# Osilodrostat

Osilodrostat is a medication used in the Cushing's disease treatment. It is classified as a cortisol synthesis inhibitor, meaning that it blocks an enzyme called 11-beta-hydroxylase that is involved in the production of cortisol in the adrenal glands.

By inhibiting cortisol production, osilodrostat can help reduce the symptoms associated with Cushing's disease, such as weight gain, high blood pressure, and abnormal glucose metabolism. It is typically used in patients who have not responded to other treatments or who are not candidates for surgery to remove the pituitary tumor that is causing the excess cortisol production.

Osilodrostat is taken orally, usually once or twice a day, and is available in tablet form. Common side effects of osilodrostat include nausea, headache, fatigue, and high blood pressure. In some cases, it can also cause liver problems or adrenal insufficiency, so patients taking osilodrostat require close monitoring by a healthcare provider.

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Cushing's disease (CD) is caused by endogenous hypercortisolism as a result of adrenocorticotropin (ACTH) secretion from a pituitary tumor. The condition is associated with multiple comorbidities and increased mortality. First-line therapy for CD is pituitary surgery, performed by an experienced pituitary neurosurgeon. Hypercortisolism may often persist or recur after initial surgery. Patients with persistent or recurrent CD will generally benefit from medical therapy, often administered to patients who underwent radiation therapy to the sella and are awaiting its salutary effects. There are three groups of medications directed against CD, including pituitary-targeted medications that inhibit ACTH secretion from tumorous corticotroph cells, adrenally-directed medications that inhibit adrenal steroidogenesis and a glucocorticoid receptor (GR) antagonist. The focus of this review is osilodrostat, a steroidogenesis inhibitor. Osilodrostat (LCI699) was initially developed to lower serum aldosterone levels and control hypertension. However, it was soon realized that osilodrostat also inhibits 11-beta hydroxylase (CYP11B1), leading to a reduction in serum cortisol levels. The focus of drug development then shifted from treatment of hypertension to treatment of hypercortisolism in CD. In a series of studies (LINC 1 through 4), osilodrostat was shown to be effective in normalizing 24-h urinary free cortisol (UFC) in the majority of treated patients and was approved for patients with CD who have failed surgery or are not surgical candidates. Further study is needed to examine the role of combination therapy as well as long-term outcomes of treated patients. Osilodrostat was shown to have an overall good safety profile. Most common adverse effects include nausea, headache, fatigue, arthralgias, dizziness, prolonged QTc interval, hypokalemia. In females, the drug can cause hirsutism and acne. Osilodrostat is administered twice daily, making it a good choice for patients with difficulty adhering to more complex regimens. Osilodrostat has an important, albeit adjunctive, role in the management of patients with CD.

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Yuen KCJ. Osilodrostat: A Review Of Recent Clinical Studies And Practical Recommendations Of Its Use In The Treatment of Cushing Disease. Endocr Pract. 2021 Aug 10:S1530-891X(21)01107-1. doi: 10.1016/j.eprac.2021.06.012. Epub ahead of print. PMID: 34389514.