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 moderate hepatic impairment or if dose reduction is needed

Dose modifications for adverse reactions included on the following page.

INDICATIONS AND IMPORTANT SAFETY INFORMATION

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.

WARNINGS AND PRECAUTIONS

Hypertension and Hypertensive Crisis: Hypertension was reported in 45% of FOTIVDA-treated patients with 22% of the events ≥ 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.

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, March 2021.

Please see Important Safety Information on the following page and full Prescribing Information.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypertension and Hypertensive Crisis: Hypertension was reported in 45% of FOTIVDA-treated patients with 22% of the events ≥ 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 Failure: Cardiac failures were reported in 1.6% of FOTIVDA-treated patients, with 1% of events reported as ≥ Grade 3; 0.6% of events were fatal. Monitor for signs or symptoms of cardiac failure throughout treatment with FOTIVDA. Manage with dose interruption, dose reduction, or discontinuation.

Cardiac Ischemia and Arterial Thromboembolic Events: Cardiac ischemia in FOTIVDA-treated patients were reported in 3.2%; 0.4% of events were fatal. Arterial thromboembolic events were reported in 2.0% of FOTIVDA-treated patients, including death due to ischemic stroke (0.1%). Closely monitor patients who are 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: Venous thromboembolic events were reported in 2.4% of FOTIVDA-treated patients, including 0.3% fatal events. Closely monitor patients who are at increased risk for these events. Discontinue FOTIVDA in patients who develop serious venous thromboembolic events.

Hemorrhagic Events: Hemorrhagic events were reported in 11% of FOTIVDA-treated patients; 0.2% of events were fatal. FOTIVDA should be used with caution in patients who are at risk for or who have a history of bleeding.

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

Thyroid Dysfunction: Thyroid dysfunction events were reported in 11% of FOTIVDA-treated patients, with 0.3% of events reported as ≥ Grade 3. Monitor thyroid function before initiation and throughout treatment with FOTIVDA.

Wound Healing Complications: Withhold FOTIVDA for at least 24 days prior to elective surgery. Do not administer FOTIVDA for at least 2 weeks after major surgery and until adequate wound healing is observed. The safety of resumption of FOTIVDA after resolution of wound healing complications has not been established.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS): RPLS, a syndrome of subcortical vasogenic edema diagnosed by MRI, can occur with FOTIVDA. Evaluate for RPLS in patients presenting with seizures, headache, visual disturbances, confusion, or altered mental function. Discontinue FOTIVDA 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) as an imprint ink which may cause allergic-type reactions (including bronchial asthma) in certain susceptible patients.

ADVERSE REACTIONS

The most commonly reported (≥20%) adverse reactions were: fatigue/asthenia, hypertension, diarrhea, decreased appetite, nausea, dysphonia, hypothyroidism, cough, and stomatitis. Serious adverse reactions reported in >2% of patients included bleeding (3.5%), venous thromboembolism (3.5%), arterial thromboembolism (2.9%), acute kidney injury (2.3%), and hepatobiliary disorders (2.3%).

DRUG INTERACTIONS

Strong CYP3A4 Inducers: Avoid coadministration of FOTIVDA with strong CYP3A4 inducers.

USE IN SPECIFIC POPULATIONS

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

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

Hepatic Impairment: 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.

AVEO ONCOLOGY an LG Chem company

FOTIVDA® (tivozanib) capsules