DRUG QUANTITY MANAGEMENT POLICY – PER RX

POLICY: Oncology – Vitrakvi Drug Quantity Management Policy – Per Rx
- Vitrakvi® (larotrectinib capsules and oral solution – Bayer)

REVIEW DATE: 05/02/2025

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, 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 CUSTOMER'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 CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES 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 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. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. 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. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Vitrakvi, a kinase inhibitor, is indicated in adult and pediatric patients for the treatment of **solid tumors** that have a **neurotrophic receptor tyrosine kinase (NTRK) gene fusion:** without a known acquired resistance mutation; are metastatic or where surgical resection is likely to result in severe morbidity; have no satisfactory alternative treatments or that have progressed following treatment.[1] Patients should be selected for therapy based on an FDA-approved test.

Dosing

The recommended dose of Vitrakvi in patients with a body surface area (BSA) ≥ 1 m^2 is 100 mg twice daily (BID) until disease progression or unacceptable toxicity.[1] For pediatric patients with a BSA < 1 m^2, the recommended dose of Vitrakvi is 100 mg/m^2 BID. Dose adjustments to 75 mg BID, 50 mg BID, or 100 mg once daily (if

BSA ≥ 1 m^2) or 75 mg/m^2 BID, 50 mg/m^2 BID, or 25 mg/m^2 BID (if BSA < 1 m^2) may be needed to manage adverse events.

Use of Vitrakvi with strong cytochrome P450 (CYP)3A4 inhibitors or inducers should be avoided. However, if coadministration with a strong CYP3A4 inhibitor cannot be avoided, the dose of Vitrakvi should be reduced by 50%. Conversely, if coadministered with a moderate or strong CYP3A4 inducer, the dose of Vitrakvi should be doubled. Additionally, the starting dose of Vitrakvi should be reduced by 50% in patients with moderate to severe hepatic impairment.

Guidelines

Vitrakvi is addressed in the National Comprehensive Cancer Network (NCCN) guidelines for the following:

- **Solid Tumors:** NCCN Compendium notes Vitrakvi as an option for the treatment of the following cancers with NTRK gene fusion-positive tumors as category 2A recommendations: ampullary adenocarcinoma, breast cancer, central nervous system cancers, cervical cancer, cholangiocarcinoma (intrahepatic and extrahepatic), colon cancer, cutaneous melanoma, endometrial carcinoma, epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer, Erdheim-Chester disease, esophageal and esophagogastric cancer, gallbladder cancer, gastric cancer, gastrointestinal stromal tumors, head and neck cancer, hepatocellular carcinoma, Langerhans Cell histiocytosis, neuroendocrine and adrenal tumors, non-small cell lung cancer, ovarian/endometrial/serous carcinoma, occult primary, pancreatic cancer, pediatric diffuse high-grade gliomas, rectal cancer, Rosai-Dorfman disease, salivary gland tumors, small bowel adenocarcinoma, soft tissue sarcoma, thyroid carcinoma, uterine sarcoma, and vulvar cancer.[2]
- **Pediatric Central Nervous System Cancers:** Guidelines (version 2.2025 – January 17, 2025) recommend Vitrakvi for *NTRK* fusion-positive disease in the adjuvant setting or for recurrent or progressive disease (both category 2A).[3] The guideline refers to children and adolescents ≤ 21 years of age.

Availability

Vitrakvi is available as 25 mg and 100 mg capsules supplied in bottles of 60 capsules each.[1] It is also available as a 20 mg/mL oral solution in 50 mL bottles (supplied in packages of 2 bottles each) and 100 mL bottles.

POLICY STATEMENT

This Drug Quantity Management program has been developed to promote the safe, effective, and economic use of Vitrakvi. If the Drug Quantity Management rule is not met for the requested medication at the point of service, coverage will be determined by the Criteria below. All approvals are provided for 1 year in duration.

Drug Quantity Limits

Product	Strength and Dosage Form	Retail Maximum Quantity per Rx	Home Delivery Maximum Quantity per Rx
Vitrakvi® (larotrectinib capsules and oral solution)	25 mg capsules	180 capsules	540 capsules
	100 mg capsules	60 capsules	180 capsules
	20 mg/mL oral solution	300 mL	900 mL

EXCEPTIONS TO THE QUANTITY LIMITS LISTED ABOVE ARE COVERED AS MEDICALLY NECESSARY WHEN THE FOLLOWING CRITERIA ARE MET. ANY OTHER EXCEPTION IS CONSIDERED NOT MEDICALLY NECESSARY.

CRITERIA

Vitrakvi 25 mg capsules

1. If the patient is taking a moderate or strong cytochrome P450 (CYP)3A4 inducer, approve 360 capsules per dispensing at retail or 1,080 capsules per dispensing at home delivery.
Note: Moderate/strong CYP3A inducers include, but are not limited to, apalutamide, carbamazepine, enzalutamide, mitotane, phenytoin, rifampin, St. John's wort, bosentan, efavirenz, phenobarbital, and primidone.

Vitrakvi 100 mg capsules

1. If the patient is taking a moderate or strong cytochrome P450 (CYP)3A4 inducer, approve 120 capsules per dispensing at retail or 360 capsules per dispensing at home delivery.
Note: Moderate/strong CYP3A inducers include, but are not limited to, apalutamide, carbamazepine, enzalutamide, mitotane, phenytoin, rifampin, St. John's wort, bosentan, efavirenz, phenobarbital, and primidone.

Vitrakvi 20 mg/mL oral solution

1. If the patient is taking a moderate or strong cytochrome P450 (CYP)3A4 inducer, approve 600 mL per dispensing at retail or 1,800 mL per dispensing at home delivery.
Note: Moderate/strong CYP3A inducers include, but are not limited to, apalutamide, carbamazepine, enzalutamide, mitotane, phenytoin, rifampin, St. John's wort, bosentan, efavirenz, phenobarbital, and primidone.

REFERENCES

1. Vitrakvi® capsules and oral solution [prescribing information]. Whippany, NJ: Bayer; April 2025.The NCCN Drugs & Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed April 18, 2025. Search terms: larotrectinib.
2. The NCCN Pediatric Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 2.2025 – January 17, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 18, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	Policy was updated to reflect the existing quantity limits when a product is obtained via home delivery. **Vitrakvi 25 mg capsules:** Override criteria were updated to approve an additional quantity if the patient is taking a moderate or strong cytochrome P450 3A4 inducer. Previously, criteria approved if the patient was taking a strong cytochrome P450 3A inducer. **Vitrakvi 100 mg capsules:** Override criteria were updated to approve an additional quantity if the patient is taking a moderate or strong cytochrome P450 3A4 inducer. Previously, criteria approved if the patient was taking a strong cytochrome P450 3A inducer. **Vitrakvi 20 mg/mL oral solution:** Override criteria were updated to approve an additional quantity if the patient is taking a moderate or strong cytochrome P450 3A4 inducer. Previously, criteria approved if the patient was taking a strong cytochrome P450 3A inducer.	05/17/2023
Annual Revision	**Vitrakvi 20 mg/mL oral solution:** The number of bottles were removed from the override criteria as Vitrakvi is now available in multiple bottle sizes. The same override remains in place to approve 600 mL per dispensing at retail or 1,800 mL per dispensing at home delivery if the patient is taking a moderate or strong cytochrome P450 (CYP)3A4 inducer.	05/15/2024
Annual Revision	No criteria changes.	05/02/2025

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