Qinlock (ripretinib)

NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Qinlock
- **Generic name:** Ripretinib
- **Pharmacologic class:** Kinase inhibitor
- **Strength and Formulation:** 50mg; tablets
- **Manufacturer:** Dicephera
- **How supplied:** Tabs—90
- **Legal Classification:** Rx

Qinlock


NDC: 73207-101-30
Rx only
QINLOCK™
(ripretinib) tablets
50 mg
Attention: Dispense and store QINLOCK™ in the original container to protect from moisture and light.
Dispense the enclosed Patient Information Leaflet to each patient.
90
TABLETS

MPR

Indication

- Treatment of adult patients with advanced **gastrointestinal stromal tumor** (GIST) who have received prior treatment with 3 or more kinase inhibitors, including imatinib

MPR

Dosage and Administration

- Swallow whole.
- 150mg once daily until disease progression or unacceptable toxicity.
- Recommended dose reduction for adverse reactions: 100mg once daily
- Permanently discontinue in patients unable to tolerate 100mg once daily.

Dosage Modifications for Adverse Reactions

- *Palmar-Plantar Erythrodysesthesia Syndrome (PPES)*
  - **Grade 2**: Withhold until Grade ≤1 or baseline; if recovered within 7 days, resume at same dose, otherwise resume at reduced dose. Consider re-escalating if maintained at Grade ≤1 or baseline for at least 28 days. If PPES recurs, withhold until Grade ≤1 or baseline and then resume at reduced dose regardless of time to improvement.
  - **Grade 3**: Withhold for at least 7 days or until Grade ≤1 or baseline (maximum 28 days); resume at reduced dose. Consider re-escalating if maintained at Grade ≤1 or baseline for at least 28 days.

MPR

Dosage Modifications for Adverse Reactions

- *Hypertension*
  - **Grade 3**: If symptomatic, withhold until symptoms have resolved and blood pressure (BP) is controlled. If BP controlled to Grade ≤1 or baseline, resume at same dose; otherwise, resume at reduced dose. If Grade 3 hypertension recurs, withhold until symptoms have resolved and BP controlled; resume at reduced dose.
  - **Grade 4**: Permanently discontinue.
- *Left Ventricular Systolic Dysfunction*
  - **Grade 3 or 4**: Permanently discontinue.

Dosage Modifications for Adverse Reactions

- *Arthralgia or Myalgia*
  - **Grade 2**: Withhold until Grade ≤1 or baseline; if recovered within 7 days, resume at same dose; otherwise resume at reduced dose. Consider re-escalating if maintained at Grade ≤1 or baseline for at least 28 days. If arthralgia or myalgia recurs, withhold until Grade ≤1 or baseline and then resume at reduced dose regardless of time to improvement.
  - **Grade 3**: Withhold for at least 7 days or until Grade ≤1 or baseline (maximum of 28 days); resume at reduced dose. Consider re-escalating if maintained at Grade ≤1 or baseline for at least 28 days.
- *Other Adverse Reactions*
  - **Grade 3 or 4**: Withhold until Grade ≤1 or baseline (maximum 28 days), and then resume at reduced dose; otherwise permanently discontinue. Consider re-escalating if no recurrence of adverse reaction for at least 28 days. If Grade 3 or 4 recurs, permanently discontinue.

MPR

Considerations for Special Populations

- **Pregnancy:** Can cause fetal harm.
- **Nursing mothers:** Not recommended during and for ≥1 week after the last dose.
- **Pediatric**: Not established.
- **Geriatrics**: Studies did not include sufficient numbers of patients aged 65 and older to determine response difference.
- **Hepatic impairment**: Not established in patients with moderate or severe impairment.

MPR

Warnings and Precautions

- Risk of new primary cutaneous malignancies.
- Perform skin exams prior to initiation and during therapy.
- Manage suspicious skin lesions with excision and dermatopathologic evaluation.
- Uncontrolled hypertension: Do not initiate.
- Control BP prior to initiation; monitor and treat during therapy as appropriate.
- Cardiac dysfunction
- Assess ejection fraction by echocardiogram or MUGA scan prior to initiation, during therapy, and as clinically indicated.
- Permanently discontinue if Grade 3/4 left ventricular systolic dysfunction occurs.

MPR

Warnings and Precautions

- Impaired wound healing: Withhold for ≥1 week prior to elective surgery; do not give for ≥2 weeks after major surgery and until adequate healing.
- Safety of resuming therapy after resolution of wound healing complications has not been established.
- Moderate or severe hepatic impairment
- Severe renal impairment
- Advise females of reproductive potential and males (w. female partners) to use effective contraception during and for ≥1 week after the last dose.
- Pregnancy: Exclude status prior to initiation.

MPR

Interactions

- Potentiated by strong CYP3A4 inhibitors; monitor frequently.
- May be antagonized by strong CYP3A4 inducers; avoid.

Adverse Reactions

- **Most common (≥ 20%):** alopecia, fatigue, nausea, abdominal pain, constipation, myalgia, diarrhea, decreased appetite, palmar-plantar erythrodysesthesia, vomiting
- **Most common Grade 3 or 4 lab abnormalities (≥4%):** increased lipase, decreased phosphate

MPR

Mechanism of Action

- Ripretinib is a **tyrosine kinase inhibitor** that inhibits KIT proto-oncogene receptor tyrosine kinase (KIT) and platelet derived growth factor receptor A (PDGFRA) kinase, including wild type, primary, and secondary mutations.

Pharmacokinetics

- Primarily metabolized by CYP3A4; also CYP2C8, CYP2D6, CYP2E1 (minor)
- Effective elimination half-life:
  - Ripretinib: 14.8 hours
  - DP-5439 (active metabolite): 17.8 hours
- Excretion pathway: fecal (major)

Clinical Trials

- Efficacy was evaluated in INVICTUS, a double-blind, placebo-controlled trial (NCT03353753).
- Patients had unresectable, locally advanced or metastatic gastrointestinal stromal tumor and had received prior treatment with imatinib, sunitinib, and regorafenib.
- Patients received ripretinib 150mg (n=85) or placebo (n=44) orally once daily until disease progression or unacceptable toxicity.
- Major efficacy outcome measure was progression free survival (PFS).
- Additional outcome measures were objective response rate (ORR) and overall survival (OS).

Clinical Trials

Patient demographics

- Median age: 60 years; 57% male; 75% White
- 92% had Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- 63% received 3 prior therapies
- 37% received 4 or more prior therapies
- 66% of patients randomized to placebo switched to ripretinib after disease progression

Clinical Trials

- Ripretinib significantly reduced the risk of disease progression or death by 85% (hazard ratio [HR] 0.15; 95% CI, 0.09-0.25; *P* <.0001) with a median PFS of 6.3 months compared with 1 month in the placebo arm.
- ORR was 9% (95% CI, 4.2-18) in the ripretinib arm vs 0% (95% CI, 0-8) in the placebo arm (*P* =.05).
- Median OS was 15.1 months in the ripretinib arm vs 6.6 months in the placebo arm (HR 0.36; 95% CI, 0.21-0.62).

MPR

New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/qinlock/