



CIGNA PHARMACY COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

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Coverage Policy Number 1020

Subject **Pazopanib (Votrient™)**

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Hyperlink to Related Coverage Policies

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2010 CIGNA

Coverage Policy

CIGNA covers pazopanib (Votrient™) as medically necessary for treatment of advanced renal cell carcinoma (RCC).

FDA Approved Indications

Votrient is indicated for the treatment of patients with advanced renal cell carcinoma (RCC).

FDA Recommended Dosing

The recommended dose of Votrient is 800 mg orally once daily without food. The dose of should not exceed 800 mg. Do not crush tablets due to the potential for increased rate of absorption which may affect systemic exposure. If a dose is missed, it should not be taken if it is less than 12 hours until the next dose.

Black Box Warning

Severe and fatal hepatotoxicity has been observed in clinical studies. Monitor hepatic function and interrupt, reduce, or discontinue dosing as recommended.

Drug Availability

The 200 mg tablets of Votrient are modified capsule-shaped, gray, film-coated with GS JT debossed on one side and are available in bottles of 120.

General Background

Pharmacology

Pazopanib is a multi-tyrosine kinase inhibitor labeled for the treatment of advanced renal cell carcinoma (RCC). Vascular endothelial growth factor is a key element in tumor growth. Pazopanib inhibits vascular endothelial growth factor receptors (VEGFR1, VEGFR2, and VEGFR3). Pazopanib also inhibits other receptors implicated in tumor pathogenesis including platelet-derived growth factor receptors (PDGFR-alpha and PDGFR-beta), cytokine receptor (Kit), and fibroblast growth factor receptors (FGFR1 and FGFR3). Additionally, pazopanib inhibits interleukin-2 receptor inducible T-cell kinase (Itk), leukocyte-specific protein tyrosine kinase (Lck), and transmembrane glycoprotein receptor tyrosine kinase (c-Fms).

Peak plasma concentration occurs 2 to 4 hours (median) after oral administration. The bioavailability of pazopanib is significantly increased if the tablet is crushed or administered with food. Pazopanib is over 99% protein bound. Metabolism is hepatic, via isoenzymes CYP3A4 (major pathway), CYP1A2 (minor) and CYP2C8 (minor). The mean half-life is 30.9 hours.

Clinical Efficacy

Pazopanib has not been compared to other agents for the treatment of RCC in clinical trials. Two published clinical trials have evaluated pazopanib in RCC. In one randomized, double-blind trial, median progression free survival was improved with pazopanib (9.2 months) compared to placebo (4.2 months, $p < 0.0001$); more patients experienced a complete or partial response with pazopanib (30%) compared to placebo (3%, $p < 0.001$). In one open-label trial, 35% of patients experienced a complete or partial response. Median progression free survival was 52 weeks. The median duration of response ranged from 58.7 to 68 weeks.

Guidelines

The National Comprehensive Cancer Network (NCCN) recommends Votrient for RCC as follows:

- First-line therapy as a single agent for relapsed or medically unresectable stage IV disease with predominant clear cell histology in selected patients (grade 1)
- Subsequent therapy as a single agent for relapsed or medically unresectable stage IV disease with predominant clear cell histology in patients who have progressed on prior first-line therapy (grade 1)

Adverse Reactions / Interactions

The most common adverse events with pazopanib were diarrhea, hypertension, hair color changes, nausea, vomiting, and anorexia; elevations in ALT and AST (all grades) were reported in 53% of patients. Pazopanib carries a black box warning for potentially severe or fatal hepatotoxicity. Other serious adverse events include hemorrhagic events, proteinuria, gastrointestinal perforation or fistula, arterial thrombotic events, QT prolongation, torsades de pointes, hypothyroidism, and lipase elevation. Pazopanib may impair wound healing.

Significant pharmacokinetic and pharmacodynamic interactions are possible with pazopanib. Consider pazopanib dosing adjustment if used concomitantly with strong CYP3A4 inhibitors. Avoid pazopanib with strong CYP3A4 inducers. Avoid pazopanib with substrates of CYP3A4, CYP2C8, or CYP2D6 that have a narrow therapeutic index. Pazopanib may affect serum concentrations of drugs dependent on UGT1A1 or OATP1B1 for elimination. Use pazopanib cautiously with concomitant agents known to affect the QT interval including antiarrhythmics.

Coding/Billing Information

Note: This section is not in use.

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