Turalio®
pexidartinib
125 mg capsules

Prior authorization for **TURALIO® (pexidartinib)**

Considerations for prior authorization submissions to help ensure that your patients can start and stay on TURALIO

IMPORTANT NOTE: It is the healthcare provider's responsibility to determine the appropriate medical diagnosis, codes, and treatment and to submit valid and accurate claims for products and services rendered. Coding, coverage, and reimbursement may vary significantly by payer, plan, patient, and setting of care. Actual coverage and reimbursement decisions are made by individual payers following the receipt of claims. It is the responsibility of the provider to contact third-party payers for specific information on their coding, coverage, and payment policies. Information and materials provided by Daiichi Sankyo, Inc., are for the purposes of assisting healthcare providers, but the responsibility to determine coverage, reimbursement, and appropriate coding for a particular patient and/or procedure remains with the provider. Even if all information provided is valid and accurate, there is not a guarantee of coverage or reimbursement from payers for any product or service.

Indication and Important Safety Information

Indication and Usage

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.**
- **TURALIO is available only through a restricted program called the TURALIO Risk Evaluation and Mitigation Strategy (REMS) Program.**

Important Safety Information continues on pages 4-5.
Please see accompanying full Prescribing Information, including **Boxed WARNING**, and Medication Guide.

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Completing a prior authorization (PA) for TURALIO

Remember, PA request forms may vary by health insurance plan. The list below contains important considerations about TURALIO that may affect the PA process.

Key points to keep in mind when completing and submitting a PA for TURALIO

- **TURALIO has a REMS program** (please see www.turalioREMS.com and/or call 1-833-887-2546 for more information about the program).
- **TURALIO prescriptions require an appropriate ICD-10-CM code.** View possible codes on the following page.
- **Documentation of the patient's TGCT diagnosis** (eg, MRI report) may be required.
- **Prior surgeries and treatments for TGCT that the patient has received** (as well as duration of treatment and reason[s] for failure) may be requested.
- **Documentation of *why the patient's TGCT is not amenable to surgery*** may be required.

Visit www.DSIAccessCentral.com/HCP/TURALIO to download helpful information; examples include a sample letter of medical necessity and a sample letter of appeal.

Helping your patients access TURALIO

It is important to remember that the completion and submission of coverage- or reimbursement-related documentation is the responsibility of the patient and his or her healthcare provider. Daiichi Sankyo Access Central and its service providers (eg, Biologics) are committed to helping your patients achieve timely approval for TURALIO. Biologics is able to help you with:

- Verifying payer-specific PA requirements
- Offering information on initiating and completing the authorization process
- Tracking the PA request status
- Providing status updates to you and your patient throughout the process

Call Biologics at 1-800-850-4306 for assistance.

NDC for TURALIO

Strength	Packaging configuration	NDC
125 mg	Bottle of 120	65597-407-20

Abbreviations: ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; NDC, National Drug Code; TGCT, tenosynovial giant cell tumor.

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TURALIO prescriptions require an appropriate ICD-10-CM code

Possible ICD-10-CM codes for patients prescribed TURALIO

This table is provided for informational purposes only. Healthcare providers have the responsibility to assure claims and codes submitted are accurate, complete, and applicable. Coding and documentation are the responsibility of the provider, and the provider should confirm with each payer.

Code	Description
M12.2[a]	**Villonodular synovitis (pigmented)**
M12.20	Villonodular synovitis (pigmented), unspecified site
M12.28	Villonodular synovitis (pigmented), other specified site
M12.29	Villonodular synovitis (pigmented), multiple sites
M12.21[a]	**Villonodular synovitis (pigmented), shoulder**
M12.211	Villonodular synovitis (pigmented), right shoulder
M12.212	Villonodular synovitis (pigmented), left shoulder
M12.219	Villonodular synovitis (pigmented), unspecified shoulder
M12.22[a]	**Villonodular synovitis (pigmented), elbow**
M12.221	Villonodular synovitis (pigmented), right elbow
M12.222	Villonodular synovitis (pigmented), left elbow
M12.229	Villonodular synovitis (pigmented), unspecified elbow
M12.23[a]	**Villonodular synovitis (pigmented), wrist**
M12.231	Villonodular synovitis (pigmented), right wrist
M12.232	Villonodular synovitis (pigmented), left wrist
M12.239	Villonodular synovitis (pigmented), unspecified wrist
M12.24[a]	**Villonodular synovitis (pigmented), hand**
M12.241	Villonodular synovitis (pigmented), right hand
M12.242	Villonodular synovitis (pigmented), left hand
M12.249	Villonodular synovitis (pigmented), unspecified hand
M12.25[a]	**Villonodular synovitis (pigmented), hip**
M12.251	Villonodular synovitis (pigmented), right hip
M12.252	Villonodular synovitis (pigmented), left hip
M12.259	Villonodular synovitis (pigmented), unspecified hip

Code	Description
M12.26[a]	**Villonodular synovitis (pigmented), knee**
M12.261	Villonodular synovitis (pigmented), right knee
M12.262	Villonodular synovitis (pigmented), left knee
M12.269	Villonodular synovitis (pigmented), unspecified knee
M12.27[a]	**Villonodular synovitis (pigmented), ankle and foot**
M12.271	Villonodular synovitis (pigmented), right ankle and foot
M12.272	Villonodular synovitis (pigmented), left ankle and foot
M12.279	Villonodular synovitis (pigmented), unspecified ankle and foot
D21.1[a]	**Benign neoplasm of connective and other soft tissue of upper limb, including shoulder**
D21.10	Benign neoplasm of connective and other soft tissue of unspecified upper limb, including shoulder
D21.11	Benign neoplasm of connective and other soft tissue of right upper limb, including shoulder
D21.12	Benign neoplasm of connective and other soft tissue of left upper limb, including shoulder
D21.2[a]	**Benign neoplasm of connective and other soft tissue of lower limb, including hip**
D21.20	Benign neoplasm of connective and other soft tissue of unspecified lower limb, including hip
D21.21	Benign neoplasm of connective and other soft tissue of right lower limb, including hip
D21.22	Benign neoplasm of connective and other soft tissue of left lower limb, including hip
D21.9	**Benign neoplasm of connective and other soft tissue, unspecified**
D48.1	**Neoplasm of uncertain behavior of connective and other soft tissue**

[a]This is a nonbillable diagnosis code that indicates a subcategory. For reporting purposes, only codes with the full number of required characters are permissible.

Abbreviation: ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification.

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Indication and Usage

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WARNING: HEPATOTOXICITY

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- **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.**
- **TURALIO is available only through a restricted program called the TURALIO Risk Evaluation and Mitigation Strategy (REMS) Program.**

Contraindications

None.

Warnings and Precautions

Hepatotoxicity

TURALIO can cause serious and potentially fatal liver injury and is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS).

Hepatotoxicity with ductopenia and cholestasis 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 with advanced cancer and ongoing liver toxicity died 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.

In ENLIVEN, 3 of 61 (5%) patients who received TURALIO developed signs of serious liver injury, defined as ALT or 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 patients 1 to 7 months after discontinuing TURALIO.

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. Rechallenge with a reduced dose of TURALIO may result in a recurrence of increased serum transaminases, bilirubin, or ALP. Monitor liver tests weekly for the first month after rechallenge.

TURALIO REMS

TURALIO is available only through a restricted program under a REMS, because of the risk of hepatotoxicity.

Notable requirements of the TURALIO REMS Program 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 dispense only to patients who are authorized (enrolled in the REMS patient registry) to receive TURALIO.

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

Embryo-fetal toxicity

Based on animal studies and its mechanism of action, TURALIO may cause fetal harm when administered to pregnant women. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use an effective nonhormonal method of contraception, since 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.

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Important Safety Information *(cont'd)*

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). Consider referring patients to a dietician as deemed necessary.

Adverse Reactions

The safety of TURALIO was evaluated in ENLIVEN, in which patients received TURALIO without food at a dose of 400 mg in the morning and 600 mg in the evening orally for 2 weeks followed by 400 mg orally twice daily until disease progression or unacceptable toxicity.

Serious adverse reactions were reported in 13% of patients who received TURALIO. The most frequent serious adverse reactions (occurring in >1 patient) included abnormal liver tests (3.3%) and hepatotoxicity (3.3%).

Permanent discontinuation due to adverse reactions occurred in 13% of patients who received TURALIO. The most frequent adverse reactions (occurring in >1 patient) requiring permanent discontinuation included increased ALT (4.9%), increased AST (4.9%), and hepatotoxicity (3.3%).

Dose reductions or interruptions occurred in 38% of patients who received TURALIO. The most frequent adverse reactions (occurring in >1 patient) requiring a dosage reduction or interruption were increased ALT (13%), increased AST (13%), nausea (8%), increased ALP (7%), vomiting (4.9%), increased bilirubin (3.3%), increased GGT (3.3%), dizziness (3.3%), and abdominal pain (3.3%).

The most common adverse reactions for all grades (>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%).

Clinically relevant adverse reactions occurring in <10% of patients were blurred vision, photophobia, diplopia, reduced visual acuity, dry mouth, stomatitis, mouth ulceration, pyrexia, cholangitis, hepatotoxicity, liver disorder, cognitive disorders (memory impairment, amnesia, confusional state, disturbance in attention, attention deficit/hyperactivity disorder), alopecia, skin pigment changes (hypopigmentation, depigmentation, discoloration, hyperpigmentation), and photosensitivity reactions.

Drug Interactions

- Use with hepatotoxic products: TURALIO can cause hepatotoxicity. In patients with increased serum transaminases, total bilirubin, or direct bilirubin (>ULN) or active liver or biliary tract disease, avoid coadministration of TURALIO with other products known to cause hepatotoxicity.
- Moderate or strong CYP3A inhibitors: Concomitant use of a moderate or strong CYP3A inhibitor may increase pexidartinib concentrations. Reduce TURALIO dosage if concomitant use of moderate or strong CYP3A inhibitors cannot be avoided.
- Strong CYP3A inducers: Concomitant use of a strong CYP3A inducer decreases pexidartinib concentrations. Avoid concomitant use of strong CYP3A inducers.
- Uridine diphosphate glucuronosyltransferase (UGT) inhibitors: Concomitant use of a UGT inhibitor increases pexidartinib concentrations. Reduce TURALIO dosage if concomitant use of UGT inhibitors cannot be avoided.
- Acid-reducing agents: Concomitant use of a proton pump inhibitor (PPI) decreases pexidartinib concentrations. Avoid concomitant use of PPIs. Use histamine-2 receptor antagonists or antacids if needed.
- CYP3A substrates: TURALIO is a moderate CYP3A inducer. Concomitant use of TURALIO decreases concentrations of CYP3A substrates. Avoid coadministration of TURALIO with hormonal contraceptives and other CYP3A substrates where minimal concentration changes may lead to serious therapeutic failure. Increase the CYP3A substrate dosage in accordance with approved product labeling if concomitant use is unavoidable.

Important Safety Information *(cont'd)*

Use in Specific Populations

- **Pregnancy:** TURALIO may cause embryo-fetal harm when administered to pregnant women. Advise pregnant women of the potential risk to a fetus.
- **Lactation:** Because of the potential for serious adverse reactions in the breastfed child, advise women to not breastfeed during treatment with TURALIO and for at least 1 week after the final dose.
- **Females and males of reproductive potential:** 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, since TURALIO can render hormonal contraceptives ineffective, during treatment with TURALIO and for 1 month after the final dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TURALIO and for 1 week after the final dose.
- **Renal impairment:** Reduce the dose when administering TURALIO to patients with mild to severe renal impairment (CLcr 15 to 89 mL/min, estimated by Cockcroft-Gault [C-G] using actual body weight).
- **Hepatic impairment:** Reduce the dosage of TURALIO for patients with moderate hepatic impairment (total bilirubin greater than 1.5 and up to 3 times ULN, not due to Gilbert's syndrome, with any AST). TURALIO has not been studied in patients with severe hepatic impairment (total bilirubin greater than 3 to 10 times ULN and any AST)

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.

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