PDL DRUG REVIEW

Proprietary Name: Truseltiq®
Common Name: infigratinib
PDL Category: Antineoplastics

Comparable Products	Preferred Drug List Status
Pemazyre	Non-Recommended with Conditions

Summary

Pharmacology/Usage: Infigratinib, the active ingredient of Truseltiq®, is a small molecule kinase inhibitor.

Indication: For the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test.

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

There is no pregnancy category for this medication; however, the risk summary indicates that based on findings in animal studies and its mechanism of action, Truseltiq® can cause fetal harm or loss of pregnancy when administered to a pregnant woman. There are no available data on the use of Truseltiq® during pregnancy. Advise pregnant women of the potential risk to a fetus. Furthermore, verify pregnancy status of females of reproductive potential prior to starting Truseltiq®. Advise females of reproductive potential and males that are partnered with females of reproductive potential to use effective contraception during treatment and for one month after the final dose. The safety and efficacy of use in the pediatric population have not been established.

Dosage Form: Capsules: 25mg, 100mg. (Do not crush, chew, or dissolve capsules)

Recommended Dosage: Select patients for the treatment of unresectable locally advanced or metastatic cholangiocarcinoma with Truseltiq® based on the presence of an FGFR2 fusion or rearrangement, as detected by an FDA-approved test. Information on FDA-approved test(s) for the detection of FGFR2 fusion or rearrangements in cholangiocarcinoma is available at http://www.fda.gov/CompanionDiagnostics.

The recommended dosage is 125mg (one 100mg capsule and one 25mg capsule) PO QD for 21 consecutive days followed by 7 days off therapy, in 28-day cycles. Continue treatment until disease progression or unacceptable toxicity. Take on an empty stomach at least 1 hour before or 2 hours after food, at about the same time each day. Swallow capsules whole with a glass of water. If a dose is missed by ≥4 hours or if vomiting occurs, instruct patients to resume the regular daily dose schedule for Truseltiq® the next day.

Dose modifications may be needed for adverse reactions, such as retinal pigment epithelial detachment (RPED), hyperphosphatemia, or other adverse reactions. Refer to the prescribing information for additional information.

The recommended dosage for patients with mild to moderate renal impairment is 100mg PO QD for 21 consecutive days followed by 7 days off of therapy, in 28-day cycles. The recommended dosage has not been established for patients with severe renal impairment or for patients with end-stage renal disease receiving intermittent hemodialysis. For mild hepatic impairment, the recommended dosage is 100mg QD for 21 consecutive days followed by 7 days off therapy, in 28-day cycles. For moderate hepatic impairment, the recommended dosage is 75mg QD for 21 consecutive days followed by 7 days off therapy, in 28-day cycles. The recommended dosage of Truseltiq® has not been established in patients with severe hepatic impairment.

Drug Interactions: Concomitant use of Truseltiq® with a strong or moderate CYP3A inhibitor may increase infigratinib concentrations. Avoid concomitant use of Truseltiq® with strong or moderate CYP3A inhibitors.

Concomitant use of Truseltiq® with a strong or moderate CYP3A inducer may decrease infigratinib plasma levels, which may reduce Truseltiq® anti-tumor activity. Avoid concomitant use of Truseltiq® with strong or moderate CYP3A inducers.

The concomitant use of Truseltiq® with a gastric acid reducing agent may decrease infigratinib plasma levels. Avoid concomitant use of Truseltiq® with proton pump inhibitors, H2-antagonists, and locally-acting antacids. If coadministration of H2-antagonists or locally acting antacids cannot be avoided, stagger administration of Truseltiq®. For H2-antagonists, separate administration of Truseltiq® by 2 hours before or 10 hours after. For locally-acting antacids, separate administration of Truseltiq® by 2 hours before or after.

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 (Truseltiq®) for all grades. Please note that there was no placebo data to compare with in the prescribing information.* The most frequently reported adverse event included nail toxicity (57%), alopecia (38%), palmar-plantar erythrodysesthesia syndrome (33%), dry skin (23%), stomatitis (56%), constipation (30%), abdominal pain (26%), dry mouth (25%), diarrhea (24%), vomiting (21%), nausea (19%), dyspepsia (17%), dry eye (44%), eyelash changes (25%), vision blurred (21%), fatigue (44%), edema (17%), pyrexia (15%), arthralgia (32%), pain in extremity (17%), dysgeusia (32%), headache (17%), decreased appetite (22%), epistaxis (18%), and weight loss (15%). Select laboratory abnormalities included decreased hemoglobin (53%), decreased lymphocytes (43%), decreased platelets (37%), decreased leukocytes (26%), decreased neutrophils (14%), increased creatinine (93%), increased phosphate (90%), decreased phosphate (64%), increased alkaline phosphatase (54%), increased alanine aminotransferase (51%), increased lipase (44%), increased calcium (43%), decreased sodium (41%), increased triglycerides (38%), increased aspartate aminotransferase (38%), increased urate (37%), decreased albumin (24%), increased bilirubin (24%), decreased potassium (21%), increased cholesterol (18%), increased potassium (17%), and decreased calcium (10%).

Truseltiq® can cause retinal pigment epithelial detachment (RPED), which may cause symptoms such as blurred vision. Perform a comprehensive ophthalmic exam including optical coherence tomography (OCT) prior to the start of treatment, at 1 month, at 3 months, and then every 3 months thereafter during treatment. Refer patients for ophthalmic evaluation urgently for onset of visual symptoms, and follow-up every 3 weeks until resolution or discontinuation of treatment.

Among 351 patients who received Truseltiq® across clinical trials, dry eye occurred in 29% of patients. Treat patients with ocular demulcents (mucoprotective agents) as needed.

Truseltiq® can cause hyperphosphatemia leading to soft tissue mineralization, cutaneous calcinosis, non-uremic calciphylaxis, vascular calcification, and myocardial calcification. Increases in phosphate levels are a pharmacodynamic effect of Truseltiq®. Of 351 patients treated with Truseltiq® across clinical trials, hyperphosphatemia was reported in 82% of patients based on laboratory values above the upper limit of normal. The median time to onset of hyperphosphatemia was 8 days. Phosphate binders were received by 83% of patients treated with Truseltiq®. Monitor for hyperphosphatemia throughout treatment. Initiate phosphate lowering therapy when serum phosphate level is >5.5mg/dL. For serum phosphate level >7.5mg/dL, withhold Truseltiq® and

start phosphate lowering therapy. Withhold, reduce dose, or permanently discontinue Truseltiq® based on duration and severity of hyperphosphatemia.

Contraindications: There are no contraindications listed with this product.

Manufacturer: QED Therapeutics

Analysis: The safety and efficacy of Truseltiq® were assessed in a multicenter, open-label, single-arm study that assessed the efficacy of Truseltiq® in adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with an FGFR2 fusion or rearrangement as determined for enrollment by local (89%) or central testing (11%). Patients received Truseltiq® until disease progression or unacceptable toxicity.

The median age of included adults was 53 years (range 23 to 81 years), while 62% were female, 72% were white, and 99% had a baseline Eastern Cooperative Oncology Group (ECOG) performance status of 0 (42%) or 1 (57%). In addition, 99% had metastatic (Stage IV) disease at the time of study entry. All patients had received at least 1 prior line of systemic therapy, 32% had 2 prior lines of therapy, and 29% had 3 or more prior lines of therapy. Furthermore, 99% received prior gemcitabine-based therapy and most (88%) had progressed on their prior gemcitabine-based therapy.

The major efficacy outcome measures were overall response rate (ORR) and duration of response (DOR), as determined by blinded independent central review (BICR) per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Efficacy results can be seen in the table below, which was adapted from the prescribing information. Note that the median time to response was 3.6 months (range 1.4 to 7.4 months).

Efficacy Parameter	Truseltiq® (N=108)
ORR	23%
Complete Response, n (%)	1 (1%)
Partial Response, n (%)	24 (22%)
Median DOR, months	5.0
Patients with DOR ≥6 months, n (%)	8 (32%)
Patients with DOR ≥12 months, n (%)	1 (4%)

Place in Therapy: Truseltiq®, an oral kinase inhibitor, is indicated for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). In a open-label, single-arm trial that included patients with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with an FGFR2 fusion or rearrangement, the ORR was 23%.

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

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

References

[1] Truseltiq [package insert]. Brisbane, CA: QED Therapeutics, In; 2021.