Turalio (pexidartinib)

NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Turalio
- **Generic name:** Pexidartinib
- **Pharmacological class:** Kinase inhibitor
- **Strength and Formulation:** 200mg; capsules
- **Manufacturer:** Daiichi Sankyo
- **How supplied:** Bottles—28, 120
- **Legal Classification:** Rx

Turalio


NDC 65597-402-20
Rx only
Turalio™
(pexidartinib)
capsules
200 mg
120 capsules
for oral use
Dispense the accompanying
Medication Guide to each patient.
Daiichi-Sankyo
T10

Indication

- Treatment of adults with symptomatic **tenosynovial giant cell tumor** (TGCT) associated with severe morbidity or functional limitations and not amenable to improvement with surgery

Dosage & Administration

- Swallow whole
- Take on an empty stomach (at least 1hr before or 2hrs after a meal/snack)
- 400mg twice daily until disease progression or unacceptable toxicity
- Mild to severe renal impairment (CrCl 15–89mL/min): 200mg in the AM and 400mg in the PM
- Dose modifications for adverse reactions, concomitant strong CYP3A or UGT inhibitors, acid-reducing agents: see full labeling

Considerations for Special Populations

- **Pregnancy:** May cause embryo-fetal harm; advise pregnant women of the potential risk to a fetus
- **Nursing mothers:** advise women not to breastfeed during treatment and for at least 1 week after the last dose
- **Pediatric:** not established
- **Geriatric:** studies did not include sufficient number of patients 65yrs and older to determine whether they respond differently
- **Renal impairment:** reduce dose with mild to severe impairment
- **Hepatic impairment:** recommended dose not established for moderate to severe impairment

Boxed Warning

- Can cause **serious and potentially fatal liver injury**
- Monitor liver tests prior to initiation and at specified intervals during treatment
- Withhold and dose reduce or permanently discontinue based on severity of hepatotoxicity
- Turalio is available only through a restricted program called the Turalio Risk Evaluation and Mitigation Strategy (REMS) Program

Turalio REMS

- Notable requirements include the following:
  - Prescribers must be certified with the program by enrolling and completing training
  - Patients must complete and sign an enrollment form for inclusion in a patient registry
  - Pharmacies must be certified with the program and must only dispense to patients who are authorized to receive Turalio

- Further information is available at **www.turalioREMS.com** or 1-833-887-2546

Warnings/Precautions

- Risk of liver injury (may be fatal)
- Avoid in patients with pre-existing increased serum transaminases, total/direct bilirubin >ULN, or active liver or biliary tract disease, including increased ALP
- Monitor LFTs prior to initiation, weekly for the first 8 weeks, every 2 weeks for the next month, and then every 3 months thereafter
- Withhold and reduce dose or permanently discontinue based on severity of hepatotoxicity
- Moderate to severe hepatic impairment

Warnings/Precautions

- Embryo-fetal toxicity
- Advise use of effective contraception during and for 1 month (females) or for 1 week (males w. female partners) after last dose
- Pregnancy: exclude status prior to initiation
- Nursing mothers: not recommended (during and for 1 week after last dose)

Interactions

- **Avoid** concomitant other products known to cause hepatotoxicity
- **Potentiated by** strong CYP3A (including grapefruit or grapefruit juice) or UGT inhibitors; avoid; if unavoidable, reduce Turalio dose
- **Antagonized by** strong CYP3A inducers (including St. John's wort) or proton pump inhibitors (alternatively, can use antacids or H_2-blockers); avoid

Adverse Reactions

- **Most common** (≥20%): increased lactate dehydrogenase, increased aspartate aminotransferase, hair color changes, fatigue, increased alanine aminotransferase, decreased neutrophils, increased cholesterol, increased alkaline phosphatase, decreased lymphocytes, eye edema, decreased hemoglobin, rash, dysgeusia, and decreased phosphate

Mechanism of Action

- Pexidartinib is a small molecule **tyrosine kinase inhibitor** that targets colony stimulating factor 1 receptor (CSF1R), KIT proto-oncogene receptor tyrosine kinase (KIT), and FMS-like tyrosine kinase 3 (FLT3) harboring an internal tandem duplication (ITD) mutation
- Overexpression of the CSF1R ligand promotes cell proliferation and accumulation in the synovium
- *In vitro*, pexidartinib inhibited proliferation of cell lines dependent on CSF1R and ligand-induced autophosphorylation of CSF1R
- Pexidartinib also inhibited the proliferation of a CSF1R dependent cell line *in vivo*

Clinical Trials

- The efficacy of Turalio was evaluated in ENLIVEN, a double-blind, randomized, placebo-controlled, trial in patients with symptomatic TGCT for whom surgical removal of the tumor would be associated with worsening functional limitation or severe morbidity
- Patients were randomized to placebo (n=59) or Turalio (n=61) 400mg in the morning and 600mg in the evening for 2 weeks followed by 400mg twice daily
- Treatment continued until unacceptable toxicity or disease progression

Clinical Trials

- Major efficacy outcome measure was overall response rate (ORR) as assessed by blinded independent central review (BICR) at Week 25 using RECIST v1.1
- Additional efficacy outcome measures were mean change from baseline in range of motion of the affected joint at Week 25 and ORR as assessed by BICR at Week 25 using tumor volume score (TVS)

Clinical Trials

- Results showed an ORR of 38% in the Turalio arm (complete response: 15%; partial response: 23%) vs 0% for placebo (*P* <.0001)
  - ORR by tumor volume score was 56% in patients randomized to the Turalio arm and 0% in patients randomized to the placebo arm (*P* <.0001).
- Patients treated with Turalio showed a statistically significant improvement in the mean change from baseline in range of motion of the affected joint at Week 25 compared with placebo

New Product Monograph

- For more information view the product monograph available at:

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