

FDA REQUIRED REMS SAFETY INFORMATION

[Month/Day/Year]

- Subject:**
- Vanishing bile duct syndrome added to Prescribing Information, including Boxed Warning: Risk of serious and potentially fatal liver injury, including vanishing bile duct syndrome, associated with TURALIO® (pexidartinib)
 - FDA required TURALIO REMS with restricted distribution

Dear [Healthcare Provider]:

The purpose of this letter is to inform you about the updated TURALIO® (pexidartinib) Prescribing Information that now includes vanishing bile duct syndrome. The Boxed Warning has been updated to state:

- TURALIO can cause serious and potentially fatal liver injury, including vanishing bile duct syndrome.

TURALIO 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.

The U.S. Food and Drug Administration (FDA) has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary to mitigate the risk of serious and potentially fatal liver injury, including vanishing bile duct syndrome.

TURALIO is only available through a restricted distribution program: the TURALIO REMS. Only certified prescribers, certified pharmacies and enrolled patients can prescribe, dispense, and receive TURALIO.

Serious Risk of TURALIO

- TURALIO can cause serious and potentially fatal liver injury, including vanishing bile duct syndrome.
- Monitor liver tests, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (TBIL), direct bilirubin (DBIL), alkaline phosphatase (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 severity of hepatotoxicity.
- Monitoring and prompt cessation of TURALIO may not eliminate the risk of serious and potentially fatal liver injury.
- Refer patients to a hepatologist if liver tests do not return to normal.

See the Prescribing Information for TURALIO for more information on the risk of hepatotoxicity, liver monitoring frequency and dose reductions.

As part of the TURALIO REMS

- Healthcare providers that prescribe TURALIO must be certified.
 - To become certified, healthcare providers must review the TURALIO Prescribing Information, REMS Overview and Prescriber Training, and complete and submit a Knowledge Assessment and Prescriber Enrollment Form.
 - **Visit www.TURALIOREMS.com to begin the certification process.**
- Prescribers must counsel the patient using the Patient Guide prior to treatment and complete the Patient Enrollment Form with the patient.



Daiichi-Sankyo

Phone: 1-833-TURALIO

www.TURALIOREMS.com

Fax: 1-833-TRL-REMS

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- During treatment:
 - monitor the patient's liver tests and modify the TURALIO dose as needed
 - submit a Patient Status Form for the patient every month for the first 3 months of treatment, at month 6, month 9, and month 12, and every 6 months thereafter
 - report liver adverse events using the Liver Adverse Event Reporting Form
- Patients must be enrolled in the TURALIO REMS to receive TURALIO.
- Pharmacies must be certified to dispense TURALIO.

Adverse Event Reporting

Report any adverse events including those of serious and potentially fatal liver injury, including vanishing bile duct syndrome, by contacting the REMS at 1-833-TURALIO (1-833-887-2546), to Daiichi Sankyo, Inc. at 1-877-4DS-PROD (1-877-437-7763) or to FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.

Additional details about the REMS, including educational and certification materials for the TURALIO REMS can be found at www.TURALIOREMS.com. For more information, contact the TURALIO REMS at 1-833-TURALIO (1-833-887-2546).

The information in this letter is not intended as a complete description of benefits and risks associated with the use of TURALIO. Please see accompanying full Prescribing Information including Medication Guide.

Sincerely,
[Signatory]

Enclosures:
TURALIO Full Prescribing Information including Medication Guide



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