Pharmacy Policy Bulletin: J-0849 NTRK and ROS1 Inhibitors – Commercial and Healthcare Reform	
Number: J-0849	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Quantity Limits (1., 2., 3., or 4.)** **1.** Rx Mgmt Quantity Limits = Safety/ Specialty **2.** Rx Mgmt Quantity Limits = Safety/Specialty + Dose Opt **3.** Rx Mgmt Quantity Limits = Safety/Specialty + Dose Opt + Watchful **4.** Quantity Limits = QPC = Yes **Healthcare Reform**: Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0849-013	**Original Date:** 01/30/2019
Effective Date: 10/08/2025	**Review Date:** 09/17/2025

Drugs Product(s):	• Augtyro (repotrectinib) • Ibtrozi (taletrectinib) • Vitrakvi (larotrectinib) • Rozlytrek (entrectinib)

FDA-Approved Indication(s):	• Augtyro
	  ○ Treatment of adult patients with locally advanced or metastatic *ROS1*-positive non-small cell lung cancer (NSCLC)
	  ○ Treatment of adult and pediatric patients 12 years of age and older with solid tumors that:
	  ▪ have a neurotrophic tyrosine kinase (*NTRK*) gene fusion and
	  ▪ are locally advanced or metastatic or where surgical resection is likely to result in severe morbidity, and
	  ▪ have progressed following treatment or have no satisfactory treatment options.
	• Ibtrozi
	  ○ Treatment of adult patients with locally advanced or metastatic *ROS1*-positive NSCLC.
	• Vitrakvi

	○ 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 lead to severe morbidity; and ▪ Have no satisfactory alternative or have progressed following treatment. ○ Select patients for therapy based on an FDA-approved test. • Rozlytrek ○ Adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are *ROS1*-positive as detected by an FDA-approved test. ○ Adult and pediatric patients older than one month of age 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.

Background:	• Augtyro and Ibtrozi are inhibitors of *ROS1* and tropomyosin receptor tyrosine kinases (TRKA, TRKB, and TRKC). By inhibiting these kinases, Augtyro and Ibtrozi inhibit the signaling that leads to unconstrained cell proliferation. • Vitrakvi inhibits tropomyosin receptor kinases (TRK) TRKA, TRKB, and TRKC (which are encoded by the *NTRK* gene), which leads to decreased cell proliferation and cell death. • Rozlytrek inhibits TRK's TRKA, TRKB, and TRKC (which are encoded by the *NTRK* gene), as well as *ROS1*, which can lead to decreased cell proliferation and cell death. • In the treatment of *NTRK* fusion positive cancer, Vitrakvi and Rozlytrek do not target a specific cell site but rather target the *NTRK* gene fusion mutation. As such, Vitrakvi and Rozlytrek have been used to treat a broad range of cancers including soft tissue sarcoma, infantile fibrosarcoma, and tumors of the salivary gland, thyroid, lung, colon, breast, and pancreas, among others. • Companion diagnostic tests FDA-approved for genetic testing include for Vitrakvi and Rozlytrek FoundationOne CDx. For additional information regarding FDA-approved companion diagnostics, please visit: https://www.fda.gov/medical-devices/vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-vitro-and-imaging-tools • ICD-10-Code Information: ○ ICD-10: C80 "Malignant neoplasm without specification of site" and multiple other ICD-codes may apply to a diagnosis of solid tumors for Augtyro and Rozlytrek. • Prescribing Considerations: ○ The member should be under the supervision of an oncologist. ○ The dose of Vitrakvi should be doubled if coadministration of a strong CYP3A4 inducer cannot be avoided. After the inducer has been discontinued for 3 to 5 elimination half-lives, the dose of Vitrakvi may be resumed at the dose prior to initiating the CYP3A4 inducer. ○ The dose of Vitrakvi should be reduced by 50% if coadministration of a strong CYP3A4 inhibitor cannot be avoided. After the inhibitor has been discontinued for 3 to 5 elimination half-lives, the dose of Vitrakvi may be resumed at the dose prior to initiating the CYP3A4 inhibitor. ○ Avoid coadministration of Rozlytrek with moderate and strong CYP3A inducers.

Starting dose*	Moderate CYP3A inhibitor	Strong CYP3A inhibitor
200 mg	50 mg once daily	50 mg on alternate days
300 mg	100 mg once daily	50 mg once daily
400 mg	200 mg once daily	50 mg once daily
600 mg	200 mg once daily	100 mg once daily
* For pediatric patients with a starting dose less than 200 mg, avoid coadministration with moderate or strong CYP3A inhibitors		

- The dose of Rozlytrek should be reduced in adults and pediatrics 2 years of age and older if coadministration of a moderate or strong CYP3A cannot be avoided, based on the table above.
- Augtyro should be avoided in concomitant use with strong and moderate CYP3A inhibitors, P-gp inhibitors, strong and moderate CYP3A inducers, certain CYP3A substrates and hormonal contraceptives.
- Concomitant use of strong and moderate CYP3A inhibitors/inducers, gastric acid reducing agents (proton pump inhibitors, and histamine-2 receptor antagonists), and drugs that prolong the QTc interval with Ibtrozi should be avoided.

Approval Criteria

I. Initial Authorization

A. Augtyro

1. NSCLC

When a benefit, coverage of Augtyro may be approved when all of the following criteria are met **(a., b., and c.)**:

a. The member is 18 years of age or older.

b. The member has a diagnosis of NSCLC (ICD-10: C34), classified as locally advanced or metastatic.

c. The member's tumor status is *ROS1*-positive.

2. Solid Tumors

When a benefit, coverage of Augtyro may be approved when all of the following criteria are met **(a. through e)**:

a. The member is 12 years of age or older.

b. The member has a diagnosis of solid tumors (No ICD-10 code).

c. Disease harbors a *NTRK* gene fusion.

d. The member meets one (1) of the following **(i. or ii.)**:

i. Disease is locally advanced or metastatic.

ii. Surgical resection is likely to result in severe morbidity.

e. The member meets one (1) of the following **(i. or ii)**:

i. Disease has progressed following treatment.

ii. The member has no satisfactory alternative treatment options.

B. Ibtrozi

When a benefit, coverage of Ibtrozi may be approved when all of the following criteria are met **(1., 2., and 3.)**:

1. The member is 18 years of age or older.

2. The member has a diagnosis of locally advanced or metastatic NSCLC (ICD-10: C34).

3. Disease is *ROS1*-positive.

C. Vitrakvi

When a benefit, coverage of Vitrakvi may be approved when all of the following criteria are met **(1., 2., and 3.):**

1. The member has an *NTRK* gene fusion without a known acquired resistance mutation, as detected by an FDA-approved test.

2. The member meets one (1) of the following criteria **(a. or b.)**:

a. The member's tumors are metastatic.
b. Surgical resection is likely to result in severe morbidity.

3. The member meets one (1) of the following criteria **(a. or b.)**:
a. The member has no satisfactory alternative treatments.
b. The tumors have progressed following treatment.

D. Vitrakvi Quantity Limits

When a benefit, additional quantities of Vitrakvi 100 mg capsules, up to four capsules per day; or Vitrakvi 20 mg/mL solution, up to 20 mL/day, may be approved when the following criterion is met **(1.)**:

1. The member is taking a strong CYP3A4 inducer.

E. Rozlytrek

When a benefit, coverage of Rozlytrek may be approved when one (1) of the following criteria is met **(1 or 2.)**:

1. The member has a diagnosis of metastatic NSCLC (ICD-10: C34) and meets all of the following criteria **(a. and b.)**:
a. The member is at least 18 years of age or older.
b. The member's tumor status is *ROS1*-positive as detected by an FDA-approved test.

2. The member has solid tumors and meets all of the following criteria **(a. through d.)**:
a. The member is older than one (1) month of age.
b. The member has an *NTRK* gene fusion, as detected by an FDA-approved test, without a known acquired resistance mutation.
c. The member meets one (1) of the following criteria **(i. or ii.)**:
i. The member's tumors are metastatic.
ii. Surgical resection is likely to result in severe morbidity.
d. The member meets one (1) of the following criteria **(i. or ii.)**:
i. The member has no satisfactory alternative treatments.
ii. The tumors have progressed following treatment.

II. Reauthorization

When a benefit, reauthorization of Augtyro, Ibtrozi, Vitrakvi, or Rozlytrek may be approved when the following criterion is met **(A.)**:

A. The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as either one (1) of the following **(1. or 2.)**:
1. Disease improvement
2. Delayed disease progression

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

IV. Coverage of oncology medications listed in this policy may be approved on a case-by-case basis per indications supported in the most current NCCN guidelines.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 2 year authorization may be granted.

Automatic Approval Criteria

None

References:

1. Augtyro [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; June 2024.
2. Ibtrozi [package insert]. Burlington, MA: Nuvation Bio Inc.; June 2025.
3. Vitrakvi [package insert]. Stamford, Connecticut: Loxo Oncology, Inc.; November 2023.
4. Rozlytrek [package insert]. South San Francisco, California: Genentech, Inc.; January 2024.
5. U.S Food & Drug Administration. List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools). Available at: https://www.fda.gov/medical-devices/vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-vitro-and-imaging-tools. Accessed November 6, 2023.