

Taletrectinib (IBTROZI)

National Drug Mini-Monograph

August 2026

VHA Pharmacy Management Services and National Formulary Committee

The purpose of VA PBM Services drug monographs is to provide a focused drug review for making formulary decisions. The Product Information or other resources should be consulted for detailed and most current drug information.

Abbreviations: AC, active-controlled; CO, crossover; DB, double-blind; GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; MC, multicenter; MN, multinational; PC, placebo-controlled; Q, GRADE quality of evidence; RCT, randomized clinical trial

FDA PRESCRIBING INFORMATION

Description / MOA	Taletrectinib is an inhibitor of tyrosine kinase ROS1, including ROS1 resistance mutations. Fusion proteins including ROS1 drive unconstrained cell proliferation.
Indication Under Review	Locally advanced or metastatic ROS1 fusion positive non-small lung cancer (NSCLC)
Dosage Regimen	600 mg orally once a day on an empty stomach until disease progression or unacceptable toxicity.
Dosage Forms Under Review	200mg capsules
Pretreatment Procedures	☐ Liver function tests ☐ ECG and electrolytes for baseline QTc interval ☐ Serum uric acid

EFFICACY CONSIDERATIONS

Trial 1	TRUST-1 (NCT04395677) ¹																																												
Design	Trust-1: open-label, single-arm, nonrandomized phase 2 in LA/M ROS1 positive NSCLC in China with 2 cohorts: 1) TKI-naïve and 2) previous crizotinib; primary endpoint: independent review committee confirmed objective response rate (cORR)																																												
Population	Overall populations (n=173) Med Age 55, females 57.8%, never smokers 73.4%, brain mets 26.6%,																																												
Intervention	Taletrectinib 600mg orally daily until progression, death, unacceptable toxicity, withdrawal																																												
Comparator	None																																												
Results	<table><tr><th>Outcome</th><th>TKI naïve</th><th>Prev crizotinib</th></tr><tr><td>cORR</td><td>90.6%</td><td>51.5%</td></tr><tr><td>CR</td><td>3.8%</td><td>N/A</td></tr><tr><td>Med DOR</td><td>NR</td><td>10.6 mos</td></tr><tr><td>Med PFS</td><td>NR</td><td>7.6 mos</td></tr><tr><td>24 month DOR</td><td>78.6%</td><td></td></tr><tr><td>24 month PFS</td><td>70.5%</td><td></td></tr><tr><td>Baseline brain mets</td><td>cORR: 87.5%</td><td>cORR: 73.3%</td></tr><tr><td colspan="3">Long-Term f/u²</td></tr><tr><td>cORR</td><td>90.3%</td><td>51.5%</td></tr><tr><td>CR</td><td>4.9%</td><td></td></tr><tr><td>Med DOR</td><td>49.7 mos</td><td>13.2 mos</td></tr><tr><td>Med PFS</td><td>49.6 mos</td><td>7.6 mos</td></tr><tr><td>3-yr OS</td><td>65.3%</td><td>Med OS: 25.6 mos</td></tr></table>			Outcome	TKI naïve	Prev crizotinib	cORR	90.6%	51.5%	CR	3.8%	N/A	Med DOR	NR	10.6 mos	Med PFS	NR	7.6 mos	24 month DOR	78.6%		24 month PFS	70.5%		Baseline brain mets	cORR: 87.5%	cORR: 73.3%	Long-Term f/u ²			cORR	90.3%	51.5%	CR	4.9%		Med DOR	49.7 mos	13.2 mos	Med PFS	49.6 mos	7.6 mos	3-yr OS	65.3%	Med OS: 25.6 mos
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DOR=duration of response; PFS=progression-free survival; OS=overall survival																																													

Authors' Conclusions	<ul style="list-style-type: none">Taletrectinib demonstrated meaningful efficacy outcomes in both TKI-naïve and crizotinib-pretreated ROS1+ NSCLC.High and durable ORR was observed in both populations, along with high intracranial ORR.Taletrectinib has favorable safety, with low rates of discontinuation and dose-reduction. There was a low incidence of CNS adverse events which were mostly grade 1 compared to crizotinib and entrectinib.																					
Trial 2	TRUST-I (NCT04395677) and TRUST-II (NCT04919811) pooled cohorts ³																					
Design	TRUST-I: open-label, single-arm, nonrandomized phase 2 in LA/M ROS1 positive NSCLC in China with 2 cohorts: 1) TKI-naïve and 2) previous crizotinib TRUST II: open-label, single-arm, nonrandomized global phase 2 in LA/M ROS1 positive NSCLC with 2 cohorts: 1) TKI-naïve and 2) previous crizotinib or entrectinib Primary Endpoint: independent review committee confirmed objective response rate (cORR)																					
Population	Overall populations (n=273) Med Age 56, females 57.1%, never smokers 66.7%, brain mets 33.7%,																					
Intervention	Taletrectinib 600mg orally daily until progression, death, unacceptable toxicity, withdrawal																					
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Results	<table><tr><th>Outcome</th><th>TKI naïve (N=160)</th><th>Prev crizotinib (N=113)</th></tr><tr><td>cORR</td><td>88.8%</td><td>55.8%</td></tr><tr><td>CR</td><td>5%</td><td>4.4%</td></tr><tr><td>Med DOR</td><td>44.2 mos</td><td>16.6 mos</td></tr><tr><td>Med PFS</td><td>45.6 mos</td><td>9.7 mos</td></tr><tr><td>36-mos OS</td><td>66.3%</td><td>12 month OS: 77.5%</td></tr><tr><td>Baseline brain mets</td><td>76.5%</td><td>65.6%</td></tr></table> <p>DOR=duration of response; PFS=progression-free survival; OS=overall survival</p>	Outcome	TKI naïve (N=160)	Prev crizotinib (N=113)	cORR	88.8%	55.8%	CR	5%	4.4%	Med DOR	44.2 mos	16.6 mos	Med PFS	45.6 mos	9.7 mos	36-mos OS	66.3%	12 month OS: 77.5%	Baseline brain mets	76.5%	65.6%
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Authors' Conclusions	<ul style="list-style-type: none">Taletrectinib demonstrated robust cORR and DOR in both TKI-naïve and TKE pretreated populations in advanced ROS1+ NSCLC.Results are applicable globally.																					
NCCN Guidelines	ROS1 Gene Fusion in NSCLC Preferred 1 st line: Crizotinib or Entrectinib or Repotrectinib or Taletrectinib																					
VA Clinical Pathway	Current ROS1 Gene Fusion NSCLC: Entrectinib																					

SAFETY CONSIDERATIONS

Boxed Warnings	None
Contraindications	None
Other Warnings	<p>Hepatotoxicity: drug-induced liver injury and fatal adverse reactions (88% increase in AST and 85% increase in ALT). Interstitial Lung Disease (ILD)/Pneumonitis: Can cause severe, life-threatening, or fatal pulmonary symptoms (2.3%). QTc Interval Prolongation: Increases risk for ventricular tachyarrhythmias or sudden death (2.6% increase to >500 msec). Hyperuricemia: increased serum uric acid levels requiring treatment (14% had increase with 16% requiring therapy). Myalgia with CPK Elevation: Can cause muscle pain with or without enzyme elevation (10%). Skeletal Fractures: Increases risk of fractures, including those involving the ribs and spine (3.4%). Embryo-Fetal Toxicity: Can cause fetal harm when administered to pregnant women.</p>
Top 5 AEs	AST increased (75.7%), Diarrhea (69.9%), ALT increased (67.6%), Anemia (54.9%), and Vomiting (54.3%).
Drug Interactions	Avoid concomitant use with strong or moderate CYP3A inhibitors and inducers , as these alter taletrectinib exposure. Avoid concomitant use with proton pump inhibitors (PPIs) and H2 receptor antagonists . Avoid drugs known to prolong the QTc interval . Avoid grapefruit and grapefruit products .
Pregnancy	Taletrectinib can cause fetal harm.
Lactation	Advise women not breastfeed during therapy and for 3 weeks after the last dose.

THERAPEUTIC ALTERNATIVES AND THEIR PLACE IN THERAPY

DRUG	VANF	CFU	FDA	VA Clinical Pathways
Crizotinib	PA-F	Yes	Metastatic NSCLC and ALK or ROS1 positive	None
Entrectinib	PA-F	Yes	Metastatic NSCLC and ROS1 positive	NSCLC-1 st Line ROS1 or NTRK positive

POTENTIAL PLACE IN THERAPY OF —

1. Taletrectinib is an inhibitor of tyrosine kinase ROS1, including some resistance mutations. It also has intracranial activity.
2. Taletrectinib has 1 FDA indication: for patients with locally advanced or metastatic ROS1-positive non-small cell lung cancer.
3. In advanced **ROS1 fusion-positive NSCLC**, there are multiple TKIs with FDA indication for ROS1 fusion positive NSCLC. Next generation TKIs, including repotrectinib and taletrectinib, offer improved Progression-Free Survival, better CNS penetration, and activity against resistance mutations compared to first generation TKIs like crizotinib and entrectinib. Although repotrectinib and taletrectinib have good CNS penetration, taletrectinib has lower rates of CNS adverse events but higher rates of GI and transaminase elevation.
4. Currently, entrectinib is listed on VA Oncology Clinical Pathway for Lung Cancer for patients with ROS1 fusion positive NSCLC.
5. Consider adding taletrectinib as PA-F and replacement of entrectinib with taletrectinib for advanced ROS1 fusion positive NSCLC on the VA Oncology Clinical Pathway for Lung Cancer.

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References

- ¹ Li, et al. Efficacy and safety of taletrectinib in Chinese patients with ROS1+ non-small cell lung cancer: the phase II TRUST-I study. *J Clin Oncol* 2024; 42: 2660-2670.
- ² Li, et al. Long-term efficacy and safety of taletrectinib in patients with ROS1+ non-small cell lung cancer: results from the TRUST-I study. *J Clin Oncol* 2026; 44: 1670-1675.
- ³ Perol, et al. Taletrectinib in ROS1+ non-small cell lung cancer: TRUST. *J Clin Oncol* 2025; 43: 1920-1929.