



## Positive Quality Intervention: Ripretinib (Qinlock®) for Treatment of Adults with Advanced Gastrointestinal Stromal Tumors

**Description:** The purpose of this PQI is to summarize the process for initiating and monitoring ripretinib therapy in patients with advanced gastrointestinal stromal tumor (GIST).

**Background:** Ripretinib is a tyrosine kinase inhibitor (TKI) that inhibits KIT proto-oncogene tyrosine kinase and platelet derived growth factor receptor A (PDGFRA) kinases. Ripretinib also inhibits PDGFRB, TIE2, VEGFR2, and BRAF. Ripretinib is approved for the treatment of advanced GIST who have received prior treatment with 3 or more kinase inhibitors including imatinib. NCCN has designated ripretinib a category 2A preferred regimen for patients intolerant of second-line sunitinib and category 1 preferred for fourth line patients. Also of note, NCCN recommends ripretinib dose escalation to 150 mg BID (if previously treated with ripretinib 150 mg daily) as an additional option after progression on approved therapies.<sup>1-2</sup> The efficacy of ripretinib in advanced GIST, after 3 prior TKIs, was demonstrated in the INVICTUS trial.<sup>3</sup> Ripretinib is a switch control tyrosine kinase inhibitor specifically designed to broadly inhibit KIT and PDGFRA mutated kinases with a unique dual mechanism of action. Ripretinib binds to both the switch pocket region and the activation loop securing the target kinase into an inactive conformation, resulting in the inhibition of downstream signaling and cell proliferation.

**PQI Process:** Identify patients with advanced, unresectable metastatic GIST in the fourth line; upon receipt of a prescription for ripretinib

- Initial dose 150 mg daily - available as 50 mg tablets
  - Consider dose escalation to 150 mg BID upon progression with once daily dosing<sup>4</sup>
- Drug interactions
  - If concurrent strong CYP3A inhibitors monitor more frequently for adverse reactions
  - Avoid concomitant use with strong CYP3A inducers
  - Avoid concomitant use with moderate CYP3A inducers
    - If cannot be avoided, increase dosing frequency to 150 mg twice daily
    - If the concomitant moderate CYP3A inducer is discontinued, resume dose back to 150 mg daily 14 days after the discontinuation of the moderate CYP3A inducer
- Monitor blood pressure (BP) at baseline and as clinically indicated throughout therapy
  - Adequately control BP prior to initiation if indicated
- Monitor for palmar plantar erythrodysesthesia (PPE) and arthralgias/myalgias during therapy
  - See [Drug Induced Hand-Foot Syndrome](#) PQI
- Assess cardiac ejection fraction at baseline and then during treatment if clinically indicated
- Perform dermatologic evaluations when initiating and routinely during treatment
- Dose modifications for adverse effects (see Supplemental Section)
- Hold for at least 1 week prior to elective surgeries and for at least 2 weeks following major surgery and until adequate wound healing

### Patient-Centered Activities:

- Provide [Oral Chemotherapy Education \(OCE\)](#) and [Oral Chemotherapy Education Supplemental](#) Sheet
  - Advise patients to limit direct UV exposure during treatment with ripretinib and for at least 1 week after discontinuation of treatment
  - Females of reproductive potential and males with female partners of reproductive potential

**IMPORTANT NOTICE:** NCODA has developed this Positive Quality Intervention platform. This platform is intended as an educational aid, does not provide individual medical advice, and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication. The materials contained in this platform do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA. NCODA does not ensure the accuracy of the information presented and assumes no liability relating to its accuracy. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional. It is the individual's sole responsibility to seek guidance from a qualified healthcare professional. *Updated 2.8.24*

should use effective contraception during treatment and for 1 week after the last dose

- Administration: Can be taken with or without food
  - Take a missed dose if remembered within 8 hours of the due time
    - Ripretinib 150 mg daily: take replacement dose only if within 8 hours of missed dose
    - Ripretinib 150 mg twice daily: take replacement dose only if within 4 hours of missed dose
  - Do not take an additional dose if one is vomited up
- Patient Assistance: [NCODA Financial Assistance Tool](#)

## References:

1. [Qinlock \(riporetinib\) \[prescribing information\]](#).
2. Gastrointestinal Stromal Tumor (GIST). NCCN. Retrieved June 30, 2023, from [https://www.nccn.org/guidelines/category\\_1](https://www.nccn.org/guidelines/category_1)
3. Blay JY, Serrano C, Heinrich MC, et al. Ripretinib in patients with advanced gastrointestinal stromal tumors (INVICTUS): a double-blind, randomized, placebo-controlled, phase 3 trial. *Lancet Oncol.* 2020;21:923-934.
4. Zalberg JR, Heinrich MC, George s, et al. Clinical benefit of ripretinib dose escalation after disease progression in advanced gastrointestinal stromal tumor. *Oncologist* 2021;25:1-8.

## Supplemental Information: Adverse Reaction and Dose Modification

Dose reduction for adverse reactions: 100 mg orally once daily; permanently discontinue in patients who are unable to tolerate 100 mg orally once daily

Adverse Reaction	Severity	Dose Modification
<b>Palmar-Plantar Erythrodysesthesia</b>	Grade 2	Hold until Grade $\leq$ 1 or baseline. If recovered within 7 days, resume at same dose; otherwise resume at reduced dose. Consider re-escalating if maintained at Grade $\leq$ 1 or baseline for at least 28 days. If PPE recurs, hold until Grade $\leq$ 1 or baseline and then resume at a reduced dose regardless of time to improvement.
	Grade 3	Hold for at least 7 days or until Grade $\leq$ 1 or baseline (max 28 days). Resume at a reduced dose. Consider re-escalating if maintained at Grade $\leq$ 1 or baseline for at least 28 days.
<b>Hypertension</b>	Grade 3	If symptomatic, hold until symptoms have resolved and BP is controlled. If BP is controlled to Grade $\leq$ 1 or baseline, resume at the same dose; otherwise, resume at reduced dose. If Grade 3 hypertension recurs, hold until symptoms have resolved and BP is controlled. Resume at a reduced dose.
	Grade 4	Permanently discontinue
<b>Left Ventricular Systolic Dysfunction</b>	Grade 3/4	Permanently discontinue
<b>Arthralgia/Myalgia</b>	Grade 2	Hold until Grade $\leq$ 1 or baseline. If recovered within 7 days, resume at same dose; otherwise resume at reduced dose. Consider re-escalating if maintained at Grade $\leq$ 1 or baseline for at least 28 days. If arthralgia or myalgia recurs, hold until Grade $\leq$ 1 or baseline and then resume at a reduced dose regardless of time to improvement.
	Grade 3	Hold for at least 7 days or until Grade $\leq$ 1 or baseline (max of 28 days). Resume at a reduced dose. Consider re-escalating if maintained at Grade $\leq$ 1 or baseline for at least 28 days.
<b>Other</b>	Grade 3/4	Hold until Grade $\leq$ 1 or baseline (maximum 28 days), and then resume at a reduced dose; otherwise permanently discontinue. Consider re-escalating if no recurrence of the adverse reaction for at least 28 days. If Grade 3 or 4 recurs, permanently discontinue.