



Multi-Targeted Tyrosine Kinase Inhibitors (Multi-TKI) EOCCO POLICY

Policy Type: PA/SP

Pharmacy Coverage Policy: EOCCO166

Description

Lenvatinib (Lenvima), pazopanib (Votrient), and sorafenib (Nexavar) are orally administered multi-tyrosine kinase inhibitors (multi-TKIs), which limit angiogenesis via the inhibition of the bindings of multiple tyrosine kinase enzymes to cell surface receptors (e.g., VEGF, FGFR, IL-2 receptor)

Length of Authorization

- Initial: Three months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
lenvatinib (Lenvima)	Unresectable Hepatocellular Carcinoma; Advanced Renal Cell Carcinoma; Recurrent, High-risk or Metastatic Endometrial Carcinoma; Locally Recurrent or Metastatic Progressive Thyroid Cancer	4 mg capsule therapy pack	30 capsules/30 days*
		10 mg capsule therapy pack	30 capsules/30 days*
		14 mg capsule therapy pack	60 capsules/30 days*
	Unresectable Hepatocellular Carcinoma	8 mg capsule therapy pack	60 capsules/30 days*
		12 mg capsule therapy pack	90 capsules/30 days*
	Advanced Renal Cell Carcinoma; Recurrent, High-risk or Metastatic Endometrial Carcinoma	18 mg capsule therapy pack	90 capsules/30 days*
		20 mg capsule therapy pack	60 capsules/30 days*
	Locally Recurrent or Metastatic Progressive Thyroid Cancer	24 mg capsule therapy pack	90 capsules/30 days*
pazopanib (Votrient)	Advanced Renal Cell Carcinoma; Advanced Soft Tissue Sarcoma	200 mg tablets	120 tablets/30 days
sorafenib (Nexavar)	Unresectable Liver Carcinoma; Advanced Renal Cell Carcinoma; Locally Recurrent or Metastatic Progressive Thyroid Cancer	200 mg tablets	120 tablets/30 days

**Quantity limits are based on recommended daily dose of lenvatinib (Lenvima) for each indication; QL exceptions allowed only for dose reductions*



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Initial Evaluation

- I. Lenvatinib (Lenvima), pazopanib (Votrient), or sorafenib (Nexavar) may be considered medically necessary when the following criteria are met:
 - A. The member is 18 years of age or older; **AND**
 - B. The medication is prescribed by, or in consultation with, an oncologist; **AND**
 - C. The member has not experienced disease progression while on other multi-TKIs [e.g., lenvatinib (Lenvima), pazopanib (Votrient), sorafenib (Nexavar)] unless outlined below (e.g., Renal Cell Carcinoma); **AND**
 - D. A diagnosis of one of the following:
 1. **Renal Cell Carcinoma (RCC); AND**
 - i. The member has advanced (relapsed, stage III) or metastatic (stage IV) disease; **AND**
 - ii. The request is for first-line systemic therapy; **AND**
 - a. Lenvatinib (Lenvima) is being requested in combination with pembrolizumab (Keytruda); **OR**
 - iii. The request is for subsequent-line systemic therapy; **AND**
 - a. The member has had disease progression on, or intolerance to, **one** anti-angiogenic therapy unless all are contraindicated (e.g., axitinib [Inlyta], bevacizumab [Avastin], cabozantinib [Cabometyx]); **AND**
 - i. The request is for Lenvatinib (Lenvima) in combination with everolimus (Afinitor); **OR**
 - ii. The request is for monotherapy with pazopanib (Votrient) OR sorafenib (Nexavar); **OR**
 2. **Hepatocellular Carcinoma (HCC); AND**
 - i. The member has unresectable, advanced (stage III) or metastatic (stage IV) disease; **AND**
 - ii. The medication will be used as monotherapy; **AND**
 - iii. The request is for sorafenib (Nexavar); **AND**
 - a. Provider attests the member is Child-Pugh Class A or Class B7; **OR**
 - iv. The request is for lenvatinib (Lenvima); **AND**
 - a. Provider attests the member has Child-Pugh Class A; **OR**
 3. **Thyroid Carcinoma; AND**
 - i. The member has locally recurrent or metastatic (stage IV) disease; **AND**
 - ii. The member has one of the following subtypes of differentiated thyroid carcinoma:
 - a. Papillary thyroid carcinoma; **OR**
 - b. Follicular thyroid carcinoma; **OR**



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- c. Hurthle cell thyroid carcinoma; **AND**
 - iii. The disease is refractory to radioactive iodine treatment (RAI); **AND**
 - iv. The request is for monotherapy with lenvatinib (Lenvima); **OR**
 - v. The request is for monotherapy with sorafenib (Nexavar); **OR**
 - 4. **Soft Tissue Sarcoma (STS); AND**
 - i. The member has advanced (unresectable) or metastatic (stage IV) soft tissue sarcoma (STS); **AND**
 - ii. The diagnosis of soft tissue sarcoma (STS) does **not** include the following histological subtypes:
 - a. Gastrointestinal Stromal Tumors (GIST); **OR**
 - b. Adipocytic Sarcoma (Liposarcoma); **AND**
 - iii. The request is for pazopanib (Votrient); **AND**
 - a. The medication will be used as monotherapy; **AND**
 - b. The member has had disease progression on at least one anthracycline-based chemotherapy regimen unless all are contraindicated (e.g., doxorubicin, epirubicin, ifosfamide); **OR**
 - 5. **Endometrial Carcinoma (EC); AND**
 - i. The member has advanced, or metastatic endometrial carcinoma (EC); **AND**
 - ii. The disease is NOT microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); **AND**
 - iii. The member had disease progression on, or after, at least ONE platinum-based systemic chemotherapy in the first-line setting; **AND**
 - iv. The request is for lenvatinib (Lenvima); **AND**
 - a. lenvatinib (Lenvima) will be used in combination with pembrolizumab (Keytruda)
- II. Sorafenib (Nexavar) is considered not medically necessary when criteria above are not met and/or when used for:
 - A. Sorafenib (Nexavar) in combination with erlotinib for Hepatocellular Carcinoma
- III. Lenvatinib (Lenvima), pazopanib (Votrient), sorafenib (Nexavar) are considered investigational when used for all other conditions, including but not limited to:
 - A. Gastrointestinal Stromal Tumor
 - B. Adipocytic Sarcoma/Liposarcoma
 - C. Sorafenib (Nexavar) for the treatment of desmoid tumors (aggressive fibromatosis)



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Renewal Evaluation

- I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
- II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
- III. Disease response to treatment defined by stabilization of disease or decrease in tumor size or spread.

Supporting Evidence

- I. Multi-kinase inhibitors [lenvatinib (Lenvima), pazopanib (Votrient), sorafenib (Nexavar)] exert their actions by inhibiting activities of multiple tyrosine kinases by depriving access to the Cdc37-Hsp90 molecular chaperone unit. This inhibitory activity leads to limiting angiogenesis via various cell surface receptors (e.g., VEGF, FGFR, IL-2 receptor). Multi-kinase inhibitors (multi-TKI) listed under this policy have received FDA-approval for patients 18 years and older. Efficacy and safety of these agents have not been established in the pediatric population.
- II. Many treatment options exist for the conditions listed in this policy (e.g., renal cell carcinoma, hepatocellular carcinoma, thyroid carcinoma and soft tissue carcinoma). Initial and further line therapies in these settings are contingent upon patient specific characteristics. Given the complexities surrounding diagnosis and treatment choices, targeted drug therapies such as multi-kinase inhibitors must be prescribed by, or in consultation with, an oncologist.
- III. Multi-kinase inhibitors are considered medically necessary when used as monotherapy. Efficacy and safety of these agents has not been studied in combination with other agents, with the following exceptions: lenvatinib in combination with everolimus for the treatment of renal cell carcinoma, and lenvatinib in combination with pembrolizumab for the treatment of endometrial carcinoma and first-line therapy of renal cell carcinoma.
- IV. **Renal Cell Carcinoma (RCC):**
 - Sorafenib (Nexavar) was studied in one randomized, double-blind, placebo-controlled, multicenter, Phase 3 trial and one randomized, Phase 2 discontinuation trial. The Phase 2 trial enrolled 202 patients with advanced RCC and included patients with no prior therapy and tumor histology other than clear cell carcinoma. Patients were on therapy for 12 weeks and then randomized to continue sorafenib (Nexavar) or switch to placebo. Sorafenib (Nexavar) had a progression free survival (PFS) of 163 days compared to 41 days for placebo (p=0.0001). The Phase 3 trial included 769 patients with advanced RCC who had received on prior systemic therapy. The primary endpoints included OS and PFS. The



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median PFS was 167 days for sorafenib (Nexavar) compared to 84 days for placebo with a HR of 0.44 (95% CI 0.35, 0.55).

- Recently, the NCCN guidelines have been updated to favor the use of multi-TKI in combination with immune checkpoint inhibitors (e.g., nivolumab, pembrolizumab). Lenvatinib (Lenvima) in combination with pembrolizumab (Keytruda) was recently studied in a phase 3, randomized, open-label trial (CLEAR study, N=1069) in comparison with lenvatinib (Lenvima) + everolimus (Afinitor), and sunitinib (1:1:1 randomization). PFS was longer with lenvatinib plus pembrolizumab than with sunitinib (median, 23.9 vs. 9.2 months; HR 0.39; 95% CI, 0.32 to 0.49; P<0.001) and was longer with lenvatinib plus everolimus than with sunitinib (median, 14.7 vs. 9.2 months; HR 0.65). Additionally, overall survival (OS) was longer with lenvatinib plus pembrolizumab than with sunitinib (HR 0.66; 95% CI, 0.49 to 0.88; P = 0.005). However, OS was not statistically different in lenvatinib plus everolimus when compared to sunitinib (HR 1.15; 95% CI, 0.88 to 1.50; P = 0.30).
- Additionally, lenvatinib (Lenvima) was studied in combination with everolimus (Afinitor) as a second-line regimen in one randomized, open-label, active-controlled, multicenter, Phase 1b/2 trial with 153 patients with advanced or metastatic RCC who had previously received anti-angiogenic therapy. The PFS for lenvatinib (Lenvima) in combination with everolimus (Afinitor) was 14.6 months compared to 5.5 months for everolimus (Afinitor) alone with a HR of 0.37 (95% CI 0.22, 0.62).
- Current NCCN guideline recommends pazopanib (Votrient) as ‘other recommended regimen’ in the first-line treatment setting, while sorafenib (Nexavar) has moved to ‘useful in certain circumstances’ as a subsequent-line option only with a category 3 recommendation. Circumstances for the use of sorafenib (Nexavar) are not defined in the NCCN guideline. Meta-analysis of clinical trials involving head-to-head comparison between multi-TKI shows that newer multi-TKI have better efficacy profile compared to sorafenib (Nexavar). Clinical trial for sorafenib (Nexavar) included patients with previous trials of interferon or cytokine-based regimens only, which are no longer used in the first-line setting.

V. Hepatocellular Carcinoma (HCC):

- Sorafenib (Nexavar) was studied in one randomized, double-blind, placebo-controlled, multicenter, Phase 3 trial in 602 patients with unresectable hepatocellular carcinoma (HCC). The primary endpoint was OS. Sorafenib (Nexavar) had an OS of 10.7 months compared to 7.9 months for placebo with a hazard ratio (HR) of 0.69 (95% CI 0.55, 0.87). The median time to progression was 5.5 months for sorafenib (Nexavar) and 2.8 months for placebo with a HR of 0.58 (95% CI 0.45, 0.74).
- Lenvatinib (Lenvima) was studied in one randomized, open-label, active-controlled, non-inferiority, Phase 3 trial in patients with previously untreated unresectable HCC (N=954). The primary efficacy endpoint was OS. Lenvatinib (Lenvima) had a median OS of 13.6 months compared to 12.3 months for sorafenib (Nexavar) with a HR of 0.92 (95% CI 0.79,



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1.06). Lenvatinib (Lenvima) had a median PFS of 7.3 months compared to 3.6 months for sorafenib (Nexavar) with a HR of 0.64 (95% CI 0.55, 0.75).

- NCCN guideline for HCC was recently updated to include atezolizumab (Tecentriq) and bevacizumab (Avastin) as the preferred first-line therapy (category 1 recommendation). Sorafenib (Nexavar) and lenvatinib (Lenvima) are other recommended monotherapy options for first-line therapy (category 1) in patients with a Child-Pugh Class A score [or class A/ B7 for sorafenib (Nexavar)], and those who are treatment naïve in the first-line setting. Additionally, lenvatinib (Lenvima) and sorafenib (Nexavar) are also recommended as second-line agents with category 2A NCCN recommendations should there be progression on first-line therapy with atezolizumab (Tecentriq) and bevacizumab (Avastin). Additionally, it should be noted that incidence of hematological, respiratory, and hepatic adverse reactions is significant with a Tecentriq/Avastin regimen. In many situations, members discontinue the regimen due to adverse reactions and transition to multi-TKI agents without having progressed on the first-line therapy.
- NCCN guideline notes that sorafenib (Nexavar) may be used after disease progression on lenvatinib (Lenvima). However, there is no clinical data to support the use of lenvatinib (Lenvima) after disease progression with sorafenib (Nexavar). Neither of these therapies have been studied in large scale clinical trials to support the use after progression on the other. NCCN guidelines for HCC advise caution while using sorafenib (Nexavar) in patients with Child-Pugh Class B7. More than 95% of participants enrolled in the studies of sorafenib (Nexavar) as well as lenvatinib (Lenvima) had Child-Pugh score class A liver function. Safety data for patients with Child-Pugh score classes B or C are limited, and the recommended dose is uncertain. Additionally, in a systematic review meta-analysis of 8678 patients treated with first-line sorafenib therapy for advanced HCC, Child-Pugh B liver function was associated with a significantly worse OS compared with Child-Pugh A liver function (HR, 2.82 [95% CI, 2.04 to 3.92]; 4 studies). Estimated median OS was 7.2 months for the entire cohort, 8.8 months in patients with Child-Pugh A, and 4.6 months in patients with Child-Pugh B7.

VI. Thyroid Carcinoma:

- In the setting of thyroid carcinoma, sorafenib (Nexavar) was studied in one randomized, double-blind, placebo-controlled, multicenter, Phase 3 trial with 417 patients, who had locally recurrent or metastatic, progressively differentiated thyroid carcinoma. All participants were refractory to radioactive iodine (RAI) regimen. The primary efficacy outcome was PFS. Sorafenib (Nexavar) had a median PFS of 10.8 months compared to 5.8 months for placebo with a HR of 0.59 (95% CI 0.46, 0.76).
- Lenvatinib (Lenvima) was studied in one randomized, double-blind, placebo-controlled Phase 3 trial in patients with locally recurrent or metastatic differentiated thyroid cancer refractory to RAI (N=392). The primary efficacy endpoint was PFS. Lenvatinib (Lenvima) had



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a median PFS of 18.3 months compared to 3.6 months for placebo with a HR of 0.21 (95% CI 0.16, 0.28).

- NCCN guidelines recommend lenvatinib (Lenvima) as the preferred regimen and sorafenib (Nexavar) as other recommended regimen for advanced and metastatic thyroid carcinoma (category 2A recommendations). NCCN considers lenvatinib (Lenvima) to be the preferred agent due to its response rate of 65% compared to 12% for sorafenib (Nexavar), although these agents have never been compared in head-to-head trials. Additionally, lenvatinib (Lenvima) and sorafenib (Nexavar) have not been studied in the settings of medullary and anaplastic thyroid carcinomas.

VII. **Soft Tissue Sarcoma (STS):**

- Pazopanib (Votrient) was studied as a targeted therapy option for the treatment of advanced Soft Tissue Sarcoma (STS) in one randomized, double-blind, placebo-controlled, multicenter, Phase 3 trial (N=369). Enrolled patients had metastatic STS who had failed at least one anthracycline-based chemotherapy regimen. Although patients with most histological subtypes of STS were included in this trial, patients with gastrointestinal stromal tumors (GIST) and adipocyte tumors (liposarcoma) were excluded (of note, there are around 50 histological subtypes of STS). Histological subtype patient distribution for this trial consisted of 47% leiomyosarcoma, 10% synovial sarcoma, and 47% other soft tissue sarcomas. The primary endpoint was PFS. Pazopanib (Votrient) significantly prolonged PFS at 4.6 months vs 1.6 months for placebo ($p < 0.0001$). There was no statistical difference between pazopanib (Votrient) and placebo for OS. NCCN guidelines recommend pazopanib (Votrient) as an option for palliative therapy for patients with progressive, unresectable, or metastatic STS with a category 2A recommendation.

VIII. **Endometrial Carcinoma (EC):**

- Advanced endometrial carcinomas have a poor prognosis, continued annual increase in incidence and disease related mortality. Nearly 84% of patients with recurrent endometrial carcinoma (EC) have microsatellite stable (MSS) or microsatellite-indeterminate tumors. Based on historical clinical trial data, although pembrolizumab is effective for microsatellite instability-high (MSI-H) disease (objective response rate (ORR), 57.1%), it appears less effective for MSS disease (best response was PR, 2/18 patients). Similarly, in a phase II study of lenvatinib monotherapy for advanced, previously treated, endometrial cancer, the ORR was 14.3% and the median PFS was 5.4 months. Thus, as monotherapy, lenvatinib and pembrolizumab do not have substantial evidence of efficacy for advanced EC. However, a novel approach to use these two agents in combination has been considered. Subsequent to FDA-approval, NCCN guideline for uterine carcinoma has provided a category 2A recommendation to the use of above combination, for the treatment of recurrent, high-risk and metastatic EC as a subsequent-line treatment option.
- Surgery is often the initial treatment for early-stage endometrial cancer and consists of a hysterectomy, often along with a salpingo-oophorectomy, and removal of lymph nodes.



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In some cases, depending on localized metastases, debulking may be required. Post-surgical adjuvant regimens may utilize radiation therapy and/ or platinum-based chemotherapy as preferred treatment options. For advanced stage (stage III or IV) EC, or when a member is not a candidate for surgery, systemic chemotherapy (platinum-based regimen preferred), and hormone therapy (e.g., tamoxifen, fulvestrant) are first-line treatment options.

- In a pivotal trial leading to US-FDA approval, Lenvatinib (Lenvima) was studied in combination with pembrolizumab (Keytruda) in a single-arm, open-label, Phase 1b/2 trial (Keynote146/ Study111; N=108) in patients with metastatic endometrial carcinoma after progression on at least one prior systemic therapy. All patients in this trial were exposed to platinum-based chemotherapy in the first-line setting. The primary efficacy outcome, ORR at week 24, was 38.3% (95% CI, 28.8, 47.8). Median duration of response (DoR) for responding participants was 21.2 months (95%CI; 7.6-NR). Additionally, a median PFS of 7.4 months (95% CI; 5.3-8.7) and a median OS of 16.7 months (95% CI; 15.0-NE) were reported. This led to an accelerated FDA approval of lenvatinib (Lenvima) for the treatment of EC in combination with pembrolizumab (Keytruda).
- As of August 2021, efficacy and safety outcomes from a follow-up single-arm, open-label, randomized, active-controlled phase 3 trial have been reported. Keynote-775 / Study 309 (N= 827) compared efficacy and safety of the combination therapy with lenvatinib (Lenvima) and pembrolizumab (LEN+Pembro), with a treatment of physician’s choice (TPC; doxorubicin or paclitaxel) via a 1:1 randomization. Randomization was further stratified by DNA mismatch repair (MMR) status (i.e., pMMR versus dMMR) and microsatellite stability (MSI-H versus MSS). Primary efficacy outcomes were PFS and OS. All participants had prior progression on or after a platinum-based chemotherapy and no previous exposure to PD-1/ PD-L1 therapy. At median 12.2 months of follow-up, PFS was significantly improved with LEN + pembro versus TPC in pMMR advanced EC (median 6.6 vs 3.8 months: HR 0.60). OS in this population subset was significantly longer with LEN + pembro versus TPC (median 17.4 vs 12.0 months; HR 0.68). Additionally, efficacy outcomes in the overall trial population (both pMMR and dMMR EC) also favored LEN+ Pembro over TPC [median OS 18.3 vs 11.4 months (HR 0.62) and median PFS 7.2 vs 3.8 months (HR 0.56)]. However, given the majority participants in this clinical trial had MSS/pMMR EC (n=697 out of 827), the FDA approval is limited to the treatment of MSS/pMMR EC.

Investigational or Not Medically Necessary Uses

- I. Lenvatinib (Lenvima), pazopanib (Votrient), sorafenib (Nexavar) have not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
 - A. Gastrointestinal Stromal Tumor



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B. Adipocytic Sarcoma/Liposarcoma

- i. Pazopanib (Votrient) was studied as a targeted therapy option for the treatment of advanced Soft Tissue Sarcoma (STS) in one randomized, double-blind, placebo-controlled, multicenter, Phase 3 trial (N=369). Enrolled patients had metastatic STS who had failed at least one anthracycline-based chemotherapy regimen. Although patients with most histological subtypes of STS were included in this trial, patients with gastrointestinal stromal tumors (GIST) and adipocyte tumors (liposarcoma) were excluded.

C. Desmoid fibromatosis:

- i. Sorafenib (Nexavar) received a category 1 recommendation from NCCN for the treatment of desmoid tumors (aggressive fibromatosis) based on the data from a phase-3, double-blind, randomized, placebo-controlled, crossover clinical trial (N=87). However, sorafenib is not FDA-approved for this indication. Primary endpoint for this study was progression free survival rate (PFSR), which was estimated (based on Kaplan-Meier curve) at 89% (95% CI, 80,99) as compared to that for placebo 36% (95% CI; 22, 57). 54% of participants had newly diagnosed, untreated desmoid tumors. Although primary outcome was statistically significant, clinical meaningfulness of this data is uncertain due to high withdrawal rates from the trial (62%), significant response rates observed in placebo arm, and lack of patient quality of life (HRQoL) measures. It should be noted that desmoid tumors are slow growing benign tumors, which often regress spontaneously without treatment. hence, efficacy of therapeutic intervention in an untreated patient population, on the basis of PFSR, may not be conclusive.

D. Sorafenib (Nexavar) in combination with erlotinib for Hepatocellular Carcinoma

- i. Sorafenib (Nexavar) in combination with erlotinib, was studied in a randomized, placebo-controlled, Phase 3 trial in 720 patients with advanced HCC. Results found that the combination did not significantly improve survival relative to sorafenib (Nexavar) in combination with placebo. The combination had a significantly lower disease control rate (p=0.021) and a shorter treatment duration of 86 days compared to 123 days for sorafenib/erlotinib and sorafenib/placebo, respectively.

References

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Policy Implementation/Update:

Action and Summary of Changes	Date
Rearranged and updated Lenvima dosing and quantity limits based on recommended maximum dose for each indication; QL exceptions would be allowed only for dose reductions	02/2022
Moved "Sorafenib (Nexavar) for the treatment of desmoid tumors (aggressive fibromatosis)" out of the "Not Medically Necessary" section to "Investigational Use" section; Changed policy name from "lenvatinib (Lenvima™), pazopanib (Votrient®), sorafenib (Nexavar®)" to "Multi-Targeted Tyrosine Kinase Inhibitors (Multi-TKI)"	10/2021
Updated policy to include Lenvima and pembrolizumab combination therapy for endometrial carcinoma and as first-line therapy for RCC; In the HCC setting: removed criteria requiring member being treatment-naïve allowing coverage in first-line as well as 2 nd -line settings, added requirement for Child-Pugh class A/B7. Updates to supporting evidence sections.	09/2021
Added clinical trial data for sorafenib (Nexavar) in the setting of desmoid tumors to the supporting evidence (investigational and not medically necessary uses: C.ii)	04/2021
Updated supporting evidence for investigational indication of endometrial carcinoma for Lenvima	12/2020
Transitioned criteria to policy format and merged into one policy; Updated criteria to include lenvatinib (Lenvima) requires failure of at least one anti-angiogenic therapy and combination therapy of lenvatinib (Lenvima) with everolimus (Afinitor); Updated disease staging requirements for most indications; Updated information on endometrial cancer for lenvatinib (Lenvima); Updated supporting evidence section	10/2020



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<p>Previous reviews</p> <ul style="list-style-type: none"> • Lenvima: Updated indication to include advanced renal cell carcinoma (2017), updated indication to include unresectable hepatocellular carcinoma (2018) • Votrient: Updated to reflect FDA approved indications and quantity limits (2016) • Nexavar: Updated to reflect FDA approved indications (2016) 	<p>10/2018, 06/2017, 03/2016, 03/2016</p>
<p>Criteria created</p> <ul style="list-style-type: none"> • Lenvima: 2015 • Votrient: 2012 • Nexavar: 2012 	<p>03/2015 02/2012 03/2012</p>