PDL DRUG REVIEW

Proprietary Name: Qinlock®
Common Name: ripretinib
PDL Category: Antineoplastics

Summary

Pharmacology/Usage: Ripretinib, the active ingredient of Qinlock®, 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.

Indication: For the treatment of adult patients with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with 3 or more kinase inhibitors, including imatinib.

There is no pregnancy category for this medication; however, the risk summary indicates that based on findings from animal studies and its mechanism of action, Qinlock® can cause fetal harm when administered to a pregnant woman. There are no available data on use in pregnant women to inform a drug-associated risk. Advise pregnant women of the potential risk to the fetus. In addition, verify pregnancy status of females of reproductive potential prior to the start of treatment. Advise this population, as well as males with female partners of reproductive potential, to use effective contraception during treatment and for at least one week after the final dose. The safety and efficacy of use in the pediatric population have not been established.

Dosage Form: Tablets: 50mg. Swallow tablets whole.

Recommended Dosage: Take 150mg PO QD with or without food until disease progression or unacceptable toxicity. Take a missed dose if less than 8 hours have passed since the missed scheduled dose. Do not take an additional dose if vomiting occurs after taking Qinlock® and continue with the next dose as scheduled.

The recommended dose reduction for an adverse reaction is 100mg PO QD. Permanently discontinue Qinlock® in patients who are unable to tolerate 100mg PO QD. Dosage medications may be required for adverse reactions, such as palmar-plantar erythrodysesthesia, hypertension, left ventricular systolic dysfunction, arthralgia or myalgia, or other adverse reactions. Refer to the prescribing information for further information.

Dose adjustments are not required with mild hepatic impairment. A recommended dosage of Qinlock® has not been established for patients with moderate or severe hepatic impairment. Clinically significant differences in the pharmacokinetics of ripretinib were not seen with mild to moderate renal impairment. The effects of severe renal impairment have not been studied.

Drug Interactions: Avoid the concomitant use of Qinlock® with strong CYP3A inducers.

The coadministration of Qinlock® with a strong CYP3A inhibitor increased the exposure of ripretinib and its active metabolite, which may increase the risk of adverse reactions. Monitor patients more frequently for adverse reactions.

Box Warning: There is no box warning listed with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Qinlock®) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.* The most frequently reported adverse events included alopecia (47.3%), palmar-plantar erythrodysesthesia (21%), dry skin (6%), pruritus (6.3%), fatigue (19%), peripheral edema (10%), asthenia (0%), nausea (27%), abdominal pain (6%), constipation (15%), diarrhea (14%), vomiting (14%), stomatitis (11%), myalgia (20%), arthralgia (13.3%), muscle spasms (10.3%), decreased appetite (6%), decreased weight (7%), headache (14.3%), hypertension (9.3%), and dyspnea (13%).

Select laboratory abnormalities included increased activated partial thromboplastin time (26%), increased INR (6%), decreased neutrophil count (7.5%), increased lipase (19%), decreased phosphate (23.5%), increased triglycerides (3%), decreased calcium (15%), increased blood bilirubin (17%), increased creatine phosphokinase (11%), decreased sodium (7%), increased creatinine (0%), increased serum amylase (8%), and increased ALT (7%).

In a clinical trial, cutaneous squamous cell carcinoma (cuSCC) occurred in 4.7% treated with Qinlock® (out of 85 patients), with a median time to event of 4.6 months (range 3.8 to 6 months). Melanoma occurred in 2.4% of patients who received Qinlock® (out of 85 patients). Perform dermatological exams when starting Qinlock® and routinely during treatment. Manage suspicious lesions with excision and evaluation.

Grade 1-3 hypertension occurred in 14% of patients treated with Qinlock® in a clinical trial, including 7% with Grade 3 hypertension. Do not start Qinlock® in patients with uncontrolled hypertension. Adequately control blood pressure prior to starting Qinlock®. Monitor blood pressure as clinically indicated during treatment with Qinlock® and initiate or adjust antihypertensive therapy as appropriate. Based on severity, withhold Qinlock® and then resume at the same or reduced dose or permanently discontinue.

Cardiac failure was reported in patients treated with Qinlock® in a clinical trial (1.2% of the 85 patients who received treatment). In the pooled safety population, cardiac dysfunction (including cardiac failure, acute left ventricular failure, diastolic dysfunction, and ventricular hypertrophy) occurred in 1.7% of 351 patients, including Grade 3 adverse reactions in 1.1%. Grade 3 decreased ejection fraction occurred in 2.7% of 77 patients who received Qinlock® and had a baseline and at least one post-baseline echocardiogram. Cardiac dysfunction led to dose discontinuation in 1.2% of the 85 patients who received Qinlock®. The safety of Qinlock® has not been assessed in patients with a baseline ejection fraction below 50%. Assess ejection fraction by echocardiogram or MUGA scan prior to starting Qinlock® and during treatment, as clinically indicated.

Impaired wound healing complications can occur in patients who receive drugs that inhibit the vascular endothelial growth factor (VEGF) signaling pathway. Thus, Qinlock® has the potential to adversely affect wound healing. Withhold Qinlock® for at least 1 week prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing.

Contraindications: There are no contraindications listed with this product.

Manufacturer: Decipera Pharmaceuticals

Analysis: The safety and efficacy of Qinlock® were assessed in a multicenter, randomized, double-blind, placebo-controlled trial that included patients who had unresectable, locally advanced or metastatic GIST and who had received prior treatment with imatinib, sunitinib, and regorafenib (N=129). Those included in the trial had a median age of 60 years (range 29 to 83 years), while 39% were aged ≥65 years, 57% were male, 75% were White, 92% had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, 63% received 3 prior therapies, and 37% received 4 or more prior therapies. In addition, 66% of patients randomized to placebo switched to Qinlock® after disease progression.

The major efficacy outcome measure was progression-free survival (PFS) based on disease assessment by blinded independent central review (BICR) using modified RECIST 1.1 criteria, in which lymph nodes and bone lesions were

not target lesions and a progressively growing new tumor nodule within a pre-existing tumor mass must meet specific criteria to be considered unequivocal evidence of progression. Additional efficacy outcome measures included objective response rate (ORR) and overall survival. Patients randomized to placebo could be treated with Qinlock® at the time of disease progression. Efficacy results can be seen in the table below, which was adapted from the prescribing information.

	Qinlock® (N=85)	Placebo (N=44)
Progression-Free Survival (PFS)		
Number of events (%)	51 (60%)	37 (84%)
Progressive Disease	46 (54%)	32 (73%)
Deaths	5 (6%)	5 (11%)
Median PFS (months)	6.3	1.0
Hazard ratio; p-value	0.15; p<0.0001	
Overall Response Rate (ORR)		
Overall Response Rate (%)	9%	0%
p-value	0.0504 (not statistically significant)	
Overall Survival (OS)		
Number of deaths (%)	26 (31%)	26 (59%)
Median OS (months)	15.1	6.6
Hazard Ratio	0.36	

Place in Therapy: Qinlock®, a tyrosine kinase inhibitor, is indicated for the treatment of adult patients with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with 3 or more kinase inhibitors, including imatinib. In a placebo-controlled trial, Qinlock® significantly prolonged progression-free survival and overall survival in a patient population with unresectable, locally advanced or metastatic GIST who had received prior treatment with imatinib, sunitinib, and regorafenib.

It is recommended that Qinlock® should be non-recommended with conditions in order to confirm the appropriate diagnosis and clinical parameters for use.

PDL Placement: ☐ **Recommended**
☒ **Non-Recommended with Conditions**

References

[1] Qinlock [package insert]. Waltham, MA: Deciphera Pharmaceuticals, LLC; 2020.

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