Vimseltinib cap, oral (ROMVIMZA) in Tenosynovial Giant Cell Tumor
National Drug Mini-Monograph
June 2026
VA Pharmacy Benefits 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: 2L, second-line; AC, active-controlled; ALP, alkaline phosphatase; ALT, alanine transaminase; ARD, absolute risk difference; AST, aspartate transaminase; CO, crossover; DB, double-blind; GGT, gamma-glutamyl transferase; GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; MC, multicenter; MN, multinational; PC, placebo-controlled; PFS, progression-free survival; P-gp, P-glycoprotein; Q, GRADE quality of evidence; RCT, randomized clinical trial; RECIST, Response Evaluation Criteria in Solid Tumors; REMS, Risk Evaluation and Mitigation Strategy; RR, relative risk; ULN, upper limit of normal

FDA PRESCRIBING INFORMATION[1]	
Description / MOA	Kinase inhibitor and antagonist of macrophage colony-stimulating factor 1 receptors (CSF1Rs).
Indication Under Review	Treatment of adults with symptomatic tenosynovial giant cell tumor (TGCT) for which surgical resection will potentially cause worsening functional limitation or severe morbidity.
Dosage Regimen	30 mg orally twice weekly, with a minimum of 72 hours between doses, on the same days each week. Modify dosage for adverse reactions including hepatotoxicity and avoid concomitant use with P-glycoprotein (P-gp) substrates if possible. See prescribing information for details.
Dosage Forms Under Review	14, 20, and 30-mg capsules
Pretreatment Procedures	□ Assess liver tests, including AST, ALT, total bilirubin, direct bilirubin, ALP, and GGT. □ Verify pregnancy status. □ Advise pregnant women on the potential risk to the fetus. □ Advise women of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment and for 1 month after the last dose. □ Advise lactating women not to breastfeed/provide breastmilk to infants.
Treatment Monitoring	□ Liver tests twice a month for the first 2 months and once every 3 months for the first year then as clinically indicated. □ Renal function using measures other than serum creatinine (drug-lab interaction).

EFFICACY CONSIDERATIONS	
Trial	**Vimseltinib versus placebo for tenosynovial giant cell tumour (MOTION): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial[2]**
Design	Part 1, Weeks 0–24: Phase 3, multinational, double-blind, placebo-controlled randomized clinical trial (RCT; 2:1); stratified by tumor location (lower limb vs all other) and region (USA vs non-USA) Part 2, Weeks 25–49: Patients could enter an open-label period at end of Week 24. Patients on placebo in part 1 could cross over to vimseltinib. Long-term Extension, Beyond Week 49: Patients could continue vimseltinib. *Primary Endpoint*: Objective response rate (complete response or partial response) as assessed by independent radiologic (MRI) review using Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 at the beginning of Week 25 in the intent-to-treat population.
Population	*Inclusion Criteria:* Age ≥ 18 years; histologically confirmed TGCT for which surgical resection might worsen functional limitation or cause severe morbidity; ≥ 1 lesion measuring ≥ 2 cm in size. *Exclusion Criteria*: Previous systemic therapy targeting CSF1 or CSF1R (the nonselective inhibitors imatinib and nilotinib were permitted). *Baseline Characteristics (N = 123)*: Median age 44 years; male 41%; White 65%; USA/CN 15.4%; affected the knee 67.5%; previous TGCT surgery or procedure 74.0%; previous systemic therapy 22.8% (18.7% imatinib; 4.9% nilotinib).
Interventions	Vimseltinib 30 mg or Placebo twice weekly on Days 1 and 5 in 28-day cycles for 24 weeks, with at least 24 hours between doses.
Results	**Primary and Selected Secondary Endpoints at Week 25 (Part 1 of Trial)**

Outcome	Vimseltinib	Placebo	RR (95% CI)	ARD (95% CI)	Q
Objective Response, n/N (%)	33/83 (40)	0/40 (0)	NC	40 (29, 51)	Mod[α]
Complete Response, n/N (%)	4/83 (5)	0/40 (0)	NC	—	
Partial Response, n/N (%)	29/83 (35)	0/40 (0)	NC	—	
Median (Range) DOR, mos	NR (0.03, 11.7)	NA	—	—	
LSM CFB in PROMIS-PF	4.6	1.3	—	3.3 (1.4, 5.2)	
LSM CFB in EQ-VAS Health Status	13.5	6.1	—	7.4 (1.4, 13.4)	
BPI-30, n/N (%)	40/83 (48)	9/40 (23)	2.1 (1.16, 3.97)	26 (4, 42)	Mod[α]

ARD, Absolute risk difference; BPI-30, Brief Pain Inventory worst pain response rate (≥ 30% improvement without a ≥ 30% increase in narcotic analgesic use); CFB, change from baseline; LSM, least squares mean; DOR, duration of response; EQ, EuroQoL; Mod, moderate; NC, not calculable; PROMIS-PF, Patient-Reported Outcomes Measurement Information System physical function, TGCT-specific; VAS, Visual Analogue Scale

[α] Downgraded for indirectness (endpoint is not a final clinical outcome) and imprecision (optimal information size not met)

Subgroup Analyses

- No statistically significant difference was seen in the small subgroup of patients aged ≥ 65 years: 2/5 (40%) vs 0/4 (0%) for vimseltinib vs placebo, respectively; ARD (95% CI), 40% (–3, 83).
- A significant treatment difference was seen in patients aged 50 to < 65 years.

Authors' Conclusions	Vimseltinib showed significant antitumor activity, a favorable safety profile, clinically meaningful improvements in active range of motion, and improvements in stiffness, physical function, health status, and pain in patients with TGCT who are not surgical candidates.

SAFETY CONSIDERATIONS

Boxed Warnings	None
Contraindications	None
Other Warnings	Hepatotoxicity Embryofetal toxicity Allergic reactions to FD&C Yellow No. 5 (tartrazine) and No. 6 (Sunset Yellow FCF). Tartrazine sensitivity is often seen in patients with aspirin sensitivity. Increased serum creatinine without affecting renal function
Top 5 AEs (≥ 20%)	Increased AST, periorbital edema, fatigue, rash, increased cholesterol
Drug Interactions	*P-glycoprotein (P-gp) Substrates*: Avoid if possible; otherwise take vimseltinib at least 4 hours before P-gp substrates. Exposure to P-gp substrates may increase. *Breast Cancer Resistance Protein (BCRP) Substrates*: Avoid. Exposure to BCRP substrates may increase. *Organic Cation Transporter 2 (OCT2) Substrates*: Avoid. Exposure to OCT2 substrates may increase.
Pregnancy	Can cause fetal harm. Insufficient human data. Animal studies showed fetal structural abnormalities including skeletal variations and cardiac malformations.
Lactation	Avoid breastfeeding during treatment and for 1 month after the last dose.
Females & Males of Reproductive Potential	Verify pregnancy status in women of reproductive potential before initiating therapy. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during therapy and for 1 month after the last dose.
Infertility	May impair fertility.
Geriatric Use	Insufficient data to determine whether patients 65 years and older respond differently from younger patients.
Hepatic Impairment	*Mild Hepatic Impairment*: No dosage adjustment is recommended. *Moderate (bilirubin > 1.5 x to 3x upper limit of normal [ULN] and any AST) or Severe (bilirubin > 3x ULN and any AST) Hepatic Impairment*: Not studied.
MOTION Trial Safety Results	Vimseltinib vs placebo, respectively: • *Deaths*: None. • *Grade 3 or 4 Adverse Events*: 31/83 (37%) vs 4/39 (10%); RR 3.6 (95% CI 1.38, 9.60); ARD 27% (13.0, 41.2) • *Discontinuations Due to Adverse Events (DAEs)*: 4/83 (4.8%) vs 0/39 (0%); RR not calculable; ARD 4.8% (0.2, 9.4) • No evidence of cholestatic hepatotoxicity or drug-induced liver injury.

THERAPEUTIC ALTERNATIVES AND THEIR PLACE IN THERAPY				
DRUG	**On VANF**	**CFU**	**FDA-labelled indications and other considerations**	**NCCN GUIDELINES[3]**
Vimseltinib (ROMVIMZA)	TBD (cap)	TBD	Kinase inhibitor for the treatment of adults with symptomatic TGCT for which surgical resection will potentially cause worsening functional limitation or severe morbidity; MOTION (P3) n=123 ORR 40% vs. 0% (pbo) mDoR not reached No cholestatic hepatotoxicity; 10% periorbital/facial edema; twice-weekly dosing; no food restrictions	Preferred (category 1) regimen
Pexidartinib (TURALIO)	No (cap)	Yes (2L after imatinib)	Kinase inhibitor for the treatment of adults with symptomatic TGCT associated with severe morbidity or functional limitations and not amenable to improvement with surgery. ENLIVEN (P3) ORR 39% vs. 0% (pbo) mDoR not reached *Boxed Warning*: Hepatotoxicity. Drug is only available through a restricted Risk Evaluation and Mitigation Strategy (REMS) Program.	Preferred (category 1) regimen
Imatinib (GLEEVEC)	Yes, PA-F (tab) No (soln)	No	Off-label. Kinase inhibitor – not approved for TGCT Retrospective n=29; ORR 19%; 1yr PFS 71% Edema 48%; fatigue 50%	Useful in certain circumstances
Nilotinib (DANZITEN)	No (cap, tab)	No	Off-label. Kinase inhibitor – not approved for TGCT Phase 2 n=56; ORR 6% at 1yr; mPFS 77 mos Gr 3 AEs: headache, GGT elevation, pruritus	Useful in certain circumstances

Background/ Summary of therapeutic options

TGCT (formerly PVNS/giant cell tumor of tendon sheath) is a rare, CSF1-driven, locally aggressive neoplasm of the synovium, bursae, or tendon sheath. Incidence is ~10 per million (localized) and ~4 per million (diffuse). Diffuse TGCT is recurrent, impairs quality of life, and often requires repeated surgeries with significant morbidity.

Four CSF1R-targeting agents with supporting data to treat TGCT:

- Imatinib (off-label): Nonselective multikinase inhibitor with modest efficacy — 19% ORR in a small retrospective study (n=29), improving to ~29% CR+PR in longer-term follow-up. Median PFS was 21 months; 5-year PFS was 48%. Tolerability was reasonable but 21% discontinued due to adverse events.
- Nilotinib (off-label): More potent second-generation TKI but produced only 6% ORR at 1 year despite high disease control (90% progression-free at week 24). Long-term median PFS was 77 months, but the authors themselves questioned nilotinib's role in TGCT given the low objective response rate.
- Pexidartinib (FDA-approved, first-in-class): 39% ORR including 15% CR in the ENLIVEN trial. However, it carries a significant hepatotoxicity risk requiring REMS enrollment. The approved dose was subsequently reduced from 400 mg BID to 250 mg BID with a low-fat meal to mitigate overexposure and hepatic risk.
- Vimseltinib (FDA-approved): 40% ORR including 5% CR in the MOTION trial. Grade 3–4 AEs occurred in 37% but only 4.8% discontinued for toxicity. Notably, vimseltinib lacks the hepatotoxicity signal seen with pexidartinib, representing a potential safety advantage. However, duration of response data remain immature and long-term safety experience is limited. Vimseltinib may be used in patients with inadequate response, intolerance, or medical inadvisability to imatinib; no head-to-head trials exist to definitively establish sequencing of these agents.

Prepared: April 2026. By Francine Goodman, PharmD, BCPS and Berni Heron, PharmD., BCOP National Program Manager, VA Pharmacy Benefits Management Services – Formulary Management (12PBM)

References

1 ROMVIMZA (vimseltinib) capsules [prescribing information online]. Waltham, MA: Deciphera Pharmaceuticals. 2/2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219304s000lbl.pdf . Accessed: 3/11/2025.

2 Gelderblom H, Bhadri V, Stacchiotti S, Bauer S, Wagner AJ, van de Sande M, Bernthal NM, López Pousa A, Razak AA, Italiano A, Ahmed M, Le Cesne A, Tinoco G, Boye K, Martín-Broto J, Palmerini E, Tafuto S, Pratap S, Powers BC, Reichardt P, Casado Herráez A, Rutkowski P, Tait C, Zarins F, Harrow B, Sharma MG, Ruiz-Soto R, Sherman ML, Blay JY, Tap WD; MOTION investigators. Vimseltinib versus placebo for tenosynovial giant cell tumour (MOTION): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2024 Jun 22;403(10445):2709-2719. doi: 10.1016/S0140-6736(24)00885-7. Epub 2024 Jun 3. PMID: 38843860; PMCID: PMC11740396.

3 National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Soft Tissue Sarcoma v5.2024—March 10, 2025. Available at: sarcoma.pdf. Accessed: 3/11/2025