Three weeks on treatment, one week off[1]

- One 1.34-mg capsule
- Once-daily with water
- With or without food
- 21 days on / 7 days off (28-day cycle)
- 0.89-mg strength available for patients with moderate hepatic impairment or if dose reduction is needed

Dose modifications for adverse reactions included on the following page.

INDICATIONS

FOTIVDA is indicated for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypertension was reported in 45% of patients (22% ≥ Grade 3). **Hypertensive crises** were reported in 0.8% of patients. Do not initiate FOTIVDA in patients with uncontrolled hypertension. Monitor for hypertension and treat as needed. Reduce the FOTIVDA dose for persistent hypertension not controlled by anti-hypertensive medications. Discontinue FOTIVDA for severe hypertension that cannot be controlled with anti-hypertensive therapy or for hypertensive crisis.

Please see Important Safety Information on page 3 and full Prescribing Information for FOTIVDA® (tivozanib).

Dose Modifications for Adverse Reactions[1]

Adverse Reaction	Severity*	Dose Modifications
Hypertension	Grade 3	Withhold for Grade 3 that persists despite optimal antihypertensive therapy. Resume at reduced dose when hypertension is controlled at less than or equal to Grade 2.
	Grade 4	Permanently discontinue.
Cardiac Failure	Grade 3	Withhold until improves to Grade 0 to 1 or baseline. Resume at a reduced dose or discontinue depending on the severity and persistence of adverse reaction.
	Grade 4	Permanently discontinue.
Arterial Thromboembolic Events	Any Grade	Permanently discontinue.
Hemorrhagic Events	Grade 3 or 4	Permanently discontinue.
Proteinuria	2 grams or greater proteinuria in 24 hours	Withhold until less than or equal to 2 grams of proteinuria per 24 hours. Resume at a reduced dose. Permanently discontinue for nephrotic syndrome.
Reverse Posterior Leukoencephalopathy Syndrome	Any Grade	Permanently discontinue.
Other Adverse Reactions	Persistent or intolerable Grade 2 or 3 adverse reaction Grade 4 laboratory abnormality	Withhold until improves to Grade 0 to 1 or baseline. Resume at reduced dose.
	Grade 4 adverse reaction	Permanently discontinue.

*Grades are based on the National Cancer Institute Common Terminology Criteria for Adverse Events.

Reference: 1. FOTIVDA (tivozanib) [package insert]. Boston, MA: AVEO Pharmaceuticals, Inc, August 2024.

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IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypertension was reported in 45% of patients (22% ≥ Grade 3). **Hypertensive crises** were reported in 0.8% of patients. Do not initiate FOTIVDA in patients with uncontrolled hypertension. Monitor for hypertension and treat as needed. Reduce the FOTIVDA dose for persistent hypertension not controlled by anti-hypertensive medications. Discontinue FOTIVDA for severe hypertension that cannot be controlled with anti-hypertensive therapy or for hypertensive crisis.

Cardiac failures were reported in 1.6% of patients (1% ≥ Grade 3); 0.6% of events were fatal. Monitor for signs or symptoms of cardiac failure during treatment with FOTIVDA. Manage with dose interruption, dose reduction, or discontinuation.

Cardiac ischemia were reported in 3.2% of patients; 0.4% of events were fatal. **Arterial thromboembolic events** were reported in 2.0% of patients, including death due to ischemic stroke (0.1%). Closely monitor patients at risk for, or who have a history of these events. Discontinue FOTIVDA in patients who develop severe arterial thromboembolic events, such as myocardial infarction and stroke.

Venous Thrombotic Events (VTE) were reported in 2.4% of patients, including 0.3% fatal events. Closely monitor patients who are at increased risk for these events. Discontinue in patients who develop serious VTEs.

Hemorrhagic Events were reported in 11% of patients; 0.2% of events were fatal. Use FOTIVDA with caution in patients who are at risk for or who have a history of bleeding.

Proteinuria was reported in 8% of patients (2% = Grade 3). Monitor during treatment with FOTIVDA. For moderate to severe proteinuria, reduce the dose or interrupt treatment. Discontinue in patients who develop nephrotic syndrome.

Gastrointestinal (GI) Perforation including fatal cases, has been reported in patients receiving FOTIVDA. Monitor for symptoms of GI perforation or **fistula formation** periodically throughout treatment with FOTIVDA. Permanently discontinue FOTIVDA in patients who develop severe or life-threatening GI perforation.

Thyroid Dysfunction events were reported in 11% of patients (0.3% ≥ Grade 3). Monitor thyroid function before and during treatment with FOTIVDA.

Wound Healing Complications: Withhold FOTIVDA for at least 24 days prior to elective surgery and do not administer for at least 2 weeks after major surgery and until adequate wound healing is observed.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS) can occur with FOTIVDA. Evaluate for RPLS in patients presenting with seizures, headache, visual disturbances, confusion, or altered mental function. Discontinue if signs or symptoms of RPLS occur.

Embryo-fetal Toxicity: FOTIVDA can cause fetal harm. Advise patients of the potential risk to a fetus, to avoid becoming pregnant and to use contraception during treatment and for one month after the last dose of FOTIVDA. Advise males with female partners of reproductive potential to use effective contraception during treatment and for one month after the last dose of FOTIVDA.

Allergic Reaction to Tartrazine: FOTIVDA 0.89 mg capsule contains FD&C Yellow No. 5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible patients.

ADVERSE REACTIONS

Common adverse reactions include fatigue/asthenia, hypertension, diarrhea, decreased appetite, nausea, dysphonia, hypothyroidism, cough, and stomatitis.

Serious adverse reactions include bleeding (3.5%), venous thromboembolism (3.5%), arterial thromboembolism (2.9%), acute kidney injury (2.3%), and hepatobiliary disorders (2.3%).

DRUG INTERACTIONS

Avoid coadministration with strong CYP3A4 inducers.

USE IN SPECIFIC POPULATIONS

Advise women not to breastfeed during treatment and for at least 1 month after the last dose.

The recommended dosage for patients with end-stage renal disease has not been established.

Reduce the FOTIVDA dose for patients with moderate hepatic impairment. The recommended dosage in patients with severe hepatic impairment has not been established.

To report SUSPECTED ADVERSE REACTIONS, contact AVEO Pharmaceuticals, Inc. at 1-833-FOTIVDA (1-833-368-4832) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see full Prescribing Information for FOTIVDA® (tivozanib).

AVEO ONCOLOGY an LG Chem company

FOTIVDA® (tivozanib) capsules