Votrient (pazopanib)

Background
Votrient is used to treat advanced renal cell carcinoma (RCC) and advanced soft tissue sarcoma (STS) in patients who have received prior chemotherapy. Votrient works by blocking certain proteins called kinases that play a role in tumor growth and cancer progression. It has been shown to inhibit receptor tyrosine kinases including vascular endothelial growth factor receptors 1, 2 and 3, platelet-derived growth factor receptors α and β, fibroblast growth factor receptors 1 and 3, cytokine receptor (Kit), interleukin-2 receptor-inducible T-cell kinase (Itk), leukocyte-specific protein tyrosine kinase (Lck), and transmembrane glycoprotein receptor tyrosine kinase (c-Fms). These receptors are implicated in tumor blood vessel generation, tumor growth, and cancer progression (1-5).

Regulatory Status
FDA-approved indication: Votrient is an inhibitor of multiple tyrosine kinases indicated for: (1)
   1. Treatment of advanced renal cell carcinoma (RCC)
   2. Treatment of patients with advanced soft tissue sarcoma (STS) who have received prior chemotherapy

Limitation of Use: (1)
The efficacy of Votrient for the treatment of patients with adipocytic STS or gastrointestinal stromal tumors has not been demonstrated.

Off Label Uses: (2-5)
According to current oncology practice guidelines, Votrient may also be used for:
1. Metastatic Dermatofibrosarcoma Protuberans (DFSP)
2. Complete remission following primary treatment of Ovarian Cancer Stage II-IV: Epithelial Ovarian Cancer/Fallopian Tube Cancer/ Primary Peritoneal Cancer
3. Gastrointestinal Stromal Tumor after failure of therapy with imatinib, sunitinib, or regorafenib
4. Recurrent/metastatic Thyroid Carcinomas (Follicular/Hürthle Cell/Medullary/Papillary) if clinical trials or other systemic therapies are not available or appropriate.
5. Recurrent or postoperative Uterine Sarcoma

Votrient includes a boxed warning citing the risk of severe and fatal hepatotoxicity; therefore, Votrient should be used with caution in patients with hepatic impairment. Initiation of Votrient is not recommended in patients with pre-existing hepatic-impairment, defined as total bilirubin > 3 times ULN with any level of ALT. Transaminase and bilirubin levels should be obtained prior to initiation of treatment and regularly throughout therapy (1).

Votrient can cause fatal complications including hemorrhagic events, thromboembolic events, cardiac dysfunction, GI perforation, interstitial lung disease/pneumonitis, reversible posterior leukoencephalopathy syndrome (RPLS), and hypertensive crisis. Use with caution in patients at higher risk of developing these complications. Permanently discontinue Votrient if thrombotic microangiopathy (TMA) or reversible posterior leukoencephalopathy syndrome (RPLS) occurs. Votrient can cause fetal harm when administered to a pregnant woman. Females of reproductive potential should use effective contraception while taking Votrient (1).

The safety and effectiveness of Votrient in pediatric patients have not been established (1).

Related policies
Caprelsa, Cometriq, Nexavar, Stivarga, Sutent

Policy
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Votrient may be considered medically necessary in patients that are 18 years of age and older and when the conditions indicated below are met.

Votrient is considered investigational in patients that are less than 18 years of age and for all other indications.
Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have ONE of the following:

1. Advanced Renal Cell Carcinoma (RCC)

2. Advanced Soft Tissue Sarcoma (STS)
   a. Inadequate treatment response with at least one previous chemotherapy regimen

3. Metastatic Dermatofibrosarcoma Protuberans (DFSP)

4. Recurrent Ovarian Cancer Stage II-IV (Epithelial Ovarian Cancer; Fallopian Tube Cancer; or Primary Peritoneal Cancer)
   a. Complete remission following primary treatment

5. Gastrointestinal Stromal Tumor
   a. Inadequate treatment with imatinib, sunitinib, or regorafenib

6. Recurrent or metastatic Thyroid Carcinoma
   AND ONE of the following:
   a. Follicular carcinoma
   b. Hürthle cell carcinoma
   c. Papillary carcinoma
   d. Medullary carcinoma
      i. Inadequate response or contraindication to vandetanib or cabozantinib

7. Uterine Sarcoma
   AND ONE of the following:
   a. Stage II, III, or IV
   b. Stage I and the disease is medically inoperable

AND the following:
   a. NO severe hepatic impairment
i. Bilirubin levels less than 3 times ULN
ii. Agreement to monitor transaminase and bilirubin levels at least twice per month for the first 3 months and then periodically thereafter.

Prior – Approval Renewal Requirements

Age
18 years of age or older

Diagnosis

Patient must have **ONE** of the following:

1. Advanced Renal Cell Carcinoma (RCC)
2. Advanced Soft Tissue Sarcoma (STS)
3. Metastatic Dermatofibrosarcoma Protuberans (DFSP)
4. Ovarian Cancer
5. Gastrointestinal Stromal Tumor
6. Recurrent or metastatic Thyroid Carcinoma
7. Uterine Sarcoma

AND **NONE** of the following:

a. Severe hepatic impairment
   i. Bilirubin levels less than 3 times ULN
b. Disease progression or unacceptable toxicity

 Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits

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<tr>
<th>Quantity</th>
<th>200 mg</th>
<th>360 tablets per 90 days</th>
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<th>Duration</th>
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Prior – Approval Renewal Limits

Same as above
Rationale

Summary
Votrient is a multi-tyrosine kinase inhibitor indicated for the treatment of advanced renal cell carcinoma, soft tissue sarcoma after trial of prior chemotherapy, and certain cases of dermatofibrosarcoma protuberans, ovarian cancer, GI stromal tumors, thyroid carcinoma, and uterine sarcoma. Votrient should be used with caution in patients at risk for hepatic toxicity, cardiac dysfunction, hemorrhagic events, thromboembolic events, gastrointestinal perforation, interstitial lung disease, RPLS, or hypertensive crisis. The safety and efficacy of Votrient in pediatric patients have not been studied (1-5).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Votrient while maintaining optimal therapeutic outcomes.

References

Policy History

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<thead>
<tr>
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<tbody>
<tr>
<td>August 2016</td>
<td>Addition to PA</td>
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<tr>
<td>December 2016</td>
<td>Annual review</td>
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<tr>
<td>June 2017</td>
<td>Annual editorial review and reference update</td>
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<tr>
<td>September 2017</td>
<td>Annual review</td>
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<td></td>
<td>Addition of quantity limits</td>
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<tr>
<td>June 2018</td>
<td>Annual editorial review and reference update</td>
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<tr>
<td>June 2019</td>
<td>Annual review and reference update</td>
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Keywords
This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 20, 2019 and is effective on July 1, 2019.