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| **Clinical Policy Title:** | tivozanib |
| **Policy Number:** | RxA.683 |
| **Drug(s) Applied:** | Fotivda® |
| **Original Policy Date:** | 06/10/2021 |
| **Last Review Date:** | 06/10/2021 |
| **Line of Business Policy Applies to:** | All lines of business |

## Background

Fotivda® is a vascular endothelial growth factor (VEGF) tyrosine kinase inhibitor (TKI) indicated for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies.

## Dosing Information

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| tivozanib (Fotivda®) | Relapsed/refractory advanced RCC | 1.34 mg PO once daily with or without food for 21 days on treatment, followed by 7 days off treatment (28-day cycle) until disease progression or unacceptable toxicity | 1.34 mg/day |

## Dosage Forms

- Capsules: 1.34 mg and 0.89 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. Relapsed, Refractory Advanced Renal Cell Carcinoma** (must meet all):

1. Diagnosis of advanced renal cell carcinoma;
1. Failure of at least 2 prior systemic therapies at up to maximally indicated doses within the past 12 months, 1 of which includes a VEGF TKI (e.g. Sutent®, Nexavar®, Inlyta®), unless contraindicated or clinically significant adverse effects are experienced;
2. Prescribed by or in consultation with an oncologist;
3. Member is age ≥ 18 years;
4. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 (Appendix D);
5. Request meets one of the following (a or b):*

a. Dose does not exceed 1.34 mg per day on Days 1 to 21 of a 28-day cycle;
b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

**Approval Duration**
**Commercial:** 3 months
**Medicaid:** 3 months

**II. Continued Therapy Approval**

**A. Relapsed, Refractory Advanced Renal Cell Carcinoma** (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, request meets one of the following (a or b):*
   a. New dose does not exceed 1.34 mg per day on Days 1 to 21 of a 28-day cycle;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

**Approval Duration**
**Commercial:** 6 months
**Medicaid:** 6 months

**III. Appendices**

**APPENDIX A: Abbreviation/Acronym Key**
EOG: Eastern Cooperative Oncology Group
FDA: Food and Drug Administration
NCCN: National Cancer Center Network
TKI: tyrosine kinase inhibitor
VEGF: vascular endothelial growth factor

**APPENDIX B: Therapeutic Alternatives**
None.

**APPENDIX C: Contraindications/Boxed Warnings**

- Contraindication(s):
  - None.

- Boxed Warning(s):
  - None.

**APPENDIX D: General Information**

- Eastern Cooperative Oncology Group (ECOG) performance status:

| GRADE | ECOG PERFORMANCE STATUS |
|---|---|
| 0 | Fully active, able to carry on all pre-disease performance without restriction |
| 1 | Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work |
| 2 | Ambulatory and capable of all selfcare but unable to carry out any work activities; up and |

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| | about more than 50% of waking hours |
| 3 | Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours |
| 4 | Completely disabled; cannot carry on any selfcare; totally confined to bed or chair |
| 5 | Dead |

- A Phase 3, Randomized, Controlled, Multi-Center, Open-Label Study to Compare Tivozanib Hydrochloride to Sorafenib in Subjects With Refractory Advanced Renal Cell Carcinoma [NCT02627963]:
    - Results:
        - Progression-free survival (median months): 5.6 for Fotivda® vs. 3.9 for Nexavar®
        - Overall survival: 16.4 months for Fotivda® vs. 19.2 months for Nexavar®

**References**


1. Fotivda® Prescribing Information, AVEO Pharmaceuticals, Inc., March 2021. Available at: https://www.fotivdahcp.com/fotivdapi.pdf. Accessed May 07, 2021.
2. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2021. Accessed with subscription at: http://www.clinicalkey.com. Updated March 18, 2021. Accessed May 07, 2021.
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4. National Comprehensive Cancer Network. Kidney Cancer Version 4.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Updated April 19, 2021. Accessed May 07, 2021.
5. AVEO Pharmaceuticals, Inc. A Phase 3, Randomized, Controlled, Multi-Center, Open-Label Study to Compare Tivozanib Hydrochloride to Sorafenib in Subjects With Refractory Advanced Renal Cell Carcinoma. Available at: https://clinicaltrials.gov/ct2/show/NCT02627963. NLM identifier: NCT02627963. Accessed May 07, 2021.


| Review/Revision History | Review/Revision Date | P&T Approval Date |
|---|---|---|
| Policy established. | 06/10/2021 | 06/10/2021 |