

Pharmacy Policy

Neurotrophic Receptor Tyrosine Kinase (NRTK) Inhibitors – Unified Formulary

Policy Number: 9.716

Version Number: 2

Version Effective Date: 9/1/2021

Product Applicability <input type="checkbox"/> All Plan+ Products	
<p>Well Sense Health Plan</p> <input type="checkbox"/> New Hampshire Medicaid	<p>Boston Medical Center HealthNet Plan</p> <input checked="" type="checkbox"/> MassHealth- MCO <input checked="" type="checkbox"/> MassHealth- ACO <input type="checkbox"/> Qualified Health Plans/ConnectorCare/Employer Choice Direct <input type="checkbox"/> 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.
Vittrakvi® (larotrectinib) and QL >60 capsules/month and >300 mL/month	

NCCN=National Comprehensive Cancer Network, PA=prior authorization

Procedure:

Approval Diagnosis:	<ul style="list-style-type: none"> Solid tumors with neurotrophic receptor tyrosine kinase (NTRK) gene fusion without a known acquired resistance mutation (Rozlytrek®, Vittrakvi®) ROS1-positive metastatic non-small cell lung cancer (NSCLC) (Rozlytrek®)
Approval Criteria:	Prescriber provides documentation of ALL of the following:

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Rozlytrek®
(entrectinib)

Vitakvi®
(larotrectinib)

NTRK gene fusion
solid tumors

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 oral solution formulation, medical necessity for the use of an oral solution formulation (e.g. swallowing disorder)

Additional Considerations:

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

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	<ul style="list-style-type: none"> • Single agent: doxorubicin, ifosfamide, epirubicin, gemcitabine, dacarbazine, liposomal doxorubicin, temozolomide, vinorelbine, eribulin, trabectedin, pazopanib, regorafenib <p><i>Please always refer to the latest NCCN guideline prior to issuing a final decision.</i></p> <div style="border: 1px solid black; background-color: #f2f2f2; padding: 5px; text-align: center;">Requests for NTRK Gene Fusion-positive Thyroid Carcinoma</div> <p>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.</p> <p><i>Please always refer to the latest NCCN guideline prior to issuing a final decision.</i></p> <div style="border: 1px solid black; background-color: #f2f2f2; padding: 5px; text-align: center;">Other NTRK Gene Fusion-positive Solid Tumors</div> <p>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.</p> <p><i>Please always refer to the latest NCCN guideline prior to issuing a final decision.</i></p> <p>Notes:</p> <ul style="list-style-type: none"> • <i>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.</i>
<p>Approval Criteria:</p> <p>Rozlytrek® (entrectinib)</p> <p>ROS1-positive NSCLC</p>	<p>Prescriber provides documentation of ALL of the following:</p> <ol style="list-style-type: none"> 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) <p>Notes:</p>

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	<ul style="list-style-type: none"> **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:	<p>Cases that do not meet the approval criteria will be denied.</p> <p>If a request is denied and the prescriber has additional clinical documentation, a new prior authorization request must be submitted.</p>
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

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

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Policy Revisions History

05/13/2021	Moved criteria from appendix to Approval criteria for consideration of requests for NTRK Gene Fusion-positive NSCLC, Soft Tissue Sarcoma, Thyroid Carcinoma and solid tumors.		P&T Committee
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Next Review Date

5/2022

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.

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.

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