Turalio® pexidartinib 125 mg capsules

PRESCRIBING AND THE REMS PORTAL

REMS, Risk Evaluation and Mitigation Strategy.

NEXT

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About TURALIO Risk Evaluation and Mitigation Strategy (REMS)

TURALIO REMS is a safety program that manages the risks of serious and potentially fatal liver injury, including vanishing bile duct syndrome from TURALIO. The REMS Program is required by the Food and Drug Administration to help ensure that the potential benefits of TURALIO outweigh its risks. Further information is available at **www.TURALIOREMS.com** or call **1-833-887-2546**.

Because of the risk of hepatotoxicity, TURALIO is available only through a REMS Program. Under TURALIO REMS, only certified healthcare providers and pharmacies may prescribe and dispense TURALIO. In addition, a registry is used to collect information about the effects of taking TURALIO over time. Patients must complete and sign an enrollment form for the TURALIO REMS Program and the registry.

IMPORTANT SAFETY INFORMATION

WARNING: HEPATOTOXICITY

- **TURALIO can cause serious and potentially fatal liver injury, including vanishing bile duct syndrome.**
- **Monitor liver tests prior to initiation of TURALIO and at specified intervals during treatment. Withhold and dose reduce or permanently discontinue TURALIO based on severity of hepatotoxicity. Monitoring and prompt cessation of TURALIO may not eliminate the risk of serious and potentially fatal liver injury.**
- **TURALIO is available only through a restricted program called the TURALIO Risk Evaluation and Mitigation Strategy (REMS) Program.**

PREV NEXT

Please see Important Safety Information and Full Prescribing Information, including Boxed WARNING, and Medication Guide.

TURALIO REMS Certification Steps

To become certified in the TURALIO REMS Program via fax or email, prescribers must complete the following steps:

1

REVIEW

TURALIO full Prescribing Information

2

REVIEW

Program Overview and Prescriber Training

3

COMPLETE & SUBMIT

Prescriber Knowledge Assessment and Prescriber Enrollment Form

Prescribers will be notified when their certification in the TURALIO REMS Program is complete and they can prescribe TURALIO.

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Prior to Initiating Treatment

Please see the steps below to get your patients started on TURALIO.

1 Assess the patients by obtaining liver tests **(should precede initial patient visit).**

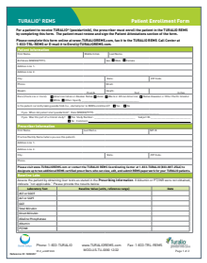
Tests: Please include all tests included on the REMS Patient Enrollment Form. To be compliant with the REMS, the following must be included: AST or SGOT, ALT or SGPT, GGT, TBIL, DBIL, and ALP.

2 Counsel patients on the TURALIO REMS Patient Guide and TURALIO Medication Guide.

NOTE: **Enroll** and **Prescribe** steps may be completed concurrently.

3 **ENROLL**

To have patients included in the patient registry, complete the form shown below, and then have them review and sign it.



TURALIO REMS
Patient Enrollment Form

Complete and submit online at **www.TURALIOREMS.com**.
Or download at **www.TURALIOREMS.com** and send completed forms by:

Email: Enroll@TURALIOREMS.com
Fax: 1-833-TRL-REMS (1-833-875-7367)

4 **PRESCRIBE**

Submit prescriptions to Biologics, a specialty pharmacy, via the form shown below.

ACCESS CENTRAL
Patient Enrollment Form

Available for download at **dsiaccesscentral.com/hcp/turalio/resources**

Fax completed forms to 1-800-823-4506.

5 Biologics, a specialty pharmacy, will process the prescriptions, and the prescribers will be notified on resolution.

6 Patients receive TURALIO.

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; DBIL, direct bilirubin; GGT, gamma-glutamyltransferase; SGOT, serum glutamic-oxaloacetic transaminase; SGPT, serum glutamic-pyruvic transaminase; TBIL, total bilirubin.

PREV NEXT

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Liver Test Monitoring and REMS Patient Status Forms Submission Schedule

During treatment

Monitor the patients' liver tests and complete and submit the Patient Status Forms to the REMS Program according to the following schedule:

	Liver Function Tests[1]	Patient Status Forms
Month 1	Weekly	Once
Month 2	Weekly	Once
Month 3	Every 2 weeks	Once
Month 4	—	—
Month 5	—	—
Month 6	Once	Once
Month 7	—	—
Month 8	—	—
Month 9	Once	Once
Month 10	—	—
Month 11	—	—
Month 12	Once	Once
After 1 year	Every 3 months	Every 6 months

Monitor patients' liver tests and modify the TURALIO dose per the Prescribing Information as needed.

Monitoring and prompt cessation of TURALIO may not eliminate the risk of serious and potentially fatal liver injury.

Visit **www.TURALIOREMS.com** to complete Patient Status Forms and Liver Adverse Event Reporting Forms.

Reference: 1. TURALIO® [package insert]. Basking Ridge, NJ: Daiichi Sankyo, Inc; 2023.

Please see Important Safety Information and Full Prescribing Information, including Boxed WARNING, and Medication Guide.

TURALIO REMS Portal Overview

TURALIO REMS Public Portal allows access for Associated Prescribers or designated Office Contacts (up to 2 each per Prescriber)

- Adding delegates can help alleviate some of the REMS requirements
- Delegating to Associated Prescribers and designated Office Contacts can:
  - —Help with timely patient enrollment
  - —Help prevent delays in reporting
  - —Streamline form submissions and updates

Roles and responsibilities of Prescribers, Associated Prescribers, and Office Contacts

	Initiate Form	Add Delegate	View Form	Edit Form	Submit Form	Remove Delegate
Prescriber	✓	✓	✓	✓	✓	✓
Associated Prescriber	✓		✓	✓	✓	
Office Contact	✓		✓	✓	Prescriber's review and approval needed to submit	

Completing all REMS forms through a single online portal reduces the need for additional follow-up and resubmission of forms, and safeguards against incomplete and erroneous submissions.

Associated Prescribers and Office Contacts will receive their own unique login to the TURALIO REMS Public Portal and will receive email notifications regarding Patient Enrollment Forms, Patient Status Forms, and Liver Adverse Event Reporting Forms where applicable.

Don't have time to complete everything at once?

All users can save Patient Enrollment Forms, Patient Status Forms, and Liver Adverse Event Forms and complete at a later time.

Please see Important Safety Information and Full Prescribing Information, including Boxed WARNING, and Medication Guide.

TURALIO REMS Support

Associated Prescribers and designated **Office Contacts** can be added via the Prescriber Portal, or by calling the TURALIO REMS Coordinating Center at 1-833-TURALIO (887-2546).

For questions regarding TURALIO REMS, please contact a team member at our Coordinating Center or visit the **TURALIO REMS website**. Our office hours are Monday–Friday, 8AM–8PM EST.

Phone
1-833-TURALIO | (1-833-887-2546)

Fax
1-833-TRL-REMS | (1-833-875-7367)

Email
Enroll@TURALIOREMS.com

Website
www.TURALIOREMS.com

Visit Website

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Daiichi-Sankyo

Indication and Important Safety Information

INDICATION

TURALIO® (pexidartinib) is indicated for the treatment of adult patients with symptomatic tenosynovial giant cell tumor (TGCT) associated with severe morbidity or functional limitations and not amenable to improvement with surgery.

IMPORTANT SAFETY INFORMATION

WARNING: HEPATOTOXICITY

- **TURALIO can cause serious and potentially fatal liver injury, including vanishing bile duct syndrome.**
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- **TURALIO is available only through a restricted program called the TURALIO Risk Evaluation and Mitigation Strategy (REMS) Program.**

CONTRAINDICATIONS: None

WARNINGS AND PRECAUTIONS
Hepatotoxicity

- Hepatotoxicity, including liver failure and life-threatening vanishing bile duct syndrome (VBDS), ductopenia, and symptomatic cholestasis (including severe pruritus) can occur in patients treated with TURALIO and can occur despite monitoring and prompt drug cessation.
- The mechanism of cholestatic hepatotoxicity is unknown and its occurrence cannot be predicted. It is unknown whether liver injury can also occur in the absence of increased transaminases.
- Of the first 609 patients who received TURALIO under the REMS program, 32 (5.3%) developed a liver injury event of concern, defined as any serious liver-related outcome or any liver abnormality that triggers drug discontinuation per the US Prescribing Information. These 32 patients developed liver toxicity within 71 days of the first dose of TURALIO; ten required hospitalization and two developed VBDS. Sixteen of the 32 patients had not fully recovered at the time of the analysis, including 6 patients followed for at least 6 months after discontinuation.
- Among 768 patients who received TURALIO in clinical trials, there were two irreversible cases of cholestatic liver injury. One patient with advanced cancer and ongoing liver toxicity died and one patient with a confirmed case of VBDS required a liver transplant.
- In ENLIVEN, 3 of 61 (5%) patients who received TURALIO developed signs of serious liver injury, defined as alanine aminotransferase (ALT) or aspartate aminotransferase (AST) ≥3 × upper limit of normal (ULN) with total bilirubin ≥2 × ULN. In these patients, peak ALT ranged from 6 to 9 × ULN, peak total bilirubin ranged from 2.5 to 15 × ULN, and alkaline phosphatase (ALP) was ≥2 × ULN. ALT, AST, and total bilirubin improved to <2 × ULN in these three patients 1 to 7 months after discontinuing TURALIO.

PREV NEXT

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Indication and Important Safety Information (CONT.)

- Avoid TURALIO in patients with preexisting increased serum transaminases, total bilirubin, or direct bilirubin (>ULN); or active liver or biliary tract disease, including increased ALP.
- Monitor liver tests, including AST, ALT, total bilirubin, direct bilirubin, ALP, and gamma-glutamyl transferase (GGT), prior to initiation of TURALIO, weekly for the first 8 weeks, every 2 weeks for the next month and every 3 months thereafter.
- Withhold and dose reduce, or permanently discontinue TURALIO based on the severity of the hepatotoxicity. Refer patients to a hepatologist if liver tests do not return to normal. Rechallenge with a reduced dose of TURALIO may result in a recurrence of increased serum transaminases, bilirubin, ALP or other signs of liver injury. Monitor liver tests weekly for the first month after rechallenge.

TURALIO REMS

- Requirements include: 1) prescribers must be certified by enrolling and completing training, 2) patients must complete and sign an enrollment form for inclusion in a patient registry, and 3) pharmacies must be certified and must dispense only to patients who are authorized (enrolled in the REMS patient registry).
- Further information is available at www.TURALIOREMS.com or 1-833-887-2546.

Embryo-Fetal Toxicity

- TURALIO may cause fetal harm when administered to a pregnant woman. Advise patients of reproductive potential of the potential risk to a fetus. Verify pregnancy status in females of reproductive potential prior to the initiation of TURALIO.
- Advise females of reproductive potential to use an effective nonhormonal method of contraception. TURALIO can render hormonal contraceptives ineffective during treatment with TURALIO and for 1 month after the final dose.
- Advise males with female partners of reproductive potential to use effective contraception during treatment with TURALIO and for 1 week after the final dose.

Potential Risks Associated with a High-Fat Meal

- Taking TURALIO with a high-fat meal increases pexidartinib concentrations, which may increase the incidence and severity of adverse reactions, including hepatotoxicity.
- Instruct patients to take TURALIO with a low-fat meal (approximately 11 to 14 grams of total fat) and to avoid taking TURALIO with a high-fat meal (approximately 55 to 65 grams of total fat).

ADVERSE REACTIONS

- The most common adverse reactions (>20%) were increased lactate dehydrogenase (92%), increased AST (88%), hair color changes (67%), fatigue (64%), increased ALT (64%), decreased neutrophils (44%), increased cholesterol (44%), increased ALP (39%), decreased lymphocytes (38%), eye edema (30%), decreased hemoglobin (30%), rash (28%), dysgeusia (26%), and decreased phosphate (25%).

DRUG INTERACTIONS

- Hepatotoxic products: Avoid coadministration in patients with increased serum transaminases, total bilirubin, or direct bilirubin (>ULN) or active liver or biliary tract disease.

PREV NEXT

Please see Important Safety Information and Full Prescribing Information, including Boxed WARNING, and Medication Guide.

Indication and Important Safety Information (CONT.)

- Moderate or strong CYP3A inhibitors and UGT inhibitors: Concomitant use may increase pexidartinib concentrations. Reduce TURALIO dosage if concomitant use cannot be avoided.
- Strong CYP3A inducers: Avoid concomitant use due to decreased pexidartinib concentrations.
- Acid-reducing agents: Avoid concomitant use of proton pump inhibitors due to decreased pexidartinib concentrations. Use histamine-2 receptor antagonists or antacids if needed.
- CYP3A substrates: Avoid concomitant use where minimal concentration changes may lead to serious therapeutic failure (e.g., hormonal contraceptives) due to decreased concentrations of CYP3A substrates.

USE IN SPECIFIC POPULATIONS

- Lactation: Advise not to breastfeed and for at least 1 week after the final dose.
- Renal impairment: Reduce the dosage for patients with mild to severe renal impairment.
- Hepatic impairment: Reduce the dosage for patients with moderate hepatic impairment. TURALIO has not been studied in patients with severe hepatic impairment.

To report SUSPECTED ADVERSE REACTIONS, contact Daiichi Sankyo, Inc. at 1-877-437-7763 or FDA at 1-800-FDA-1088 or fda.gov/medwatch.

Please see Full Prescribing Information, including Boxed WARNING, and Medication Guide.