

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

211810Orig1s000

REMS

Risk Evaluation and Mitigation Strategy (REMS) Document

TURALIO™ (pexidartinib) REMS Program

I. Administrative Information

Application Number: NDA 211810
Application Holder: Daiichi Sankyo, Inc.
Initial REMS Approval: 08/2019

II. REMS Goal

The goal of the TURALIO REMS is to mitigate the risk of serious and potentially fatal liver injury by:

1. Ensuring that prescribers are educated on the following:
 - a. approved indication for TURALIO
 - b. the risk of serious and potentially fatal liver injury associated with the use of TURALIO
 - c. the need for liver monitoring at baseline and periodically during treatment with dose modifications as described in the Prescribing Information
 - d. the need to counsel patients about the risk of serious and potentially fatal liver injury, liver monitoring at baseline and periodically during treatment with TURALIO as described in the Patient Guide and to report signs and/or symptoms of liver injury to the prescriber during therapy
2. Ensuring that prescribers adhere to the requirement of baseline and periodic monitoring as described in the Prescribing Information
3. Enrollment of all patients in a registry to further assess the safe use and acute, chronic and irreversible hepatotoxicity of TURALIO.

III. REMS Requirements

Daiichi Sankyo, Inc. must ensure that healthcare providers, patients, pharmacies, and wholesalers-distributors comply with the following requirements:

1. Healthcare Providers who prescribe TURALIO must:

To become certified to prescribe

1. Review the drug's Prescribing Information.
2. Review the following: [Program Overview](#) and [Prescriber Training](#).
3. Successfully complete the [Prescriber Knowledge Assessment](#) and submit it to the REMS.
4. Enroll in the REMS by completing the [Prescriber Enrollment Form](#) and submitting it to the REMS Program.

Before treatment initiation (first dose)	- Provide the patient with the Patient Guide. - Assess the patient's baseline liver function. Document and submit the results to the REMS Program using the Patient Enrollment Form. - Enroll the patient by completing and submitting the Patient Enrollment Form to the REMS Program.
During treatment, at least weekly for the first 8 weeks, then every 2 weeks for 1 month, then every 3 months	Assess the patient's liver function and modify the dose of TURALIO as needed as described in the Prescribing Information.
During treatment, monthly for the first 3 months	Prescribe no more than a 30 days' supply.
During treatment, monthly for the first 3 months, then month 6, 9, and 12, and every 6 months thereafter	Assess the patient by performing liver tests. Document and submit to the REMS Program using the Patient Status Form.
At all times	Report adverse events suggestive of serious and potentially fatal liver injury to the REMS Program using the Liver Adverse Event Reporting Form.

2. Patients who are prescribed TURALIO:

Before treatment initiation	- Review the Patient Guide. - Get blood tests to check your liver. - Enroll in the REMS Program by completing the Patient Enrollment Form with the prescriber. Enrollment information will be provided to the REMS Program.
During treatment, weekly for the first 8 weeks, then every 2 weeks for 1 month, then every 3 months or more often as directed by your prescriber	Get blood tests to check your liver so your prescriber can modify your TURALIO treatment, if needed.
At all times	Inform the prescriber of signs and/or symptoms of liver injury.

3. Pharmacies that dispense TURALIO must:

To become certified to dispense	1. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS Program on behalf of the pharmacy. 2. Have the authorized representative review the Program Overview. 3. Have the authorized representative enroll in the REMS by completing the Pharmacy Enrollment Form and submitting it to the REMS Program. 4. Train all relevant staff involved in dispensing TURALIO using the Program Overview.
Before dispensing	5. Obtain authorization to dispense each prescription by contacting the REMS Program to verify the prescriber is certified and the patient is enrolled and authorized to receive the drug.
Before dispensing; for the first 3 months	6. Dispense no more than a 30 days supply.
To maintain certification to dispense	7. Have the new authorized representative enroll in the REMS by completing the Pharmacy Enrollment Form and submitting it to the REMS if the authorized representative changes.
At all times	8. Report adverse events suggestive of serious and potentially fatal liver injury to the REMS Program using the Liver Adverse Event Reporting Form. 9. Do not distribute, transfer, loan, or sell TURALIO, except to certified dispensers. 10. Maintain records documenting the staff's completion of REMS training. 11. Maintain records that all processes and procedures are in place and being followed. 12. Comply with audits carried out by Daiichi Sankyo, Inc. or a third party acting on behalf of the applicant, to ensure that all processes and procedures are in place and are being followed.

4. Wholesalers-Distributors that distribute TURALIO must:

To be able to distribute	1. Establish processes and procedures to ensure that the drug is distributed only to certified pharmacies. 2. Train relevant staff involved in TURALIO distribution on the REMS requirements.
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At all times	- Distribute only to certified pharmacies. - Maintain records of all drug distributions. - Comply with audits carried out by Daiichi Sankyo, Inc. or a third party acting on behalf of the applicant to ensure that all processes and procedures are in place and are being followed.
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Daiichi Sankyo, Inc. must provide training to healthcare providers who prescribe TURALIO.

The training includes the following educational materials: [Program Overview](#), [Prescriber Training](#) and [Prescriber Knowledge Assessment](#). The training must be available online and as a hard copy format via mail or fax.

Daiichi Sankyo, Inc. must provide training to pharmacies that dispense TURALIO.

The training includes the following educational material: [Program Overview](#). The training must be available online and as a hard copy format via mail or fax.

To inform healthcare providers about the REMS and the risks and safe use of TURALIO, Daiichi Sankyo, Inc. must disseminate REMS communication materials according to the table below:

Target Audience	Communication Materials-& Dissemination Plans
Healthcare providers who are likely to prescribe TURALIO	REMS Letter: Letter for Healthcare Providers, Letter for Professional Societies - Email within 60 calendar days of the date TURALIO is first commercially distributed and again 12 months later. - Send by mail within 30 calendar days of approval of the REMS if a healthcare provider’s email address is not available or the email is undeliverable. - Send a second email within 30 calendar days of the date the first email was sent if the first email is marked as unopened. - Send by mail within 30 calendar days of the date the second email was sent if the second email is marked as unopened. - Disseminate through field-based sales and medical representatives. - Disseminate through professional societies and request the letter or content be provided to their members. - Sarcoma Alliance for Research through Collaboration; Connective Tissue Oncology Society; American Society of Clinical Oncology; and National Comprehensive Cancer Network - Disseminate at professional meetings for 12 months from the date TURALIO is first commercially distributed.

To support REMS operations, Daiichi Sankyo, Inc. must:

- Authorize dispensing for each patient based on receipt of the [Patient Enrollment Form](#) and [Patient Status Form](#) on the following schedule: Authorize the first patient shipment upon receipt of the [Patient Enrollment Form](#). If a completed [Patient Enrollment Form](#) is not received, the patient is not

authorized to receive drug. For subsequent dispensing, if the [Patient Status Form](#) is not received within 20 calendar days after the date the last [Patient Status Form](#) was due, the patient is not authorized to receive subsequent drug shipments.

2. Establish and maintain a REMS Website, www.TURALIOREMS.com. The REMS website must include the capability to complete prescriber certification and enrollment online, the capability to enroll and manage patients online including patient authorization and reporting liver injury, and the option to print the Prescribing Information and REMS materials. All product websites for consumers and healthcare providers must include prominent REMS-specific links to the REMS website. The REMS website must not link back to the promotional product website(s).
3. Make the REMS website fully operational and all REMS materials available through website and call center by the date TURALIO is first commercially distributed.
4. Establish and maintain a REMS call center for REMS participants at [1-833-887-2546].
5. Establish and maintain a validated, secure database of all REMS participants who are enrolled and/or certified in the TURALIO REMS Program.
6. Ensure prescribers are able to enroll online, by fax, and by email.
7. Ensure pharmacies are able to enroll by fax and email.
8. Ensure prescribers and pharmacies are able to report serious and potentially fatal liver injury by phone and online.
9. Ensure pharmacies are able to obtain authorization to dispense by phone and online.
10. Provide [Program Overview](#), [Prescriber Training](#), [Prescriber Knowledge Assessment](#), [Patient Enrollment Form](#), [Patient Guide](#) and the Prescribing Information to prescribers who (1) attempt to prescribe and are not yet certified or (2) inquire about how to become certified.
11. Provide [Program Overview](#), [Pharmacy Enrollment Form](#) to pharmacies that (1) attempt to order/dispense and are not yet certified or (2) inquire about how to become certified.
12. Notify prescribers and pharmacies within 2 business days after they become certified in the REMS.
13. Provide certified pharmacies access to the database of certified prescribers and enrolled patients.
14. Provide certified prescribers access to the database of certified pharmacies and their enrolled patients.
15. Provide authorized wholesalers-distributors access to the database of certified pharmacies.
16. Establish and maintain a registry which includes a reporting and collection system for all patients to provide information on acute, chronic and irreversible hepatotoxicity.
17. Ensure that once a report suggestive of serious or potentially fatal liver injury is received, Daiichi Sankyo, Inc. follows up with the healthcare provider to obtain all data required for complete adverse event reporting related to serious and potentially fatal liver injury under the REMS.
18. Report serious and potentially fatal liver injury as soon as possible to the FDA but no later than 15 calendar days from the initial receipt of the information by the applicant. This requirement does not affect the applicant's other reporting and follow-up requirements under applicable FDA regulations.

To ensure REMS participants' compliance with the REMS, Daiichi Sankyo, Inc. must:

19. Ensure the [Patient Status Form](#) is received for each patient on the following schedule: If the form is not received within 20 calendar days of the date the last [Patient Status Form](#) was due, Daiichi Sankyo, Inc. must contact the prescriber for the form. The patient is not authorized to receive the drug until the form is received.
20. Verify annually that the designated authorized representative for the pharmacy is the same. If different, the pharmacy must re-certify with a newly authorized representative.
21. Maintain adequate records to demonstrate that REMS requirements have been met, including, but not limited to records of: drug distribution and dispensing; certification of prescribers and

pharmacies; enrollment and status of patients; and audits of pharmacies and wholesalers-distributors. These records must be readily available for FDA inspections.

22. Establish a plan for addressing noncompliance with REMS requirements.
23. Monitor prescribers and pharmacies on an ongoing basis to ensure the requirements of the REMS are being met. Take corrective action if non-compliance is identified, including de-certification.
24. Audit pharmacies no later than 90 calendar days after they become certified, to ensure that all REMS processes and procedures are in place, functioning, and support the REMS requirements.
25. Audit all wholesalers-distributors no later than 90 calendar days after they become authorized to distribute the drug and annually thereafter, to ensure that all REMS processes and procedures are in place, functioning, and support the REMS requirements.
26. Take reasonable steps to improve operations of and compliance with the requirements in the TURALIO REMS based on monitoring and evaluation of the TURALIO REMS.

IV. REMS Assessment Timetable

Daichi Sankyo, Inc. must submit REMS Assessments at 6 months, 12 months and annually thereafter from the date of the initial approval of the REMS (08/02/2019). To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. Daiichi Sankyo, Inc. must submit each assessment so that it will be received by the FDA on or before the due date.

V. REMS Materials

The following materials are part of the TURALIO REMS:

Enrollment Forms

Prescriber:

1. [Prescriber Enrollment Form](#)

Patient:

2. [Patient Enrollment Form](#)

Pharmacy:

3. [Pharmacy Enrollment Form](#)

Training and Educational Materials

Prescriber:

4. [Program Overview](#)
5. [Prescriber Training](#)
6. [Prescriber Knowledge Assessment](#)

Patient:

7. [Patient Guide](#)

Pharmacy:

8. [Program Overview](#)

Patient Care Forms

9. [Patient Status Form](#)
10. [Liver Adverse Reporting Form](#)

Communication Materials

11. [Letter for Healthcare Providers](#)
12. [Letter for Professional Societies](#)

Other Materials

13. [REMS Website](#)

To become certified in the TURALIO REMS and prescribe TURALIO:

1. Review the TURALIO **Prescribing Information**
2. Review the **Program Overview** and the **Prescriber Training**
3. Complete and submit the **Prescriber Knowledge Assessment** to the TURALIO REMS
4. Complete and submit this **Prescriber Enrollment Form** to the TURALIO REMS

Submit the completed Prescriber Enrollment Form via:

- a. Online at www.TURALIOREMS.com,
- b. Fax to the TURALIO REMS at 1-833-TRL-REMS (833-875-7367), or
- c. E-mail to Enroll@TURALIOREMS.com

Prescriber Information Note: Fields marked with an * are REQUIRED.			
*First Name:	Middle Initial:	*Last Name:	
*Credentials: ☐ MD ☐ DO ☐ NP ☐ PA ☐ Other			
*Specialty: ☐ Oncology ☐ Orthopedics ☐ Other			
*National Provider Identifier (NPI) #:		State License #:	
Practice/Facility Name:			
*Street Address:	*City:	*State:	*ZIP Code:
*Office Phone Number:	*Office Fax Number:		
*E-mail:	Preferred Method of Communication (please select one): ☐ Fax ☐ E-mail ☐ Phone		Preferred Time of Contact: ☐ AM ☐ PM
Office Contact Information Note: Fields marked with an * are REQUIRED.			
First Name:		Last Name:	
Office Phone Number: ☐ Same as above	Office Fax Number: ☐ Same as above	E-mail:	
To provide additional Office Contacts please contact the TURALIO REMS Coordinating Center at 1-833-TURALIO (833-887-2546)			



Daiichi-Sankyo

Phone: 1-833-TURALIO

www.TURALIOREMS.com

Fax: 1-833-TRL-REMS



v2.0_30Jul2019

Reference ID: 4471832

Prescriber Attestations

By signing this form, I agree TURALIO is only available through the TURALIO REMS and I agree to comply with the following TURALIO REMS requirements:

I have:

- Reviewed the **Prescribing Information, Program Overview** and **Prescriber Training**.
- Successfully completed the **Prescriber Knowledge Assessment** and submitted it to the TURALIO REMS.

Before treatment initiation and with the first dose of TURALIO:

- I understand that I should counsel the patient on the risk of serious and potentially fatal liver injury, and liver test monitoring at baseline and periodically during treatment.
- I must assess the patient by obtaining baseline liver tests. I must submit the results of the assessment on the **Patient Enrollment Form**.
- I must enroll patients in the TURALIO REMS by completing and submitting the **Patient Enrollment Form**.

During treatment with TURALIO:

- I must assess the patient by obtaining liver tests weekly for the first 8 weeks, then every 2 weeks for 1 month, then every 3 months and modify the dose of TURALIO as needed in accordance with the **Prescribing Information**.
- I must prescribe no more than a 30 days supply for each of the first 3 months of treatment.
- I must complete the **Patient Status Form** every month for the first 3 months of treatment, at months 6, 9, and 12 and then every 6 months thereafter while the patient receives TURALIO.

At all times:

- I must report adverse events of serious and potentially fatal liver injury by submitting the **Liver Adverse Event Reporting Form**.

*Prescriber Signature:

*Date:



Phone: 1-833-TURALIO

www.TURALIOREMS.com

Fax: 1-833-TRL-REMS



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Reference ID: 4471832

For a patient to receive TURALIO™ (pexidartinib), the prescriber must enroll the patient in the TURALIO REMS by completing this form. The patient must review and sign the Patient Attestations section of the form.

Please complete this form online at www.TURALIOREMS.com, fax it to the TURALIO REMS Call Center at 1-833-TRL-REMS or E-mail it to Enroll@TURALIOREMS.com.

Patient Information		
First Name:	Middle Initial:	Last Name:
Birthdate (MM/DD/YYYY):		Sex: ☐ Male ☐ Female
Address Line 1:		
Address Line 2:		
City:	State:	ZIP Code:
Phone:	Email:	
Weight:	Pounds	Height: Feet Inches
Race (check one or more): ☐ American Indian or Alaskan Native ☐ Asian ☐ Black or African American ☐ Native Hawaiian or Other Pacific Islander ☐ White ☐ Other: Specify _____		
Prescriber Information		
First Name:	Last Name:	NPI #:
Practice/Facility Name (where you see this patient):		
Address Line 1:		
Address Line 2:		
City:	State:	ZIP Code:
Phone:		
Baseline Labs		
Assess the patient by obtaining liver tests as stated in the Prescribing Information . Please provide the results below.		
Laboratory Test	Baseline Value (units, reference range)	Date
AST or SGOT		
ALT or SGPT		
GGT		
Total Bilirubin		
Direct Bilirubin		
Alkaline Phosphatase		
Albumin		
PT/INR		



Current Medication (including prescription, non-prescription and herbal or dietary supplements):☐ Check box if there are no current medications

Medication

Hepatic Medical History:☐ Check box if there is no hepatic medical history

- | | | |
|--|--|--|
| ☐ Hepatitis Viral Status | ☐ Wilson's Disease | ☐ Biliary Tract Disorder |
| ☐ Hepatic Cyst | ☐ Drug Abuse | ☐ Hypertriglyceridemia |
| ☐ Ischemic Hepatitis | ☐ Gilbert's syndrome | ☐ Cirrhosis |
| ☐ Alcohol Abuse | ☐ Hypolipoproteinemia | ☐ Gallbladder Disease/ Gallstones/
Bile Duct Occlusion |
| ☐ Family History of Liver Disease | ☐ Familial Hyperbilirubinemia | ☐ Diabetes |
| ☐ Autoimmune Hepatitis | ☐ Anorexia | |

Prescriber Agreement

I have reviewed and discussed the risks of TURALIO and the requirements of the TURALIO REMS with this patient.

Prescriber Signature:

Date (MM/DD/YYYY):

Patient Attestation

In order to receive TURALIO I must be enrolled in the TURALIO REMS. The TURALIO REMS will collect data to assess the risk of serious liver problems which can be severe and lead to death as described in the **Patient Guide**.

- I agree to enroll in the Patient Registry.
- I agree to review the **Patient Guide**.
- I must get blood tests to test my liver as directed by my healthcare provider.
- I agree to tell my healthcare provider if I have signs and/or symptoms of liver injury.
- My personal information will be shared to enroll me in the Patient Registry so that my health and any liver injury can be evaluated while I am receiving TURALIO.
- Daiichi Sankyo, Inc., and its agents, may contact me by phone, mail or email to manage the TURALIO REMS.
- Daiichi Sankyo, Inc., and its agents, may use and share my personal health information, including lab tests and prescriptions as part of the TURALIO REMS. My information will be protected and will be used to enroll me into and manage the TURALIO REMS. My health information may be shared with the U.S. Food and Drug Administration (FDA) to evaluate the TURALIO REMS.

Patient or Legal Guardian Signature:

Date (MM/DD/YYYY):

Printed Patient or Legal Guardian Name:

Prescribers should always report all adverse events by contacting the REMS at 1-833-TURALIO, Daiichi Sankyo, Inc. at 1-877-4DS-PROD (1-877-437-7763) or FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.



Phone: 1-833-TURALIO

www.TURALIOREMS.com

Fax: 1-833-TRL-REMS



v2.0_30Jul2019

Reference ID: 4471832

To become certified in the TURALIO REMS and dispense TURALIO, a pharmacy must designate an Authorized Representative to:

1. Review the **Program Overview**
2. Complete and submit this **Pharmacy Enrollment Form**
3. Oversee implementation and compliance of the TURALIO REMS requirements

Submit the completed Pharmacy Enrollment Form via:

- a. Fax to the TURALIO REMS at 1-833-TRL-REMS (833-875-7367), or
- b. E-mail to Enroll@TURALIOREMS.com

Authorized Representative Attestations

As the Authorized Pharmacy Representative, I attest that:

- I have reviewed the **Program Overview**.
- I must complete the **Pharmacy Enrollment Form** and submit it to the TURALIO REMS.
- I agree to train all relevant staff involved in dispensing TURALIO using the **Program Overview**.

Before dispensing I will ensure that all pharmacy staff must:

- Obtain authorization to dispense each prescription by contacting the TURALIO REMS to verify the prescriber is certified, and the patient is enrolled and authorized to receive TURALIO.
- Dispense no more than a 30 days supply for each of the first 3 months of treatment.

On behalf of the pharmacy, we will comply with the following TURALIO REMS requirements:

- Report adverse events of serious and potentially fatal liver injury by submitting the **Liver Adverse Event Reporting Form**.
- Not distribute, transfer, loan or sell TURALIO, except to certified dispensers.
- Maintain records documenting staff's completion of training.
- Maintain records that all TURALIO REMS processes and procedures are in place and being followed.
- Maintain and submit dispensing information for all patients.
- Comply with audits carried out by Daiichi Sankyo, Inc. or third party acting on behalf of Daiichi Sankyo, Inc. to ensure that all processes and procedures are in place and are being followed.

Authorized Representative: Please PRINT your name and phone number here.

*Name: _____		*Phone Number: _____
Last First		
*Authorized Representative Signature:	*Date:	



Authorized Representative Information Note: Fields marked with an * are REQUIRED.

*First Name:	*Last Name:	Middle Initial:
*Title/Position:		
*Telephone Number:	*Fax Number:	
*E-mail:		
*Preferred Method of Communication (please select one): ☐ Fax ☐ E-mail ☐ Phone		

Pharmacy Information

Pharmacy Name:		
*Pharmacy Street Address:		
*City:	*State:	*ZIP Code:
*Pharmacy Phone Number:	*Pharmacy Fax Number:	
*Pharmacy National Provider Identifier (NPI) #:		
☐ If you are certifying more than one pharmacy location, check this box and provide the information on the following page for each site. Use as many forms as necessary.		
By completing and submitting this form as directed above and receiving certification confirmation, your pharmacy will be certified in the TURALIO REMS. You will receive confirmation of your certification via e-mail.		

Authorized Representative: Please PRINT your name and phone number here.

*Name: _____	*Phone Number: _____
Last	First



Phone: 1-833-TURALIO

www.TURALIOREMS.com

Fax: 1-833-TRL-REMS



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CERTIFYING MULTIPLE LOCATIONS

If you are certifying more than one pharmacy location, the following information will need to be provided for each site. Use additional forms as necessary.

Pharmacy Information **Note: Fields marked with an * are REQUIRED.**

Pharmacy Name:

*Pharmacy Address:

*City:

*State:

*ZIP Code:

*Pharmacy Phone Number: Area Code/Telephone Number

*Pharmacy Fax Number:

*Pharmacy National Provider Identifier (NPI) #:

Pharmacy Name:

*Pharmacy Address:

*City:

*State:

*ZIP Code:

*Pharmacy Phone Number: Area Code/Telephone Number

*Pharmacy Fax Number:

*Pharmacy National Provider Identifier (NPI) #:

Authorized Representative: Please PRINT your name and phone number here.

*Name: _____ *Phone Number: _____
Last First



Phone: 1-833-TURALIO

www.TURALIOREMS.com

Fax: 1-833-TRL-REMS



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TURALIO™ (pexidartinib)
Risk Evaluation and Mitigation Strategy
(REMS)

PROGRAM OVERVIEW



If you have any questions regarding the REMS, please visit www.TURALIOREMS.com or call 1-833-TURALIO (1-833-887-2546).

Please see Prescribing Information for complete safety profile of TURALIO.

What is TURALIO™?

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.

Warning: Hepatotoxicity

- **TURALIO can cause serious and potentially fatal liver injury.**
- **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.**

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

What is the TURALIO REMS?

This Risk Evaluation and Mitigation Strategy (REMS), is a safety program, required by the Food and Drug Administration (FDA), to ensure the potential benefits of TURALIO outweigh its risks.

TURALIO is available only through the TURALIO REMS, a restricted distribution program.

What do Healthcare Providers Need to Do Before Prescribing TURALIO?

Prescribers of TURALIO must become certified to prescribe. To become certified, prescribers must complete the following steps:

Step 1:	Review the TURALIO Prescribing Information
Step 2:	Review the Program Overview (this document) and the Prescriber Training
Step 3:	Complete and submit the Prescriber Knowledge Assessment to the TURALIO REMS
Step 4:	Complete and submit the Prescriber Enrollment Form to the TURALIO REMS

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

Prior to initiating treatment:

- counsel patients on 1) the risk of serious and potentially fatal liver injury, 2) liver test monitoring prior to and during treatment with TURALIO, and to 3) report any signs and/or symptoms of liver injury during therapy.
- enroll patient into a patient registry by completing and submitting the **Patient Enrollment Form** to the REMS.
- distribute and use the **Patient Guide** to educate and communicate these messages.
- assess the patient by obtaining liver tests.

During treatment:

- monitor the patient's liver tests and modify the TURALIO dose per the **Prescribing Information**.
- complete and submit the **Patient Status Form** to the REMS
 - monthly for the first 3 months of TURALIO treatment,
 - then every 3 months until one year of treatment,
 - then every 6 months thereafter.

Prescriptions should be limited to a 30 days' supply for each of the first 3 months of treatment.

Please see Prescribing Information for complete safety profile of TURALIO.

Adverse Event Reporting:

Prescribers should always report all adverse events including those of serious and potentially fatal liver injury 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. **Report liver adverse events using the *Liver Adverse Event Reporting Form*.**

What do Pharmacists Need to Do Before Dispensing TURALIO?

TURALIO may only be dispensed by pharmacies that have become certified to dispense. TURALIO will not be available to all pharmacies. To become certified, the pharmacy must designate an Authorized Representative to carry out the certification process and oversee implementation and compliance with the REMS on behalf of the pharmacy.

For a pharmacy to become certified, the Authorized Representative must complete the following steps:

Step 1:	Review the Program Overview (this document)
Step 2:	Complete and submit the Pharmacy Enrollment to the TURALIO REMS

By completing the Pharmacy Enrollment Form, the Authorized Representative agrees that:

- I have reviewed the **Program Overview**.
- I must complete the **Pharmacy Enrollment Form** and submit it to the TURALIO REMS.
- I agree to train all relevant staff involved in dispensing TURALIO using the **Program Overview**.

Before dispensing I will ensure that all pharmacy staff must:

- Obtain authorization to dispense each prescription by contacting the TURALIO REMS to verify the prescriber is certified, and the patient is enrolled and authorized to receive TURALIO.
- Dispense no more than a 30 days supply for each of the first 3 months of treatment.

On behalf of the pharmacy, we will comply with the following TURALIO REMS requirements:

- **Report adverse events of serious and potentially fatal liver injury by submitting the Liver Adverse Event Reporting Form.**
- Not distribute, transfer, loan or sell TURALIO, except to certified dispensers.
- Maintain records documenting staff's completion of training.
- Maintain records that all TURALIO REMS processes and procedures are in place and being followed.
- Maintain and submit dispensing information for all patients.
- Comply with audits carried out by Daiichi Sankyo, Inc. or third party acting on behalf of Daiichi Sankyo, Inc. to ensure that all processes and procedures are in place and are being followed.

If you have any questions about how to obtain TURALIO, call 1-833-TURALIO (1-833-887-2546).



TURALIO REMS Resources

For more information about the TURALIO REMS, visit www.TURALIOREMS.com or call the TURALIO REMS at 1-833-TURALIO (1-833-887-2546).

The below resources are available for download at www.TURALIOREMS.com.

PRESCRIBER	• Prescribing Information • Letter for Healthcare Providers and Letter for Professional Societies • Program Overview • Prescriber Training • Prescriber Knowledge Assessment • Prescriber Enrollment Form • Patient Enrollment Form • Patient Status Form • Liver Adverse Event Reporting Form
PHARMACY	• Program Overview • Pharmacy Enrollment Form • Liver Adverse Event Reporting Form
PATIENT	• Medication Guide • Patient Guide

Please see Prescribing Information for complete safety profile of TURALIO.



v2.0_30Jul2019

TURALIO™ (pexidartinib)
Risk Evaluation and Mitigation Strategy (REMS)

Prescriber Training



Welcome to the TURALIO™ REMS Prescriber Training

To prescribe TURALIO, you must become certified in the TURALIO REMS, which includes reviewing this training.

After reviewing this training, you must complete and submit a *Prescriber Knowledge Assessment* and a *Prescriber Enrollment Form* before you can prescribe TURALIO. You can complete these via fax (1-833-TRL-REMS), email (Enroll@TURALIOREMS.com), or online at www.TURALIOREMS.com.

For more information or to obtain any REMS materials visit www.TURALIOREMS.com

TURALIO™ (pexidartinib)
Risk Evaluation and Mitigation Strategy (REMS)

TURALIO Overview

What is TURALIO?

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.

Risk of Liver Injury

It is important to be aware of the risk of serious and potentially fatal liver injury associated with TURALIO (see *Prescribing Information for full details*).

- Hepatotoxicity with ductopenia and cholestasis has occurred in patients treated with TURALIO.
 - Across 768 patients who received TURALIO in clinical trials, there were two irreversible cases of cholestatic liver injury.
 - One patient died with advanced cancer and ongoing liver toxicity and one patient required a liver transplant.
 - The mechanism of cholestatic hepatotoxicity is unknown and its occurrence cannot be predicted. It is unknown whether liver injury occurs in the absence of increased transaminases.

TURALIO™ (pexidartinib)
Risk Evaluation and Mitigation Strategy (REMS)

TURALIO REMS Overview

What is the TURALIO REMS?

The TURALIO REMS (Risk Evaluation and Mitigation Strategy) is a safety program that manages the serious risks of TURALIO. The TURALIO REMS is required by the Food and Drug Administration (FDA) because of the serious, and potentially fatal liver injury.

- Only prescribers and pharmacies certified by the TURALIO REMS can prescribe and dispense TURALIO to patients.
- Patients must be enrolled in the TURALIO REMS patient registry and follow all the safety rules in the REMS to receive TURALIO.

What Do I Need to Do Before Prescribing TURALIO?

To prescribe TURALIO, you must become certified in the TURALIO REMS

Complete the following 4 steps to become certified:

1	Review the TURALIO Prescribing Information
2	Review the <i>Program Overview</i> and the <i>Prescriber Training</i> (this document)
3	Complete and submit the <i>Prescriber Knowledge Assessment</i> to the TURALIO REMS
4	Complete and submit the <i>Prescriber Enrollment Form</i> to the TURALIO REMS

What Do I Need to Do Prior to Initiating TURALIO?

To receive TURALIO, patients must be counseled and enrolled in the TURALIO REMS

Prior to initiating treatment, counsel patients on:

1	The risk of serious and potentially fatal liver injury
2	Liver test monitoring prior to and during treatment with TURALIO
3	Immediately reporting any signs and/or symptoms of liver injury during therapy

What Do I Need to Do Prior to Initiating TURALIO?

Prior to initiating treatment:

- Enroll the patient into the TURALIO REMS and patient registry by completing and submitting the *Patient Enrollment Form* to the REMS
- Provide the *Patient Guide* to educate and communicate these messages with each new or refill TURALIO prescription
- Assess the patient by obtaining liver tests

Prescriptions should be limited to a 30 days' supply
for each of the first 3 months of treatment

How Will My Patient Get TURALIO?

TURALIO will only be dispensed by certified pharmacies.

Enrolled patients will be contacted by a certified pharmacy to set up shipment of TURALIO.

Liver Monitoring During Treatment

Monitor aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (TBIL), direct bilirubin (DBIL), alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT).

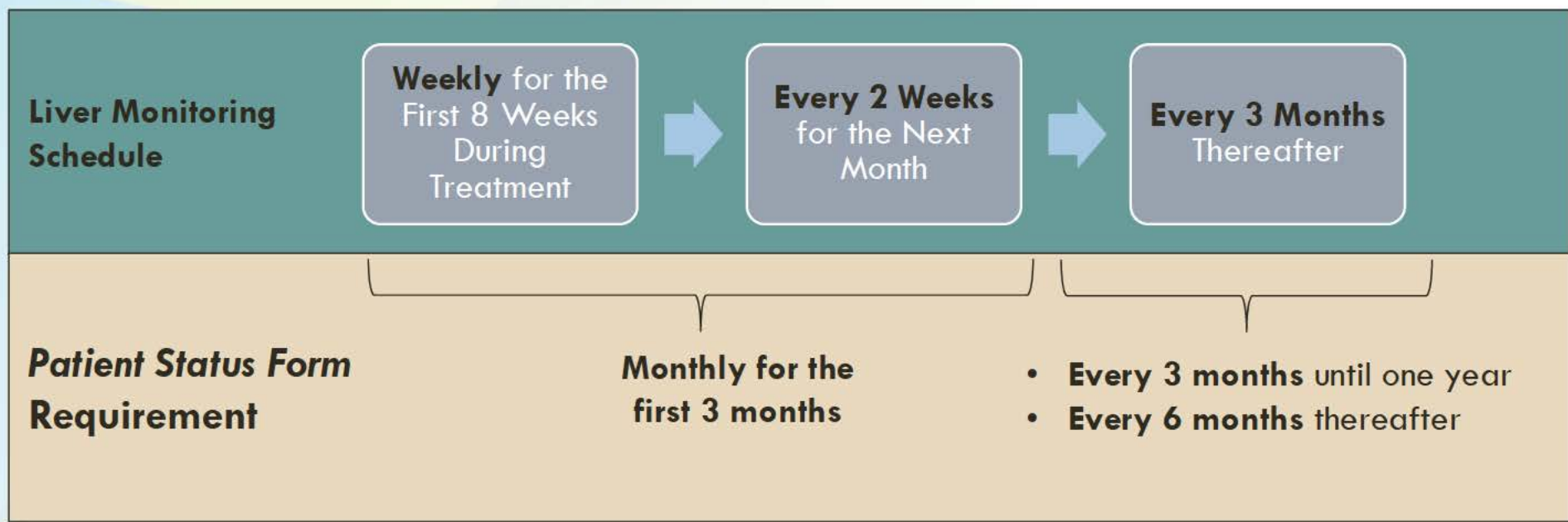
Liver Monitoring Schedule*



*More frequent monitoring is required for severe liver adverse reactions or TURALIO re-challenge.

Patient Status Form

During treatment, prescribers must complete and submit a *Patient Status Form* to the REMS



Liver Adverse Event Reporting Form

During treatment, use the *Liver Adverse Event Reporting Form* to report adverse events or laboratory abnormalities suggestive of serious and potentially fatal liver injury

Adverse events or laboratory abnormalities suggestive of serious and potentially fatal liver injury are:

- ALT or AST $> 3 \times$ ULN and TBIL $> 2 \times$ ULN
- ALT or AST $> 10 \times$ ULN with or without TBIL elevation
- TBIL $> 2 \times$ ULN without changes in ALT or AST
- Liver Transplantation
- Death

Dose Reductions For Adverse Reactions

To manage adverse reactions, interruption of treatment, dose reduction, or dose discontinuation may be needed.

Adverse Reactions	Severity	Required Modification
Increased ALT/AST	> 3-5 x ULN	- Withhold and monitor liver tests <u>weekly</u>. - If AST and ALT are less than or equal to 3 times ULN within 4 weeks, resume at reduced dose. - If AST or ALT is <u>not</u> less than or equal to 3 times ULN in 4 weeks, permanently discontinue TURALIO.
	> 5-10 x ULN	- Withhold and monitor liver tests <u>twice weekly</u>. - If AST and ALT are less than or equal to 3 times ULN within 4 weeks, resume at reduced dose. - If AST or ALT is <u>not</u> less than or equal to 3 times ULN in 4 weeks, permanently discontinue TURALIO.
	> 10 x ULN	- Permanently discontinue TURALIO. - Monitor liver tests <u>twice weekly</u> until AST or ALT is less than or equal to 5 times ULN, then <u>weekly</u> until less than or equal to 3 times ULN.

ALT = alanine aminotransferase; AST = aspartate aminotransferase; ULN = upper limit of normal

Dose reductions should be in increments of 200 mg (1 capsule)

Dose Reductions For Adverse Reactions Continued

To manage adverse reactions, interruption of treatment, dose reduction, or dose discontinuation may be needed.

Adverse Reactions	Severity	Required Modification
Increased ALP ¹ and GGT	ALP > 2 x ULN with GGT > 2 x ULN	Permanently discontinue TURALIO. Monitor liver tests <u>twice weekly</u> until ALP is less than or equal to 5 times ULN, then <u>weekly</u> until less than or equal to 2 times ULN.
Increased Bilirubin	TBIL > ULN to < 2 x ULN or DBIL > ULN and < 1.5 x ULN	- Withhold and monitor liver tests <u>twice weekly</u>. - If an alternate cause for increased bilirubin is confirmed and bilirubin is less than ULN within 4 weeks, resume at reduced dose. - If bilirubin is <u>not</u> less than ULN in 4 weeks, permanently discontinue TURALIO.
	TBIL ≥ to 2 x ULN or DBIL > 1.5 x ULN	- Permanently discontinue TURALIO. - Monitor liver tests <u>twice weekly</u> until bilirubin is less than or equal to ULN.

ALP = alkaline phosphatase; GGT = gamma-glutamyl transferase; TBIL = total bilirubin; DBIL = direct bilirubin; ULN = upper limit of normal

¹ Confirm ALP elevations as liver isozyme fraction.

Dose reductions should be in increments of 200 mg (1 capsule)

Dose Reductions For Adverse Reactions Continued

To manage adverse reactions, interruption of treatment, dose reduction, or dose discontinuation may be needed.

Adverse Reactions	Severity	Required Modification
Adverse Reactions or Other Laboratory Abnormalities	Severe or intolerable	• Withhold until improvement or resolution. • Resume at a reduced dose upon improvement or resolution.

Dose reductions should be in increments of 200 mg (1 capsule)

Dose Reductions

To manage adverse reactions, interruption of treatment, dose reduction, or dose discontinuation may be needed.

Dose Reductions

Dose Reduction	Total Daily Dose	Administration of Total Daily Dose
First	600 mg	200 mg in the morning and 400 mg in the evening
Second	400 mg	200 mg twice daily

Permanently discontinue TURALIO in patients who are unable to tolerate 200 mg orally twice daily.

Dose reductions should be in increments of 200 mg (1 capsule)



This concludes the Prescriber Training.

Prescriber Information Note: Fields marked with an * are REQUIRED.		
*First Name:	*Last Name:	Middle Initial:
*National Provider Identifier (NPI) #:		
*Phone Number:	*Fax Number:	
*E-mail:		

To become a certified prescriber in the TURALIO REMS, you have 3 attempts to answer all questions correctly.

1. Review the TURALIO **Prescribing Information**, **Prescriber Training**, and **Program Overview**.
2. Complete this **Prescriber Knowledge Assessment** and the **Prescriber Enrollment Form**.
3. Fax both pages of this form containing your responses to the 9 Prescriber Knowledge Assessment questions and the Prescriber Enrollment Form to 1-833-TRL-REMS (833-875-7367) or email them to Enroll@TURALIOREMS.com.

You will be notified via email by the TURALIO REMS on the status of your certification within 2 business days of submitting. When contacted, you will receive either:

- Confirmation of your certification in the TURALIO REMS
- OR
- Instructions on how to retake the **Prescriber Knowledge Assessment**.



QUESTIONS 1-9

1. 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.
 - ☐ True
 - ☐ False
2. TURALIO is contraindicated in patients with hepatic impairment.
 - ☐ True
 - ☐ False
3. To prescribe TURALIO, I must enroll each patient in the TURALIO REMS by completing a Patient Enrollment Form with the patient and submitting it to the TURALIO REMS.
 - ☐ True
 - ☐ False
4. Before treating each patient with TURALIO, I must (check one):
 - ☐ Become certified in the TURALIO REMS
 - ☐ Counsel the patient regarding the risk of serious and potentially fatal liver injury associated with TURALIO
 - ☐ Obtain and review baseline liver tests
 - ☐ All of the above
5. One of the primary counseling messages I must tell my patients before prescribing TURALIO is (check one):
 - ☐ Do not take TURALIO if you have vision issues
 - ☐ Patients with renal impairment should not start TURALIO at a reduced dose
 - ☐ There is a risk of liver injury associated with TURALIO and liver monitoring is required prior to treatment initiation and periodically while taking TURALIO
 - ☐ None of the above
6. I am required to educate my patients on the signs and symptoms of liver injury and the need to notify me should they experience them.
 - ☐ True
 - ☐ False
7. If any dose modifications are required, they must be done in increments of 200 mg.
 - ☐ True
 - ☐ False
8. After treatment initiation, I need to monitor liver tests weekly for the first 8 weeks of treatment, every 2 weeks for the next month, and every 3 months thereafter.
 - ☐ True
 - ☐ False
9. I must complete a Patient Status Form for each patient taking TURALIO and submit it to the TURALIO REMS:
 - ☐ Every month during treatment
 - ☐ Weekly for 8 weeks of treatment, every 2 weeks for the next month, and every 3 months thereafter
 - ☐ Every month for the first 3 months of treatment, month 6, month 9, and month 12 of treatment, and every 6 months thereafter
 - ☐ Every month for the first 6 months of treatment and every 6 months thereafter
 - ☐ None of the above



Daiichi-Sankyo

Phone: 1-833-TURALIO

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Fax: 1-833-TRL-REMS



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ANSWER KEY

1. 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.
☒ **True**
2. TURALIO is contraindicated in patients with hepatic impairment.
☒ **False**
3. To prescribe TURALIO, I must enroll each patient in the TURALIO REMS by completing a Patient Enrollment Form with the patient and submitting it to the TURALIO REMS.
☒ **True**
4. Before treating each patient with TURALIO, I must (check one):
☒ **All of the Above**
5. One of the primary counseling messages I must tell my patients before prescribing TURALIO is (check one):
☒ **There is a risk of liver injury associated with TURALIO and liver monitoring is required prior to treatment initiation and periodically while taking TURALIO**
6. I am required to educate my patients on the signs and symptoms of liver injury and the need to notify me should they experience them.
☒ **True**
7. If any dose modifications are required, they must be done in increments of 200 mg.
☒ **True**
8. After treatment initiation, monitor liver tests weekly for the first 8 weeks of treatment, every 2 weeks for the next month, and every 3 months thereafter.
☒ **True**
9. I must complete a Patient Status Form for each patient taking TURALIO and submit it to the TURALIO REMS:
☒ **Every month for the first 3 months of treatment, month 6, month 9, and month 12 of treatment, and every 6 months thereafter**



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Reference ID: 4471832

TURALIO REMS



PATIENT GUIDE

What is TURALIO™?

TURALIO™ is a prescription medicine used to treat certain adults who have tenosynovial giant cell tumor (TGCT) that is not likely to improve with surgery. TGCT is also known as giant cell tumor of the tendon sheath (GCT-TS) or pigmented villonodular synovitis (PVNS).

What are the serious risks of TURALIO?

TURALIO can cause serious liver problems, which may be severe and can lead to death.

Stop taking TURALIO and call your healthcare provider right away if you develop:

- yellowing of your skin and whites of your eyes
- dark urine

Tell your healthcare provider right away if you experience:

- lack or loss of appetite
- right upper stomach-area (abdomen) pain or tenderness
- feeling overly tired
- nausea
- vomiting
- fever
- rash
- itching

Liver problems can occur at any time after starting treatment with TURALIO.

These are not all the side effects of TURALIO.

See the Medication Guide that comes with your prescription for more information.

What do I need to do before and while taking TURALIO?

To receive TURALIO, your healthcare provider will provide you with the **Patient Guide** (this document) and discuss the risk of serious liver problems, frequency of blood tests, and symptoms of liver problems with you.

You must enroll in the TURALIO REMS and Patient Registry by completing the **Patient Enrollment Form** with your healthcare provider. The registry collects information so that your health and any liver injury can be followed over time.

It is important that you have a blood test to check your liver health before you start and while you are taking TURALIO.

Your healthcare provider will do blood tests to check for liver problems:

- before starting treatment with TURALIO
- every week for the first 8 weeks during treatment,
- every 2 weeks for the next month,
- then, every 3 months after that

Please refer to the Medication Guide for more information about TURALIO.

If you develop liver problems during treatment with TURALIO, your healthcare provider may do blood tests more often to monitor you for serious liver problems.

If you do not have these blood tests, you may no longer be able to receive TURALIO.

You or your family members should tell your healthcare provider right away if you have any symptoms of liver problems while taking TURALIO, even if they begin later in treatment. Liver problems can occur at any time after starting treatment with TURALIO.

What is a Risk Evaluation and Mitigation Strategy (REMS)?

A REMS is a safety program that the US Food and Drug Administration (FDA) can require for certain medicines with serious safety concerns. Drug companies and prescribers must take extra steps to make sure the benefits of using the drug are more than the risks.

Why does TURALIO Have a REMS?

TURALIO has a REMS because it can cause serious liver problems, which may be severe and can lead to death. The TURALIO REMS was set up to make sure healthcare providers, pharmacists and patients are aware of the serious risks. You must have blood tests to test for liver problems as part of the TURALIO REMS.

TURALIO is available only through healthcare providers and pharmacies that participate in the TURALIO REMS.

How will I get my TURALIO medicine?

Only certain pharmacies can fill your TURALIO prescription.

The pharmacies that are part of the TURALIO REMS will contact you to fill your prescription for TURALIO and ship it to your home.

If you have questions about the TURALIO REMS, you can call the TURALIO REMS.

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

Hours of Operation: 8:00 AM – 8:00 PM Eastern

www.TURALIOREMS.com

IMPORTANT SAFETY INFORMATION:

If you have any questions about your health or medicines, talk to your healthcare provider.

To report side effects,
contact the REMS at 1-833-TURALIO
(1-833-887-2546),
Daiichi Sankyo, Inc. at
1-877-4DS-PROD
(1-877-437-7763), or FDA at
1-800-FDA-1088 or
www.fda.gov/medwatch.



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Assess the patient by obtaining liver tests as stated in the Prescribing Information. Please order these tests for each of your patients taking TURALIO, and use this form to confirm that the testing has been done and reviewed.

You can complete this form online at www.TURALIOREMS.com, fax it to the TURALIO REMS Program Call Center at 1-833-TRL-REMS or E-mail it to Enroll@TURALIOREMS.com.

This form must be completed and submitted for each patient:

- Every month for the first three months of treatment
- Month 6, 9 and 12 of treatment
- Every 6 months thereafter

Note: The completion of the laboratory tests (see frequency below) and the submission of the Patient Status Form (per the schedule shown above) are done at different intervals.

Patient Information		
First Name:	Last Name:	Birthdate: (MM/DD/YYYY):
Address has not changed: ☐ or update below: Address Line 1:		
Address Line 2:		
City:	State:	ZIP Code:
Prescriber Information		
First Name:	Last Name:	NPI #:
Practice/Facility Name:		
Address has not changed: ☐ or update below: Address Line 1:		
Address Line 2:		
City:	State:	ZIP Code:
Phone:		
Hepatic Monitoring Information		
Obtain liver tests as follows: • Weekly for the first 8 weeks of treatment • Every 2 weeks for the next month • Every 3 months thereafter		
1. Is the patient still under your care? ☐ Yes ☐ No		
2. Is the patient alive? ☐ Yes ☐ No		
3. Are you monitoring the patient as recommended in the Prescribing Information? ☐ Yes ☐ No		
4. Is the patient continuing TURALIO? ☐ Yes ☐ No Withheld, reason: _____		
Discontinued, reason: _____		



Since starting TURALIO or since submission of the last Patient Status Form, whichever is later, has the patient experienced any of the following:

Laboratory Tests

5. ALT or AST >3x ULN and TBIL >2x ULN? ☐ Yes ☐ No
6. ALT or AST > 10x ULN with or without TBIL elevation? ☐ Yes ☐ No
7. TBIL >2x ULN without changes in ALT or AST? ☐ Yes ☐ No

Procedures/Imaging/Referrals

8. Liver ultrasound: ☐ Yes ☐ No
9. CT or MRI/MRA/MRV of the liver: ☐ Yes ☐ No
10. Liver biopsy: ☐ Yes ☐ No
11. Hepatology evaluation/referral: ☐ Yes ☐ No
12. Referral for liver transplantation: ☐ Yes ☐ No
13. Endoscopic retrograde cholangiopancreatography (ERCP): ☐ Yes ☐ No
14. Hepatobiliary iminodiacetic acid (HIDA) scan: ☐ Yes ☐ No
15. Hospitalization for management of liver toxicity: ☐ Yes ☐ No
16. Other procedure/referral: ☐ Yes ☐ No Describe: _____

Medications prescribed to treat liver injury:

17. Were steroids used? ☐ Yes ☐ No
18. Was ursodeoxycholic acid? ☐ Yes ☐ No
19. Other? ☐ Yes ☐ No Describe: _____

If the answer to any of the questions on this page is Yes, submit a Liver Adverse Event Reporting Form to the REMS.

Date Submitted: _____

Other Medications: Complete if Yes to any of the above questions

20. Concomitant prescription medications while on TURALIO treatment: _____
21. Concomitant non-prescription medications or herbal and dietary supplements while on TURALIO treatment: _____

Prescriber Signature:

Prescriber Signature: _____

Date (MM/DD/YYYY): _____

Prescribers should always report all adverse events by contacting the REMS at 1-833-TURALIO, Daiichi Sankyo, Inc. at 1-877-4DS-PROD (1-877-437-7763) or FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.



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Adverse events or laboratory abnormalities suggestive of serious and potentially fatal liver injury must be reported to the REMS.

Adverse events or laboratory abnormalities suggestive of serious and potentially fatal liver injury are:

- ALT or AST >3xULN and TBIL >2x ULN
- ALT or AST >10xULN with or without TBIL elevation
- TBIL >2xULN without changes in ALT or AST
- Liver Transplantation
- Death

You can complete this form online at www.TURALIOREMS.com, or fax it to the TURALIO REMS Call Center at 1-833-TRL-REMS or call the TURALIO REMS Call Center at 1-833-TURALIO (1-833-887-2546) to provide the information.

Patient Information		
First Name:	Last Name:	Birthdate (MM/DD/YYYY):
Address has not changed: ☐ or update below:		
Address Line 1:		
Address Line 2:		
City:	State:	ZIP Code:
Prescriber Information		
First Name:	Last Name:	NPI #:
Practice/Facility Name:		
Address has not changed: ☐ or update below:		
Address Line 1:		
Address Line 2:		
City:	State:	ZIP Code:
Phone		



Liver Adverse Event Reporting

1. What event triggered this report?

2. Report the following labs if they were obtained. If labs were not obtained, indicate "not applicable."

Laboratory Test	Maximum Value and Units	Reference Range Min and Max and Units	Resolved Y/N
AST or SGOT			
ALT or SGPT			
Alkaline Phosphatase			
GGT			
Total Bilirubin			
Direct Bilirubin			
PT/INR			
Albumin (minimum)			
Viral Hepatitis Status	Tests performed, date tested, and results:		



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Patient Hepatic Monitoring Information	
3. Was a hepatology referral obtained? ☐ Yes ☐ No	
4. Were any of the following procedures performed?	
Procedure ¹	Yes or No
Liver Ultrasound	
Other Imaging of the Liver	
Liver Biopsy	
ERCP	
Hospitalization	
Liver Dialysis	
Other	
¹ If the patient had imaging or the procedure more than once, please provide information about each individual procedure or imaging	
5. Medications prescribed to treat event: (circle) Yes or No	
6. What is the current status of the liver adverse event (check one)?	
☐ Resolved, date resolved: _____ ☐ Ongoing, date of last assessment: _____ ☐ Resolved with sequelae, describe: _____ ☐ Liver transplant, date: _____ ☐ Patient death, date: _____	
Signature	
Printed Name:	
Signature:	

Prescribers should always report all adverse events by contacting the REMS at 1-833-TURALIO, Daiichi Sankyo, Inc. at 1-877-4DS-PROD (1-877-437-7763) or FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.



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Reference ID: 4471832

FDA REQUIRED REMS SAFETY INFORMATION

[Month/Day/Year]

Subject: • Risk of serious and potentially fatal liver injury 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 risk of serious and potentially fatal liver injury associated with TURALIO™ (pexidartinib) and the TURALIO REMS. 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. 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.
- Monitor liver tests, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (TBIL), direct bilirubin (DBIL), alkaline phosphatase (ALP), and gamma glutamyltransferase (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.

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.
- 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.



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Turalio
pexidartinib capsules

Adverse Event Reporting

Report any adverse events including those of serious and potentially fatal liver injury 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



Phone: 1-833-TURALIO

www.TURALIOREMS.com

Fax: 1-833-TRL-REMS

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FDA REQUIRED REMS SAFETY INFORMATION

[Month/Day/Year]

Subject:

- Risk of serious and potentially fatal liver injury associated with TURALIO™ (pexidartinib)
- FDA required TURALIO REMS with restricted distribution

Dear [Professional Society]:

We encourage you to share the following information with your members.

The purpose of this letter is to inform you about the risk of serious and potentially fatal liver injury associated with TURALIO™ (pexidartinib) and the TURALIO REMS. 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. 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.
- Monitor liver tests, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (TBIL), direct bilirubin (DBIL), alkaline phosphatase (ALP), and gamma glutamyltransferase (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.

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.
- Prescribers must counsel the patient using the Patient Guide prior to treatment and complete the Patient Enrollment Form with the patient.
- 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.



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Fax: 1-833-TRL-REMS

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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



Phone: 1-833-TURALIO

www.TURALIOREMS.com

Fax: 1-833-TRL-REMS

v2.0_30Jul2019





Welcome to the TURALIO™ REMS

(Risk Evaluation and Mitigation Strategy)

[Prescribing Information](#) [Medication Guide](#)

The TURALIO REMS (Risk Evaluation and Mitigation Strategy) is a safety program that manages the risks of **serious and potentially fatal liver injury** from TURALIO. The TURALIO REMS is required by the Food and Drug Administration (FDA) to ensure the potential benefits of TURALIO outweigh its risks.

Prescribers

Prescribers must become certified in TURALIO REMS to prescribe TURALIO.

[Learn about Prescriber Certification.](#)

[LEARN MORE](#)

Pharmacies

Pharmacies must become certified in TURALIO REMS to dispense TURALIO.

[Learn about Pharmacy Certification.](#)

[LEARN MORE](#)

Patients

Patients who are prescribed TURALIO must be enrolled in TURALIO REMS.

[Learn about Patient Enrollment.](#)

[LEARN MORE](#)

If you have questions about TURALIO REMS or need help with certification or enrollment, call
1-833-TURALIO (1-833-887-2546).
Monday-Friday, 8:00am – 8:00pm ET

To learn more about the serious risks associated with TURALIO, please refer to the [Prescribing Information](#) including Boxed Warning and the [Medication Guide](#).

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.

To report adverse events of TURALIO, please contact the REMS at 1-833-TURALIO (1-833-887-2546), Daiichi Sankyo, Inc. at 1-877-4DS-PROD (1-877-437-7763) or FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.

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Welcome to the TURALIO™ REMS

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[Prescribing Information](#) [Medication Guide](#)

Prescriber Overview

TURALIO is only available through the TURALIO REMS. In order for a healthcare provider to prescribe TURALIO, they must become certified.

[Complete Prescriber Training and Certification Online](#)

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

- step 1 Read the TURALIO [Prescribing Information](#)
- step 2 Read the [Program Overview](#) and the [Prescriber Training](#)
- step 3 Complete and submit the [Prescriber Knowledge Assessment](#) and the [Prescriber Enrollment Form](#) to the TURALIO REMS
 - 3a. Via FAX (1-833-TRL-REMS)
 - 3b. Via email at Enroll@TURALIOREMS.com

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

Materials for Healthcare Providers

[Letter for Healthcare Provider](#)[Letter for Professional Societies](#)[Program Overview](#)[Prescriber Training](#)[Prescriber Knowledge Assessment](#)[Prescriber Enrollment Form](#)[Patient Enrollment Form](#)[Patient Status Form](#)[Liver Adverse Event Reporting Form](#)

Materials for Patients

[Medication Guide](#)[Patient Guide](#)

To report adverse events of TURALIO, please contact the REMS at 1-833-TURALIO (1-833-887-2546), Daiichi Sankyo, Inc. at 1-877-4DS-PROD (1-877-437-7763) or FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.

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Welcome to the TURALIO™ REMS

(Risk Evaluation and Mitigation Strategy)

Pharmacies

TURALIO is only available through the TURALIO REMS by certified pharmacies.

To become certified to dispense TURALIO, pharmacies must complete the following steps:

- step 1** Designate Authorized Representative to carry out the certification process and oversee implementation and compliance with the REMS
- step 2** Authorized Representative must review the **Program Overview**
- step 3** Authorized Representative must attest that the pharmacy will follow REMS requirements by completing and submitting a **Pharmacy Enrollment Form** to the TURALIO REMS
 - 3a.** By fax at 1-833-TRL-REMS (1-833-875-7367)
 - 3b.** By email at Enroll@TURALIOREMS.com
- step 4** Authorized Representatives will be notified when their pharmacy's certification in the TURALIO REMS is complete and they can dispense TURALIO.
- step 5** Prior to dispensing TURALIO, the Authorized Representative must train all relevant pharmacy staff on TURALIO using the **Program Overview**.
- step 6** Before Dispensing:
 - 6a.** Obtain authorization to dispense each prescription by contacting the REMS to verify the prescriber is certified and the patient is enrolled in the REMS
 - 6b.** Dispense no more than a 30 days supply for the first 3 months of treatment

Materials for Pharmacies

[Program Overview](#)[Pharmacy Enrollment Form](#)[Liver Adverse Event Reporting Form](#)

To report adverse events of TURALIO, please contact the REMS at 1-833-TURALIO (1-833-887-2546), Daiichi Sankyo, Inc. at 1-877-4DS-PROD (1-877-437-7763) or FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.

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Welcome to the TURALIO™ REMS

(Risk Evaluation and Mitigation Strategy)

Patients

Patients who are prescribed TURALIO must be enrolled in TURALIO REMS by your doctor.

Materials for Patients

[Medication Guide](#)[Patient Guide](#)

To report adverse events of TURALIO, please contact the REMS at 1-833-TURALIO (1-833-887-2546), Daiichi Sankyo, Inc. at 1-877-4DS-PROD (1-877-437-7763) or FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.

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Welcome to the TURALIO™ REMS

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Contact Us



Phone

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



Fax

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



Hours of Operation

Monday - Friday
8:00-8:00 PM Eastern

For more information on TURALIO, please read the [Medication Guide](#) and the [Patient Guide](#).

To report any adverse events, product quality complaints, medication errors, or pregnancies associated with the use of TURALIO, contact:

the REMS at 1-833-TURALIO (1-833-887-2546),
Daiichi Sankyo, Inc. at 1-877-4DS-PROD (1-877-437-7763) or
FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.

To report adverse events of TURALIO, please contact the REMS at 1-833-TURALIO (1-833-887-2546), Daiichi Sankyo, Inc. at 1-877-4DS-PROD (1-877-437-7763) or FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.

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Welcome to the TURALIO™ REMS

(Risk Evaluation and Mitigation Strategy)

Login

Login

Login is available to certified prescribers and other users authorized by the REMS Coordinating Center.

LOGIN

[Forgot Username](#)

OR

Don't have an online account?

Register

To create your web account for the TURALIO REMS, please enter your NPI Number and click "Continue".

Note: Online registration is required for Prescribers only.

* NPI Number

CONTINUE

To report adverse events of TURALIO, please contact the REMS at 1-833-TURALIO (1-833-887-2546), Daiichi Sankyo, Inc. at 1-877-4DS-PROD (1-877-437-7763) or FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.

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This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MARC R THEORET
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