BOSTON MEDICAL CENTER HEALTHNet PLAN

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**Pharmacy Policy**

# Neurotrophic Receptor Tyrosine Kinase (NRTK) Inhibitors – Unified Formulary

**Policy Number:** 9.716
**Version Number:** 1
**Version Effective Date:** 1/1/2021

Product Applicability ☐ **All Plan+ Products**

**Well Sense Health Plan**
☐ New Hampshire Medicaid

**Boston Medical Center HealthNet Plan**
☒ MassHealth- MCO
☒ MassHealth- ACO
☐ Qualified Health Plans/ConnectorCare/Employer Choice Direct
☐ Senior Care Options

Note: Disclaimer and audit information is located at the end of this document.

## Prior Authorization Policy

**Reference Table:**

| 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

**Procedure:**

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| **Approval Diagnosis:** | • Solid tumors with neurotrophic receptor tyrosine kinase (NTRK) gene fusion without a known acquired resistance mutation (**Rozlytrek®, Vitrakvi®**)<br>• ROS1-positive metastatic non-small cell lung cancer (NSCLC) (**Rozlytrek®**) |
| **Approval Criteria:** | Prescriber provides documentation of **ALL** of the following: |

+ *Plan* refers to Boston Medical Center Health Plan, Inc. and its affiliates and subsidiaries offering health coverage plans to enrolled members. The Plan operates in Massachusetts under the trade name Boston Medical Center HealthNet Plan and in other states under the trade name Well Sense Health Plan.

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| **Rozlytrek®**<br>(entrectinib)<br><br>**Vitrakvi®**<br>(larotrectinib)<br><br>NTRK gene fusion solid tumors | 1. Appropriate diagnosis*<br>2. Prescriber is an oncologist<br>3. Appropriate dosing**<br>4. **ONE** of the following:<br>a. Tumor is metastatic<br>b. Member is not a candidate for surgical resection<br>5. **ONE** of the following:<br>a. Requested agent is first-line for the requested indication<br>b. Member has no satisfactory alternative treatments options<br>c. Disease has progressed following at least one first-line treatment for the requested indication (e.g., chemotherapy, radiation, surgical intervention)<br>6. If request is for oral solution formulation, medical necessity for the use of an oral solution formulation (e.g. swallowing disorder)<br><br>***Notes:***<br>• ***The Clinical Reviewer will evaluate whether member has no satisfactory alternative treatments based on the tumor type and ensure that the gene fusion does not have a known resistance mutation.***<br>• **Please refer to Appendices for evaluation of NSCLC, soft tissue sarcoma, and thyroid carcinoma.*<br>• ***Concomitant use of larotrectinib with strong CYP3A4 inhibitors (e.g., ketoconazole, clarithromycin, indinavir), strong CYP3A4 inducers (e.g., carbamazepine, phenobarbital, phenytoin), and sensitive CYP3A4 substrates should be avoided. Product labeling provides instructions on dose modification in the concomitant use of strong CYP3A4 inhibitors (50% dose reduction of larotrectinib) and strong CYP3A4 inducers (doubling of larotrectinib dose [please evaluate for over quantity limit]) if concomitant use cannot be avoided. Concomitant use of entrectinib with moderate or strong CYP3A inducers or inhibitors should be avoided. If coadministration with moderate or strong CYP3A inhibitors is unavoidable, the entrectinib dose should be reduced.* |
| **Approval Criteria:**<br><br>**Rozlytrek®**<br>(entrectinib)<br><br>ROS1-positive NSCLC | Prescriber provides documentation of **ALL** of the following:<br>1. Appropriate diagnosis<br>2. Prescriber is an oncologist<br>3. Appropriate dosing**<br>4. Cancer is ROS1 positive (Documentation must be provided on the PA request or in attached medical records)<br><br>***Notes:***<br>• ***Concomitant use of entrectinib with moderate or strong CYP3A inducers or inhibitors should be avoided. If coadministration with moderate or strong CYP3A inhibitors is unavoidable, the entrectinib dose should be reduced.* |
| **Denial Criteria:** | Cases that do not meet the approval criteria will be denied.<br><br>If a request is denied and the prescriber has additional clinical documentation, a **new** prior authorization request must be submitted. |

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| **Duration/Quantity of Authorization:** | Prior authorization may be issued for **three months**. |
| **Recertification Criteria:** | Prescriber provides documentation of positive response to therapy and the request can be recertified for **six months**. |

**Appendix:**

**Stability**

Stability alone on Rozlytrek® (entrectinib) or Vitrakvi® (larotrectinib) is not a reason to bypass approval criteria. However, requests for members who have already started treatment on these agents should be reviewed with clinical review and approval is strongly considered for any member with any FDA-approved indication.

**Grandfathering**

Information is not applicable.

**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, which include immune checkpoint inhibitors or other systemic therapies.

- Immune checkpoint inhibitors: nivolumab, pembrolizumab, or atezolizumab
- Other therapies: docetaxel, pemetrexed, gemcitabine, or ramucirumab + docetaxel

*Please always refer to the latest NCCN guideline prior to issuing a final decision.*

**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 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

*Please always refer to the latest NCCN guideline prior to issuing a final decision.*

**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 in regard to treatment options for papillary carcinoma, follicular carcinoma, Hurthle cell carcinoma, and anaplastic carcinoma. The guidelines recommend molecular testing for actionable mutations prior to systemic treatment.

*Please always refer to the latest NCCN guideline prior to issuing a final decision.*

**Other NTRK Gene Fusion-positive Solid Tumors**

According to the NCCN guidelines, larotrectinib may be used for the treatment of pancreatic adenocarcinoma. According to the NCCN guidelines, both larotrectinib and entrectinib may be used for the treatment of colon Cancer, rectal cancer, head and neck cancers, and ovarian cancer.

*Please always refer to the latest NCCN guideline prior to issuing a final decision.*

## Clinical Background Information and References

| Original Approval Date | Original Effective Date | Policy Owner | Approved by |
|---|---|---|---|
| 12/1/2020 | 1/1/2021 | Pharmacy Services | Pharmacy & Therapeutics (P&T) Committee |

| Policy Revisions History | | | |
|---|---|---|---|
| **Review Date** | **Summary of Revisions** | **Revision Effective Date** | **Approved by** |
| 12/1/2020 | New policy create to align with MH Unified Formulary Policy | 1/1/2021 | P&T Committee |

## Next Review Date

2021

## Reference to Applicable Laws and Regulations, If Any

### Disclaimer Information

Medical Policies are the Plan's guidelines for determining the medical necessity of certain services or supplies for purposes of determining coverage. These Policies may also describe when a service or supply is considered experimental or investigational, or cosmetic. In making coverage decisions, the Plan uses these guidelines and other Plan Policies, as well as the Member's benefit document, and when appropriate, coordinates with the Member's health care Providers to consider the individual Member's health care needs.

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Plan Policies are developed in accordance with applicable state and federal laws and regulations, and accrediting organization standards (including NCQA). Medical Policies are also developed, as appropriate, with consideration of the medical necessity definitions in various Plan products, review of current literature, consultation with practicing Providers in the Plan's service area who are medical experts in the particular field, and adherence to FDA and other government agency policies. Applicable state or federal mandates, as well as the Member's benefit document, take precedence over these guidelines. Policies are reviewed and updated on an annual basis, or more frequently as needed. Treating providers are solely responsible for the medical advice and treatment of Members.

The use of this Policy is neither a guarantee of payment nor a final prediction of how a specific claim(s) will be adjudicated. Reimbursement is based on many factors, including member eligibility and benefits on the date of service; medical necessity; utilization management guidelines (when applicable); coordination of benefits; adherence with applicable Plan policies and procedures; clinical coding criteria; claim editing logic; and the applicable Plan – Provider agreement.