and cortisol.
Block-and-replace	This is a treatment regimen that involves using higher doses of medication to reach hypocortisolism and subsequently replacing it with glucocorticoids.
Complete response	Mean 24-hour urinary free cortisol less than or equal to the upper limit of normal
Cortisol	This is a steroid hormone.
Glucocorticoid	These are a class of steroid hormones.
Malignancy	This is caused by uncontrolled grown of abnormal cells, also known as cancer.
Partial response	Mean 24-hour urinary free cortisol greater than the upper limit of normal but with equal or greater than 50% reduction from baseline or mean 24-hour urinary free cortisol between the upper limit of normal and twice the upper limit of normal.
Pituitary gland	This is an endocrine (hormone-producing) gland in the brain.

References

Electronic medicines compendium (emc). Isturisa (osilodrostat). Summary of Product Characteristics. Available from: https://www.medicines.org.uk/emc/product/11587/smpc. 2021. Accessed 03 October 2023.

Lacroix A, Feelders RA, Stratakis CA, Nieman LK. Cushing's syndrome. Lancet (London, England). 2015;386(9996):913-27.