Tropomyosin Receptor Kinase (TRK) Inhibitors
Vitrakvi® (larotrectinib)
Rozyltrek® (entrectinib)
Effective 05/01/2022

Plan	☐ MassHealth ☒ MassHealth (PUF) ☐Commercial/Exchange	**Program Type**	☒ Prior Authorization ☐ Quantity Limit ☐ Step Therapy
Benefit	☒ Pharmacy Benefit ☐ Medical Benefit (NLX)		
Specialty Limitations	This medication has been designated specialty and must be filled at a contracted specialty pharmacy.		
Contact Information	**Specialty Medications**		
	All Plans	Phone: 866-814-5506	Fax: 866-249-6155
	Non-Specialty Medications		
	MassHealth	Phone: 877-433-7643	Fax: 866-255-7569
	Commercial	Phone: 800-294-5979	Fax: 888-836-0730
	Exchange	Phone: 855-582-2022	Fax: 855-245-2134
	Medical Specialty Medications (NLX)		
	All Plans	Phone: 844-345-2803	Fax: 844-851-0882
Exceptions	N/A		

Overview

VITRAKVI is a kinase inhibitor indicated for the treatment of adult and pediatric patients with 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, and
- have no satisfactory alternative treatments or that have progressed following treatment.

ROZLYTREK is a kinase inhibitor indicated for the treatment of:

- Adult patients with metastatic non-small cell lung cancer (NSCLC) that is *ROS1*-positive. (1.1)
- Adult and pediatric patients 12 years of age and older with solid tumors that:
    - have a neurotrophic tyrosine receptor kinase (*NTRK)* gene fusion without a known acquired resistance mutation,
    - are metastatic or where surgical resection is likely to result in severe morbidity, and
    - have progressed following treatment or have no satisfactory alternative therapy.
    -

Drugs that require PA	No PA
Rozlytrek® (entrectinib) and QL >30 capsules/month	Alternatives vary by disease category and may include systemic chemotherapy, radiation, or surgical intervention. Please refer to the NCCN guidelines for the most up-to-date recommendations.
Vitrakvi® (larotrectinib) and QL >60 capsules/month and >300 mL/month	

NCCN=National Comprehensive Cancer Network, PA=prior authorization

Coverage Guidelines

Authorization may be reviewed on a case by case basis for members new to AllWays Health Partners who are currently receiving treatment with the requested drugs, excluding when the product is obtained as samples or via manufacturer's patient assistance programs

OR

Authorization may be granted if the member meets all following criteria and documentation has been submitted:

Solid tumors with neurotrophic receptor tyrosine kinase (NTRK) gene fusion without a known acquired resistance mutation (Rozlytrek®, Vitrakvi®)

1. Appropriate diagnosis*
2. Prescriber is an oncologist
3. Appropriate dosing
4. **ONE** of the following:
    a. Tumor is metastatic
    b. Member is not a candidate for surgical resection
5. **ONE** of the following:
    a. Requested agent is first line for the requested indication
    b. Member has no satisfactory alternative treatments options
    c. Disease has progressed following at least one first-line treatment for the requested indication (e.g., chemotherapy, radiation, surgical intervention)
6. If request is for Vitrakvi (larotrectinib) oral solution formulation, medical necessity for the use of an oral solution formulation (e.g. swallowing disorder)
7. **ONE** of the following:
    a. For Vitrakvi (larotrectinib), request is within quantity limit of:
        i. Vitrakvi 100mg capsule ≤ 2 capsules/day
        ii. Vitrakvi 25mg capsule ≤ 6 capsules/day
        iii. Vitrakvi oral solution ≤10 mL/day
    b. For Rozlytrek (entrectinib), request is within quantity limit of:
        i. Rozlytrek 200mg ≤ 3 capsules/day
        ii. Rozlytrek 100mg ≤ 2 capsules/day

**Please refer to Appendices for evaluation of NSCLC, soft tissue sarcoma, and thyroid carcinoma.*

ROS1-positive metastatic non-small cell lung cancer (NSCLC) (Rozlytrek®)

1. Appropriate diagnosis
2. Prescriber is an oncologist
3. Appropriate dosing
4. Cancer is ROS1 positive (Documentation must be provided on the PA request or in attached medical records)
5. request is within quantity limit of:
    a. Rozlytrek 200mg ≤ 3 capsules/day
    b. Rozlytrek 100mg ≤ 2 capsules/day

Continuation of Therapy

Reauthorization requires documentation of positive response to therapy

Limitations

1. Initial authorization may be issued for **3 months**

2. Reauthorization may be issued for **6 months**
3. The following quantity limits apply:

Rozlytrek 100mg	60 capsules per 30 days
Rozlytrek 200mg	90 capsules per 30 days
Vitrakvi 25mg	180 capsules per 30 days
Vitrakvi 100mg	60 capsules per 30 days
Vitrakvi oral solution	300mL per 30 days

Appendix: Additional Information

Requests for NTRK Gene Fusion-positive NSCLC

In the NCCN guidelines, larotrectinib and entrectinib are treatment options for NTRK gene fusion positive disease. If this gene-fusion was discovered prior to first-line systemic chemotherapy, first-line therapy could be larotrectinib, entrectinib, or other initial systemic therapy options:

- **For adenocarcinoma, large cell, NSCLC NOS (PS 0-1):** No contraindications to PD-1 or PD-L1 inhibitors:
  Preferred:
  - Pembrolizumab/carboplatin/pemetrexed
  - Pembrolizumab/cisplatin/pemetrexed

  Other recommended:
  - Atezolizumab/carboplatin/paclitaxel/bevacizumab (category 1)
  - Nivolumab/ipilimumab/pemetrexed/(carboplatin/cisplatin) (category 1)
- **For adenocarcinoma, large cell, NSCLC NOS (PS 2):**
  Preferred
  - Carboplatin/pemetrexed

  If contraindications to PD-1 or PD-L1 inhibitors:
  - Refer to NCCN guidelines for list of agents useful in certain circumstances

- **For squamous cell carcinoma (PS 0-1):**No contraindications to PD-1 or PD-L1 inhibitors:
  Preferred:
  - Pembrolizumab/carboplatin/paclitaxel (category 1)
  - Pembrolizumab/carboplatin/albumin-bound paclitaxel (category1)

  Other recommended:
  - Nivolumab/ipilimumab
  - Nivolumab/ipilimumab/paclitaxel/carboplatin
- **Squamous cell carcinoma (PS 2)**
  Preferred:
  - Carboplatin/albumin-bound paclitaxel
  - Carboplatin/gemcitabine
  - Carboplatin/paclitaxel

  If contraindications to PD-1 or PD-L1 inhibitors:
  - Refer to NCCN guidelines for list of agents useful in certain circumstances

Approvals will be granted on a case by case basis per NCCN guidelines.

Requests for NTRK Gene Fusion-positive Soft Tissue Sarcoma

In the NCCN guidelines, larotrectinib and entrectinib are single agents treatment options for soft tissue sarcoma subtypes with non-specific histologies. It is the only treatment specifically for NTRK gene-fusion sarcomas. Other treatments for non-NTRK gene-fusion sarcomas include:

- Combination: AD (doxorubicin, dacarbazine); AIM (doxorubicin, ifosfamide, mesna); MAID (mesna, doxorubicin, ifosfamide, dacarbazine); ifosfamide, epirubicin, mesna; gemcitabine and docetaxel; gemcitabine and vinorelbine; gemcitabine and dacarbazine
- Single agent: doxorubicin, ifosfamide, epirubicin, gemcitabine, dacarbazine, liposomal doxorubicin, temozolomide, vinorelbine, eribulin, trabectedin, pazopanib, regorafenib

Approvals will be granted on a case by case basis per NCCN guidelines.

Requests for NTRK Gene Fusion-positive Thyroid Carcinoma
The NCCN guidelines note that larotrectinib and entrectinib are FDA approved for patients with NTRK gene fusion-positive advanced solid tumors. Larotrectinib or entrectinib are recommended treatment options for unresectable locoregional recurrent/persistent disease or soft tissue metastases in papillary carcinoma, follicular carcinoma, Hurthle cell carcinoma, and anaplastic carcinoma if NTRK gene fusion positive. The guidelines recommend molecular testing for actionable mutations prior to systemic treatment.

Approvals will be granted on a case by case basis per NCCN guidelines.

Other NTRK Gene Fusion-positive Solid Tumors
According to the NCCN guidelines, both larotrectinib and entrectinib may be used for the treatment of colon cancer, rectal cancer, biliary tract, head and neck cancers, pancreatic adenocarcinomas, melanoma and ovarian/fallopian/primary peritoneal cancer.

Approvals will be granted on a case by case basis per NCCN guidelines.

References

1. ROZLYTREK® [prescribing information]. South San Francisco, CA: Genentech USA, Inc. 2019.
2. Vaishnavi A, Le AT, Doebele RC. TRKing down an old oncogene in a new era of targeted therapy. *Cancer Discov*. 2015;5(1):25-34.
3. VITRAKVI [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals, Inc.; July 2019.
4. Amatu A, Sartore-Bianchi A, Siena S. *NTRK* gene fusions as novel targets of cancer therapy across multiple tumour types. *ESMO Open*. 2016;1(2):e000023.
5. Laetsch TW, DuBois SG, Mascarenhas L, et al. Larotrectinib for paediatric solid tumours harbouring *NTRK* gene fusions: phase 1 results from a multicentre, open-label, phase 1/2 study. *Lancet Oncol*. 2018;19(5):705-714.

Review History

10/6/20: Created criteria to follow MassHealth partial unified formulary; effective 1/1/21
03/16/2022 – Reviewed and Updated for March P&T; Guideline updated to reflect new quantity limits for both Rozlytrek and Vitrakvi to accommodate potential need for dose adjustments due to pediatric population, changes to BSA or to manage adverse reactions. Appendices section also revised based on updated NCCN guidelines and monitoring program workflow (please see Vitrakvi MCO Cover Sheet). Lastly, guideline title updated to be consistent with GPI categories- changed from Neurotrophic Receptor

Tyrosine Kinase (NTRK) Inhibitors to Tropomyosin Receptor Kinase (TRK) Inhibitors. Effective 05/01/2022

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