Clinical Policy Title:	osilodrostat
Policy Number:	RxA.633
Drug(s) Applied:	Isturisa®
Original Policy Date:	09/14/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All line of business

Background

Osilodrostat (Isturisa®) is a cortisol synthesis inhibitor indicated for the treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
osilodrostat (Isturisa®)	Cushing's disease	Initial dosing: 2 mg orally twice daily, with or without food. Dosage is titrated by 1 to 2 mg twice daily, no more frequently than every 2 weeks based on rate of cortisol changes, individual tolerability and improvement in signs and symptoms. **Hepatic Impairment** Adult Mild impairment (Child-Pugh class A): No dosage adjustment necessary. Moderate impairment (Child-Pugh class B): Initial: 1 mg twice daily. Severe impairment (Child-Pugh class C): Initial: 1 mg once daily in the evening.	Maximum recommended dosage is 30 mg twice daily.

Dosage Forms

- Tablets: 1 mg, 5 mg, and 10 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the

terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Cushing's Disease (must meet all):

1. Diagnosis of Cushing's disease;
2. Age ≥ 18 years;
3. Prescribed by or in consultation with an endocrinologist;
4. Hypokalemia and hypomagnesemia levels are corrected, and baseline electrocardiogram is obtained prior to starting therapy;
5. Documentation supporting failure of pituitary surgery or clinical inability of the patient to undergo pituitary surgery;
6. Maximum dose does not exceed 30 mg twice daily.

Approval Duration
Commercial: 3 months
Medicaid: 3 months

II. Continued Therapy Approval

A. Cushing's Disease (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 30 mg twice daily.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
mifepristone (Korlym®)	600 mg/day	1200 mg/day
Signifor®	0.6 mg twice daily	1.8 mg/day
Signifor® LAR	10 mg – 60 mg every 28 days	60 mg/28 days

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- Hypocortisolism: Monitor patients closely for hypocortisolism and potentially life-threatening adrenal insufficiency. Dosage reduction or interruption may be necessary.
- QTc Prolongation: Perform electrocardiogram in all patients. Use with caution in patients with risk factors for QTc prolongation.
- Elevations in Adrenal Hormone Precursors and Androgens: Monitor for hypokalemia, worsening of hypertension, edema, and hirsutism.

References

1. Isturisa® Prescribing Information. Lebanon, NJ: Recordati Rare Diseases, Inc. March 2020. Available at: https://www.isturisa.com/pdf/isturisa-prescribing-information.pdf. Accessed July 02, 2021.
2. Clinical Pharmacology [database online] powered by Clinical Key. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com. Accessed July 02, 2021.
3. Korlym® (mifepristone) Prescribing Information HCP. Available at: https://www.korlym.com/hcp/wp-content/uploads/sites/2/2020/05/K-00017-NOV-2019_electronic-PI_r8_FINAL.pdf. Accessed July 02, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	09/14/2020	09/14/2020
Policy was reviewed: 1. Background was updated to include generic drug name osilodrostat. 2. Dosing Information dosing regimen was updated to include hepatic impairment dosing, “Adult Mild impairment (Child-Pugh class A): No dosage…”. 3. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 4. Initial Approval Criteria I.A.4 was updated to include “Hypokalemia and hypomagnesemia levels are corrected, and baseline electrocardiogram is obtained prior to starting therapy…”. 5. Continued Therapy Approval Criteria II.A.1 was rephrased to “Member is currently receiving medication that has been authorized by RxAdvance…”. 6. Appendix A was updated to include abbreviation FDA. 7. Therapeutic Alternatives verbiage was	07/02/2021	09/14/2021

rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". 8. Statement about drug listing format in Appendix B is updated to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name®...". 9. Appendix D was updated to include warnings and precautions "Hypocortisolism…", "QTc Prolongation…", and "Elevations in Adrenal Hormone Precursors and Androgens…". 10. References were reviewed and updated. 11. Dosing regimen table was updated to include hepatic dosing adjustments.		