Indication

VOTRIENT® (pazopanib) tablets is indicated for the treatment of patients with advanced soft tissue sarcoma (STS) who have received prior chemotherapy.

Limitation of Use: The efficacy of VOTRIENT for the treatment of patients with adipocytic STS or gastrointestinal stromal tumors has not been demonstrated.

Important Safety Information for VOTRIENT® (pazopanib) tablets

WARNING: HEPATOTOXICITY
Severe and fatal hepatotoxicity has been observed in clinical trials. Monitor hepatic function and interrupt, reduce, or discontinue dosing as recommended. See “Warnings and Precautions,” Section 5.1, in complete Prescribing Information.

Please see additional Important Safety Information on pages 8 through 11. Please click here for full Prescribing Information, including Boxed WARNING, and Medication Guide.
ONCE-DAILY ORAL DOSING

The recommended starting dose is 800 mg once daily

- VOTRIENT® (pazopanib) tablets is available in 200-mg tablets
- Daily dose should not exceed 800 mg

VOTRIENT must be taken without food, at least 1 hour before or 2 hours after a meal

If a dose is missed, it should not be taken if it is less than 12 hours until the next dose

Do not crush tablets due to the potential for increased rate of absorption, which may affect systemic exposure

Dose adjustments

<table>
<thead>
<tr>
<th>STARTING DOSE</th>
<th>INCREMENTAL DOSE ADJUSTMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>800 mg</td>
<td>Dose decrease should be in 200-mg steps based upon individual tolerability</td>
</tr>
</tbody>
</table>

Interruptions, reductions, and discontinuation

In the phase 3 trial:
- 58% of patients taking VOTRIENT required a dose interruption
- 38% of patients taking VOTRIENT required a dose reduction
- 17% of patients taking VOTRIENT discontinued therapy due to adverse reactions

HEPATIC TOXICITY AND IMPAIRMENT

Dosing in patients with preexisting hepatic impairment

<table>
<thead>
<tr>
<th>MILD</th>
<th>MODERATE</th>
<th>SEVERE*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No dose adjustment is required</td>
<td>Alternatives to VOTRIENT should be considered</td>
<td>Treatment with VOTRIENT is not recommended</td>
</tr>
</tbody>
</table>

*Severe hepatic impairment is defined as total bilirubin >3 x ULN with any level of ALT.

Elevated hepatotoxicity levels observed in patients in the phase 3 trial

In patients taking VOTRIENT (n=240) vs placebo (n=123), the following hepatic adverse events were recorded:
- Isolated ALT >3 x ULN was reported in 18% and 5% of VOTRIENT and placebo patients, respectively
- Isolated ALT >8 x ULN was reported in 5% and 2% of patients, respectively
- Concurrent elevation in ALT >3 x ULN and bilirubin >2 x ULN in the absence of significant alkaline phosphatase >3 x ULN occurred in 2% and <1% of patients, respectively

Study Design: Randomized, double-blind, placebo-controlled, multicenter, phase 3 trial to evaluate the efficacy and safety of VOTRIENT in patients (N=369) with advanced soft tissue sarcoma. The primary end point was PFS, while the secondary end points were overall survival, PFS in eligible histology subtypes, overall response rates, and duration of response. The phase 3 trial population excluded patients with adipocytic STS or GIST. Patients were randomized (2:1) to receive either VOTRIENT 800 mg once daily or placebo. The study included patients with leiomyosarcoma receiving VOTRIENT (n=109) or placebo (n=49), patients with synovial sarcoma receiving VOTRIENT (n=25) or placebo (n=13), and patients with "other soft tissue sarcoma" receiving VOTRIENT (n=112) or placebo (n=61).

ALT, alanine aminotransferase; GIST, gastrointestinal stromal tumor; PFS, progression-free survival; ULN, upper limit of normal.

Important Safety Information for VOTRIENT® (pazopanib) tablets

WARNING: HEPATOTOXICITY
Severe and fatal hepatotoxicity has been observed in clinical trials. Monitor hepatic function and interrupt, reduce, or discontinue dosing as recommended. See “Warnings and Precautions,” Section 5.1, in complete Prescribing Information.

Please see additional Important Safety Information on pages 8 through 11.

Please click here for full Prescribing Information, including Boxed WARNING, and Medication Guide.
MONITORING GUIDELINES FOR HEPATIC EFFECTS¹

Monitor serum liver tests

MONITOR serum liver tests at baseline before treatment

MONITOR at weeks 3, 5, 7, and 9

MONITOR at months 3 and 4 and as clinically indicated

CONTINUE periodic monitoring after month 4

MONITORING GUIDELINES FOR HEPATIC EFFECTS¹

ELEVATED HEPATOTOXICITY LEVELS

ISOLATED ALT LEVELS BETWEEN 3 x ULN AND 8 x ULN

DOSE MODIFICATION

• Continue treatment with VOTRIENT® (pazopanib) tablets and monitor liver function tests weekly until ALT levels return to grade 1 or baseline

ISOLATED ALT LEVELS >8 x ULN

• Interrupt treatment until ALT levels return to grade 1 or baseline
• Reintroduce at a reduced dose of no more than 400 mg once daily if the potential benefit outweighs the risk of hepatotoxicity
• Monitor liver function tests weekly for 8 weeks. If ALT elevations >3 x ULN recur, permanently discontinue

ALT LEVELS >3 x ULN CONCURRENTLY WITH BILIRUBIN LEVELS >2 x ULN

• Permanently discontinue and monitor patient until resolution

Concomitant use of VOTRIENT and simvastatin increases the risk of ALT elevations and should be undertaken with caution and close monitoring. Insufficient data are available to assess the risk of concomitant administration of alternative statins and VOTRIENT.¹

Please see additional Important Safety Information on pages 8 through 11.
Please click here for full Prescribing Information, including Boxed WARNING, and Medication Guide.
**RECOMMENDED BASELINE AND PERIODIC TESTING**

<table>
<thead>
<tr>
<th>TEST</th>
<th>FREQUENCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver function</td>
<td>Baseline and at weeks 3, 5, 7, and 9, and at months 3 and 4, and periodically thereafter</td>
</tr>
<tr>
<td>Electrocardiogram</td>
<td>Baseline and periodically thereafter</td>
</tr>
<tr>
<td>Echocardiogram (only for patients at risk of cardiac dysfunction)</td>
<td>Baseline and periodically thereafter</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Before or during week 1 and frequently thereafter</td>
</tr>
<tr>
<td>Thyroid function</td>
<td>Proactive monitoring is recommended</td>
</tr>
<tr>
<td>Urine</td>
<td>Baseline and periodic urinalysis is recommended with follow up measurement of 24-hr urine protein</td>
</tr>
<tr>
<td>Electrolytes</td>
<td>Baseline and periodically thereafter</td>
</tr>
</tbody>
</table>

**DRUG INTERACTIONS**

Please note that this is not a comprehensive list of possible drug interactions.

<table>
<thead>
<tr>
<th>DRUG</th>
<th>POSSIBLE EFFECTS</th>
<th>RECOMMENDED ACTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong CYP3A4 inhibitors</td>
<td></td>
<td>• Avoid use • Consider medications with no or minimal potential to inhibit CYP3A4 • If use of a strong CYP3A4 inhibitor is warranted, reduce pazopanib to 400 mg and lower if adverse reactions occur • Avoid grapefruit and grapefruit juice</td>
</tr>
<tr>
<td>Ketoconazole</td>
<td>Increased</td>
<td>• Avoid use • Consider medications with no or minimal potential to inhibit CYP3A4 • If use of a strong CYP3A4 inhibitor is warranted, reduce pazopanib to 400 mg and lower if adverse reactions occur • Avoid grapefruit and grapefruit juice</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>concentrations</td>
<td>• Avoid use • Consider medications with no or minimal potential to inhibit CYP3A4 • If use of a strong CYP3A4 inhibitor is warranted, reduce pazopanib to 400 mg and lower if adverse reactions occur • Avoid grapefruit and grapefruit juice</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>of pazopanib</td>
<td>• Avoid use • Consider medications with no or minimal potential to inhibit CYP3A4 • If use of a strong CYP3A4 inhibitor is warranted, reduce pazopanib to 400 mg and lower if adverse reactions occur • Avoid grapefruit and grapefruit juice</td>
</tr>
<tr>
<td>Strong CYP3A4 inducers</td>
<td></td>
<td>• Avoid use • Consider medications with no or minimal enzyme induction potential • Do not use in patients who cannot avoid chronic use of strong CYP3A4 inducers</td>
</tr>
<tr>
<td>Rifampin</td>
<td>Decreased</td>
<td>• Avoid use • Consider medications with no or minimal enzyme induction potential • Do not use in patients who cannot avoid chronic use of strong CYP3A4 inducers</td>
</tr>
<tr>
<td>CYP substrates</td>
<td>Inhibition of</td>
<td>• Not recommended for use with agents with narrow therapeutic windows metabolized by CYP3A4, CYP2D6, or CYP2C8</td>
</tr>
<tr>
<td></td>
<td>metabolism and</td>
<td>• Not recommended for use with agents with narrow therapeutic windows metabolized by CYP3A4, CYP2D6, or CYP2C8</td>
</tr>
<tr>
<td></td>
<td>potential for</td>
<td>• Not recommended for use with agents with narrow therapeutic windows metabolized by CYP3A4, CYP2D6, or CYP2C8</td>
</tr>
<tr>
<td></td>
<td>serious adverse</td>
<td>• Not recommended for use with agents with narrow therapeutic windows metabolized by CYP3A4, CYP2D6, or CYP2C8</td>
</tr>
<tr>
<td></td>
<td>reactions</td>
<td>• Not recommended for use with agents with narrow therapeutic windows metabolized by CYP3A4, CYP2D6, or CYP2C8</td>
</tr>
<tr>
<td>Transport inhibitors</td>
<td></td>
<td>• Avoid use • Consider medications with no or minimal potential to inhibit PgP or BCRP</td>
</tr>
<tr>
<td>P-glycoprotein (PgP)</td>
<td></td>
<td>• Avoid use • Consider medications with no or minimal potential to inhibit PgP or BCRP</td>
</tr>
<tr>
<td>Breast cancer resistance protein</td>
<td></td>
<td>• Avoid use • Consider medications with no or minimal potential to inhibit PgP or BCRP</td>
</tr>
<tr>
<td>(BCRP)</td>
<td></td>
<td>• Avoid use • Consider medications with no or minimal potential to inhibit PgP or BCRP</td>
</tr>
<tr>
<td>Simvastatin (insufficient data to assess the risk with alternative statins)</td>
<td>Increased incidence of ALT elevations</td>
<td>• Follow dosing guidelines • Consider alternatives to pazopanib • Consider discontinuing simvastatin</td>
</tr>
<tr>
<td>Drugs that raise gastric pH</td>
<td>Decreased</td>
<td>• Avoid use • Consider short-acting antacids in place of proton pump inhibitors and H2-receptor antagonists • Separate antacid and pazopanib dosing by several hours</td>
</tr>
<tr>
<td>Esomeprazole</td>
<td>concentrations</td>
<td>• Avoid use • Consider short-acting antacids in place of proton pump inhibitors and H2-receptor antagonists • Separate antacid and pazopanib dosing by several hours</td>
</tr>
</tbody>
</table>

Please see additional Important Safety Information on pages 8 through 11.

Please click here for full Prescribing Information, including Boxed WARNING, and Medication Guide.
VOTRIENT® (pazopanib) tablets is indicated for the treatment of patients with advanced soft tissue sarcoma (STS) who have received prior chemotherapy. Limitation of Use: The efficacy of VOTRIENT for the treatment of patients with adipocytic STS or gastrointestinal stromal tumors has not been demonstrated.

**Indication**

VOTRIENT® (pazopanib) tablets is indicated for the treatment of patients with advanced soft tissue sarcoma (STS) who have received prior chemotherapy.

**Important Safety Information for VOTRIENT® (pazopanib) tablets**

**WARNING: HEPATOTOXICITY**

Severe and fatal hepatotoxicity has been observed in clinical trials. Monitor hepatic function and interrupt, reduce, or discontinue dosing as recommended. See “Warnings and Precautions,” Section 5.1, in complete Prescribing Information.

Hepatic Toxicity and Hepatic Impairment: Severe and fatal hepatotoxicity has occurred. Patients older than 65 years are at an increased risk. Increases in serum transaminase levels (ALT, AST) and bilirubin were observed. Transaminase elevations occur early in the course of treatment (92.5% of all transaminase elevations of any grade occurred in the first 18 weeks). In patients with preexisting moderate hepatic impairment, the starting dose of VOTRIENT should be reduced to 200 mg per day or alternatives to VOTRIENT should be considered. Treatment with VOTRIENT is not recommended in patients with severe hepatic impairment. Concomitant use of VOTRIENT and simvastatin increases the risk of ALT elevations and should be undertaken with caution [see Drug Interactions]. Before the initiation of treatment and regularly during treatment, monitor hepatic function and interrupt, reduce, or discontinue dosing as recommended.

QT Prolongation and Torsades de Pointes: Prolonged QT intervals and arrhythmias, including torsades de pointes, have occurred. Use with caution in patients with a history of QT interval prolongation, patients taking antiarrhythmics or other medications that may prolong QT interval, and those with relevant preexisting cardiac disease. Baseline and periodic monitoring of electrocardiograms and maintenance of electrolytes (eg, calcium, magnesium, and potassium) within the normal range should be performed.

Cardiac Dysfunction: Cardiac dysfunction, such as congestive heart failure (CHF) and decreased left ventricular ejection fraction (LVEF), has occurred. In the randomized STS trial, in patients who had baseline and follow-up LVEF measurements, myocardial dysfunction occurred in 11% (16/142) of patients on VOTRIENT compared to 5% (2/40) of patients on placebo. One percent (1/240) of patients on VOTRIENT had CHF, which did not resolve in 1 patient. Monitor blood pressure (BP), and manage promptly using a combination of antihypertensive therapy and dose modification of VOTRIENT (interruption and reinitiation at a reduced dose based on clinical judgment). Carefully monitor patients for clinical signs or symptoms of CHF. Baseline and periodic evaluation of LVEF is recommended in patients at risk of cardiac dysfunction, including previous anthracycline exposure.

Hemorrhagic Events: Hemorrhagic events have occurred and can be fatal. In the randomized STS trial, 22% (53/240) of patients treated with VOTRIENT compared to 8% (10/123) treated with placebo experienced at least 1 hemorrhagic event. The most common hemorrhagic events were epistaxis (8%), mouth hemorrhage (3%), and anal hemorrhage (2%). VOTRIENT should not be used in patients who have a history of hemoptysis, cerebral, or clinically significant gastrointestinal (GI) hemorrhage in the past 6 months.

Arterial Thromboembolic Events: Arterial thromboembolic events have occurred and can be fatal. In the randomized STS trial, 2% (4/240) of patients receiving VOTRIENT experienced myocardial infarction or ischemia, 0.4% (1/240) had a cerebrovascular accident, and there were no incidents of transient ischemic attack. No arterial thromboembolic events were reported in patients who received placebo. Use with caution in patients who are at increased risk for these events or have a history of these events. Do not use VOTRIENT in patients who have had an arterial thromboembolic event in the past 6 months.

Venous Thromboembolic Events (VTEs): VTEs have occurred, including venous thrombosis and fatal pulmonary emboli. In the randomized STS trial, VTEs were reported in 5% of patients treated with VOTRIENT compared to 2% with placebo. Fatal pulmonary embolus occurred in 1% (2/240) of STS patients receiving VOTRIENT and in no patients receiving placebo. Monitor for signs and symptoms.

Thrombotic Microangiopathy (TMA): TMA, including thrombotic thrombocytopenic purpura (TTP) and hemolytic uremic syndrome (HUS), has been reported in clinical trials of VOTRIENT as monotherapy, in combination with bevacizumab, and in combination with topotecan. VOTRIENT is not indicated for use in combination with other agents. Six of the 7 TMA cases occurred within 90 days of the initiation of VOTRIENT. Improvement of TMA was observed after treatment was discontinued. Monitor for signs and symptoms of TMA. Permanently discontinue VOTRIENT in patients developing TMA. Manage as clinically indicated.

GI Perforation and Fistula: In STS trials, GI perforation or fistula occurred in 1% (4/382) of patients receiving VOTRIENT. Fatal perforations occurred in 0.3% (1/382) of these patients. Use with caution in patients at risk for these events, and monitor for signs and symptoms.

Interstitial Lung Disease (ILD)/Pneumonitis: ILD/pneumonitis, which can be fatal, has been reported in 0.1% of patients in the clinical trials treated with VOTRIENT. Monitor patients for ILD/pneumonitis, and discontinue VOTRIENT if symptoms of ILD or pneumonitis develop.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS): RPLS has been reported and may be fatal. Permanently discontinue VOTRIENT in patients developing RPLS.

Hypertension (HTN): HTN, including hypertensive crisis, has occurred in clinical trials. HTN occurs early in the course of treatment (approximately 40% of cases occurred by Day 9, and 90% of cases occurred in the first 18 weeks). BP should be well controlled prior to initiating VOTRIENT, monitored early after starting treatment (no longer than 1 week), and frequently thereafter. Treat increased BP promptly with standard antihypertensive therapy and dose reduction or interruption of VOTRIENT, as clinically warranted. Discontinue VOTRIENT if there is evidence of hypertensive crisis or if HTN is severe and persistent despite antihypertensive therapy and dose reduction of VOTRIENT. Approximately 1% of patients required permanent discontinuation of VOTRIENT because of HTN.

Wound Healing: VOTRIENT may impair wound healing. Interruption of therapy is recommended in patients undergoing surgical procedures. Treatment with VOTRIENT should be stopped at least 7 days prior to scheduled surgery. VOTRIENT should be discontinued in patients with wound dehiscence.

Please see additional Important Safety Information on pages 10 through 11.

Please click here for full Prescribing Information, including Boxed WARNING, and Medication Guide.
VOTRIENT® (pazopanib) tablets is indicated for the treatment of patients with advanced soft tissue sarcoma (STS) who have received prior chemotherapy. Limitation of Use: The efficacy of VOTRIENT for the treatment of patients with adipocytic STS or gastrointestinal stromal tumors has not been demonstrated.

**Important Safety Information for VOTRIENT® (pazopanib) tablets (cont)**

**Hypothyroidism:** Hypothyroidism was reported in 5% (11/240) of patients treated with VOTRIENT® (pazopanib) tablets in the randomized STS trial and in no patients receiving placebo. Monitoring of thyroid function tests is recommended.

**Proteinuria:** In the randomized STS trial, proteinuria was reported as an adverse reaction in 1% (2/240) of patients, and nephrotic syndrome was reported in 1 patient treated with VOTRIENT compared to none in patients receiving placebo. Treatment was withdrawn in the patient with nephrotic syndrome. Monitor urine protein at baseline and periodically as clinically indicated. Interrupt treatment for 24-hour urine protein ≥3 grams, and discontinue for repeat episodes despite dose reductions.

**Infection:** Serious infections (with or without neutropenia), some with fatal outcomes, have been reported. Monitor for signs and symptoms, and treat active infection promptly. Consider interruption or discontinuation of VOTRIENT.

**Increased Toxicity With Other Cancer Therapy:** VOTRIENT is not indicated for use in combination with other agents. Increased toxicity and mortality have been observed in clinical trials administering VOTRIENT in combination with lapatinib or with pemetrexed. The fatal toxicities observed included pulmonary hemorrhage, GI hemorrhage, and sudden death. A safe and effective combination dose has not been established with these regimens.

**Increased Toxicity in Developing Organs:** The safety and effectiveness of VOTRIENT in pediatric patients have not been established. VOTRIENT is not indicated for use in pediatric patients. Animal studies have demonstrated pazopanib can severely affect organ growth and maturation during early postnatal development, and resulted in toxicity to the lungs, liver, heart, and kidney, and in death. VOTRIENT may potentially cause serious adverse effects on organ development in pediatric patients, particularly in patients younger than 2 years of age.

**Females and Males of Reproductive Potential:** VOTRIENT can cause fetal harm when administered to a pregnant woman based on animal reproduction studies and its mechanism of action. In animal developmental and reproductive toxicology studies, oral administration of pazopanib to pregnant rats and rabbits throughout organogenesis resulted in teratogenicty, and abortion at systemic exposures lower than that observed at the maximum recommended human dose of 800 mg.

Verify pregnancy status of females of reproductive potential prior to starting treatment with VOTRIENT. Advise females of reproductive potential to use effective contraception during treatment and for at least 2 weeks after the last dose of VOTRIENT. To avoid potential drug exposure to pregnant partners and female partners of reproductive potential, advise male patients (including those who have had vasectomies) with female partners of reproductive potential to use condoms during treatment with VOTRIENT and for at least 2 weeks after the last dose. VOTRIENT may impair fertility in females and males of reproductive potential while receiving treatment. Because of the potential for serious adverse reactions in breastfed infants from VOTRIENT, advise a lactating woman not to breastfeed during treatment with VOTRIENT and for 2 weeks after the final dose.

**Diarrhea:** Diarrhea occurred frequently and was predominantly mild to moderate in severity. Patients should be advised how to manage mild diarrhea and to notify their health care provider if moderate to severe diarrhea occurs so appropriate management can be implemented to minimize its impact.

**Pneumothorax:** Pneumothorax has occurred (8/240 STS patients [3%] treated with VOTRIENT vs 0% in the placebo group).

**Bradycardia:** In the randomized trial of VOTRIENT for the treatment of STS, bradycardia based on vital signs (<60 beats per minute) was observed in 19% (45/238) of patients treated with VOTRIENT and in 4% (5/121) of patients on the placebo arm.

**Drug Interactions:** Coadministration with strong CYP3A4 inhibitors (eg, ketoconazole, ritonavir, clarithromycin) increases concentrations of pazopanib and should be avoided, but, if warranted, reduce the dose of VOTRIENT to 400 mg. Avoid grapefruit and grapefruit juice.

Concomitant use of strong CYP3A4 inducers (eg, rifampin) should be avoided due to the potential to decrease concentrations of pazopanib. VOTRIENT should not be used in patients who cannot avoid chronic use of CYP3A4 inducers.

Concomitant treatment with strong inhibitors of P-glycoprotein (Pgp) or breast cancer resistance protein (BCRP) should be avoided due to risk of increased exposure to pazopanib.

CYP Substrates: Concomitant use of VOTRIENT with agents with narrow therapeutic windows that are metabolized by CYP3A4, CYP2D6, or CYP2C8 is not recommended. Coadministration may result in inhibition of the metabolism of these products and create the potential for serious adverse events.

Concomitant use of VOTRIENT and simvastatin increases the incidence of ALT elevations. If a patient develops ALT elevations, follow dosing guidelines for VOTRIENT, consider alternatives to VOTRIENT, or consider discontinuing simvastatin. There are insufficient data to assess the risk of concomitant administration of alternative statins and VOTRIENT.

Drugs That Raise Gastric pH: Avoid concomitant use of VOTRIENT with drugs that raise gastric pH (eg, esomeprazole) due to the potential to decrease concentrations of pazopanib. Consider short-acting antacids in place of proton pump inhibitors (PPIs) and H2 receptor antagonists. Separate antacid and pazopanib dosing by several hours.

**Adverse Reactions in the Randomized STS Trial:** A dose interruption was required for 58% of patients on VOTRIENT. The VOTRIENT dose was reduced for 38% of patients. Therapy was discontinued due to adverse reactions for 17% of patients who received VOTRIENT.

The most common adverse reactions (≥20%) in patients who received VOTRIENT vs placebo were fatigue (65% vs 48%), diarrhea (59% vs 15%), nausea (56% vs 22%), decreased weight (48% vs 15%), HTN (42% vs 6%), increased appetite (40% vs 19%), hair color changes (39% vs 2%), vomiting (33% vs 11%), tumor pain (29% vs 21%), dysgeusia (28% vs 3%), headache (23% vs 8%), musculoskeletal pain (23% vs 20%), myalgia (23% vs 9%), GI pain (23% vs 9%), and dyspnea (20% vs 17%).

Laboratory abnormalities occurring in >10% of STS patients and more commonly (≥5%) in patients receiving VOTRIENT vs placebo included increases in AST (51% vs 22%), ALT (46% vs 18%), glucose (45% vs 35%), alkaline phosphatase (32% vs 23%), total bilirubin (29% vs 7%), and potassium (16% vs 11%); decreases in albumin (34% vs 21%) and sodium (31% vs 20%); and leukopenia (44% vs 15%), lymphocytopenia (43% vs 36%), thrombocytopenia (36% vs 6%), and neutropenia (33% vs 7%).

In a pooled analysis of VOTRIENT clinical trials, East Asian patients had a higher frequency of neutropenia, thrombocytopenia, and palmar-plantar erythrodysesthesia syndrome than non-East Asian patients. (See Adverse Reactions, Section 6.1, in complete Prescribing Information.)

Please see additional Important Safety Information on pages 8 through 9.

Please click here for full Prescribing Information, including Boxed WARNING, and Medication Guide.
**ONCE-DAILY ORAL DOSING**

4 x 200 mg

- The recommended starting dose of VOTRIENT® (pazopanib) tablets is 800 mg

**Dosing in patients with preexisting hepatic impairment**

<table>
<thead>
<tr>
<th>MILD</th>
<th>MODERATE</th>
<th>SEVERE*</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No dose adjustment is required</td>
<td>• Alternatives to VOTRIENT should be considered</td>
<td>• Treatment with VOTRIENT is not recommended</td>
</tr>
<tr>
<td></td>
<td>• If VOTRIENT is used, the dose should be reduced to 200 mg per day</td>
<td></td>
</tr>
</tbody>
</table>

*Severe hepatic impairment is defined as total bilirubin >3 x ULN with any level of ALT.

**Important Safety Information for VOTRIENT® (pazopanib) tablets**

**WARNING: HEPATOTOXICITY**
Severe and fatal hepatotoxicity has been observed in clinical trials. Monitor hepatic function and interrupt, reduce, or discontinue dosing as recommended.

See “Warnings and Precautions,” Section 5.1, in complete Prescribing Information.


Please see additional Important Safety Information on pages 8 through 11.

Please click here for full Prescribing Information, including Boxed WARNING, and Medication Guide.

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080 © 2017 Novartis 8/17 VRN-1169073