NuvationConnect™

Navigating access for patients

Key considerations to support your office when prescribing IBTROZI™ (taletrectinib).

This guide is for informational purposes only and is not intended to provide medical, legal, or reimbursement advice.

INDICATION

IBTROZI™ (taletrectinib) is indicated for the treatment of adult patients with locally advanced or metastatic *ROS1*-positive non-small cell lung cancer (NSCLC).

SELECT SAFETY INFORMATION

Serious adverse and sometimes fatal reactions occurred with IBTROZI treatment. Warnings and precautions include hepatotoxicity, interstitial lung disease/pneumonitis, QTc interval prolongation, hyperuricemia, myalgia with creatine phosphokinase (CPK) elevation, skeletal fractures, and embryo-fetal toxicity.

Please see complete Important Safety Information on pages 6–8 and accompanying full Prescribing Information.

Prior Authorization

Many health plans require obtaining a prior authorization (PA) approval for patients to get a specific prescribed therapy. This process ensures that the prescribed treatment is medically necessary before the health plan agrees to cover it. Without an approved PA, the patient will not have coverage, leaving them without access to the medication or responsible for the full cost of treatment.

HOW IT WORKS

1

Submit Request

Your office sends a request to the patient's health plan, detailing why the treatment is needed.

2

Coverage Review

The health plan evaluates the PA request based on their PA policy criteria.

3

Decision

The health plan approves, denies, or requests additional information. If the PA is denied, the health plan will include information in the denial letter on how the healthcare professional (HCP) or patient may appeal.

HOW TO COMPLETE A PRIOR AUTHORIZATION

Coverage criteria may vary, so it is important to review specific health plan PA policy criteria. Some health plans may require a specific PA form. Incomplete information may lead to a denial of IBTROZI™ (taletrectinib). The following information is typically required and may be helpful when completing a prior authorization:

Patient Information

- Patient's full name
- Date of birth
- Policy number
- Group number
- Member ID
- Address
- Name of policy holder
- Relation to policy holder
- Insurance phone number
- Insurance address
- Copy of insurance card
- Completed and signed plan-specific PA form

HCP Information

- Prescriber name
- Specialty
- NPI number
- Office address
- Phone/fax number

Medical Documentation

- ICD-10-CM diagnosis code
- Clinical history
  - Tumor characteristics
  - Molecular testing
  - Performance Status
- Previous/current treatments
  - Dosage and start therapy dates
  - Documentation of history of progression, contraindication, or intolerance to other treatments
- Copy of chart notes
  - Details about diagnosis, current condition, and treatment history
- Additional evidence to support your prescribing recommendation

ICD-10-CM, International Classification of Diseases, 10th Revision, Clinical Modification; NPI, National Provider Identifier.

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SAMPLE LETTER

Medical Necessity

A Letter of Medical Necessity is a written explanation of your clinical rationale for why IBTROZI™ (taletrectinib) is necessary for your patient.

Sample Letter of Medical Necessity

[Date]
[Name of pharmacy director or payer contact]
[Contact's title]
[Phone] | [Fax] | [Email]
[Insurance Company Name]
[Address]

Patient: [Patient's name]
Date of birth: [Patient's Date of Birth]
Insurance ID: [Patient's Insurance ID]
Policy Group: [Patient's Group Number]
Diagnosis: [Patient's Diagnosis (ICD-10: C34.XX)]

Re: Requested Treatment: IBTROZI™ (taletrectinib)

Dear [Medical/Pharmacy Director]:

I am writing on behalf of [Patient's Name] to formally document the medical necessity for treatment with IBTROZI for a diagnosis of [Patient's Diagnosis]. [If prior authorization has been submitted previously, indicate date of submission and outcome.]

IBTROZI is indicated for the treatment of adult patients with locally advanced or metastatic *ROS1*-positive non-small cell lung cancer (NSCLC). This letter provides additional information and clinical rationale in support of the medical necessity for [initiating/continuing/reinitiating] treatment with IBTROZI.

Patient Clinical History:

[Patient's Name] is a [age]-year-old [gender] who was diagnosed with [specific type of NSCLC (eg, metastatic adenocarcinoma of the lung)] on [date]. Key clinical findings include:

- Tumor Characteristics: [Histology, staging, mutations]
- Molecular Testing Results: [*ROS1*]
- Previous Treatments: [List chemotherapy, immunotherapy, radiation, or prior targeted therapies]
- Disease Progression: [Describe disease status, prior responses, or resistance to standard treatments]
- Performance Status: [ECOG score or Karnofsky Performance Status]
- FOR IBTROZI **INITIATION** – patients who have not been previously treated with IBTROZI: [Include a summary of your professional opinion and potential prognosis for treatment with IBTROZI] [Include clinical rationale documenting medical necessity for initiation of treatment]
- FOR IBTROZI **CONTINUATION** – patients who are currently treated with IBTROZI: [Include a summary of patient's clinical response to treatment and impact to daily life] [Include clinical rationale documenting medical necessity for continuation of treatment]
- FOR IBTROZI DOSE **WITHHOLDING** – patients who have interrupted treatment with IBTROZI: [Include dates of IBTROZI initiation and dose withholding] [Include reason for interrupting therapy] [Include a summary of the patient's condition and a clinical rationale for dose withholding IBTROZI]

Rationale for Treatment:

IBTROZI is indicated for the treatment of adult patients with locally advanced or metastatic *ROS1*-positive non-small cell lung cancer. The clinical evidence supporting its use includes: [Summarize pivotal clinical trial data (eg, overall response rate [ORR]). Given the patient's [mutation subtype, disease progression, intolerance to previous treatments], IBTROZI represents the most appropriate treatment option, [describe your clinical rationale for IBTROZI™ rather than alternative(s)].

STEP THERAPY BEST PRACTICES

Step therapy requires the use of a health plan's preferred drug before the approval of another medication.

1. Review the health plan criteria and preferred medication(s).
2. Provide documentation to support medical necessity.
3. Include medications that the patient has tried and failed, the duration of therapy, and reason(s) why those treatments are no longer appropriate or the best option for the patient.

FORMULARY EXCLUSION REQUESTS BEST PRACTICES

A formulary exclusion list includes drugs that a health plan or pharmacy benefit manager does not cover.

1. It is possible to request a formulary exception (also known as a medical exception) for an excluded drug.
2. Specify which drugs on the health plan's formulary the patient has tried and failed or has a contraindication to.

Denials

COMMON REASONS FOR A PRIOR AUTHORIZATION DENIAL

Be sure to check your documentation carefully, as the most likely reason for denial is incorrect information or lack of required documentation. Common reasons for denial may include:

1. Original submission includes a simple administrative error of missing information about the physician or patient.
2. Patient does not meet clinical criteria for approval, such as the plan's requirement for a patient to try and fail other treatments on formulary first.
3. A need for additional information, such as missing biomarker testing.
4. Patient is currently using a contraindicated medication or another advanced therapy without a discontinuation plan.
5. For reauthorizations, denials may occur if demonstrated efficacy is not communicated.

WHEN IS A REAUTHORIZATION REQUIRED?

A reauthorization may be required after a specified time-period following initial PA approval. There are often insurance-specific requirements to show evidence of clinical response and supporting documentation. Health plans may have specific forms for reauthorization.

SAMPLE LETTER

Appeal

If a PA request or a formulary exception is denied, you or your patient may consider submitting an appeal.

An appeal is a request to your patient's health plan to reconsider its initial decision to deny coverage for IBTROZI™ (taletrectinib). These letters are tailored to the specific needs of the patient and describe why IBTROZI is the most appropriate treatment option for the patient.

Sample Letter of Appeal

[Date]
[Name of pharmacy director or payer contact]
[Contact's title]
[Phone] | [Fax] | [Email]
[Insurance Company Name]
[Address]

Patient: [Patient's name]
Date of birth: [Patient's Date of Birth]
Insurance ID: [Patient's Insurance ID]
Policy Group: [Patient's Group Number]
Diagnosis: [Patient's Diagnosis (ICD-10: C34.XX)]
Requested Treatment: IBTROZI™ (taletrectinib)
Denial Reference Number: [Denial Number from Insurer]

Re: Appeal of coverage denial for [Patient's Name]

Dear [Medical/Pharmacy Director]:

I am writing this letter to formally appeal the denial of coverage for IBTROZI on behalf of my patient, [Patient's Name], who has been diagnosed with [Patient's Diagnosis]. IBTROZI is FDA-approved for patients with *ROS1*-positive advanced non-small cell lung cancer (NSCLC).

Reason for Appeal

On [date of denial], your organization cited [indicate reason for denial] as the reason for denial of IBTROZI. However, I strongly believe that treatment with IBTROZI is medically necessary based on the FDA-approved indication.

IBTROZI is medically necessary for [Patient's Name] as documented by:

- Clinical rationale #1: [Provide rationale]
- Clinical rationale #2: [Provide rationale]

The denial was based on [incorrect criteria, outdated guidelines, failure to consider mutation status, requirement for step therapy, etc]. [If denial is based on a requirement for step therapy, consider including rationale for why the alternative treatment(s) suggested in the denial are not appropriate (eg, toxicity, contraindications, or previous failure).].

In summary, based on my clinical opinion, IBTROZI is medically necessary for [Patient's Name]. This is consistent with both the FDA-approved indication and the current standards of care.

Please review this appeal as soon as possible. If additional information is needed, I can be reached at [Physician's Contact Information]. Thank you for your prompt reconsideration.

Sincerely,

[Physician's signature]
[Physician name] [Name of practice]

APPEAL BEST PRACTICES

1. Review denial rationale from the health plan, so your appeal can address specific reasons for denial.
2. Confirm the health plan's preferred method of appeal submission.
3. Confirm appeal filing limits and turnaround time.

For support navigating access challenges, contact NuvationConnect™ at:

1-877-NUV-CON1 (1-877-688-2661)
Monday-Friday, 8 AM-8 PM EST

Visit us at
NuvationConnect.com

IMPORTANT SAFETY INFORMATION FOR IBTROZI™ (taletrectinib)

WARNINGS AND PRECAUTIONS

Hepatotoxicity: Hepatotoxicity, including drug-induced liver injury and fatal adverse reactions, can occur. 88% of patients experienced increased AST, including 10% Grade 3/4. 85% of patients experienced increased ALT, including 13% Grade 3/4. Fatal liver events occurred in 0.6% of patients. Median time to first onset of AST or ALT elevation was 15 days (range: 3 days to 20.8 months).

Increased AST or ALT each led to dose interruption in 7% of patients and dose reduction in 5% and 9% of patients, respectively. Permanent discontinuation was caused by increased AST, ALT, or bilirubin each in 0.3% and by hepatotoxicity in 0.6% of patients.

Concurrent elevations in AST or ALT ≥3 times the ULN and total bilirubin ≥2 times the ULN, with normal alkaline phosphatase, occurred in 0.6% of patients.

Monitor liver function tests (AST, ALT, and bilirubin) prior to treatment, every 2 weeks during the first 2 months, and then monthly thereafter as clinically indicated. Test more frequently if transaminase elevations occur. Advise patients to immediately report symptoms of hepatotoxicity. Based on severity and resolution, withhold, then resume at a reduced dose or permanently discontinue.

Interstitial Lung Disease (ILD)/Pneumonitis: Severe, life-threatening, or fatal ILD or pneumonitis can occur. ILD/pneumonitis occurred in 2.3% of patients, including 1.1% Grade 3/4. One fatal ILD case occurred at the 400 mg daily dose. Median time to first onset of ILD/pneumonitis was 3.8 months (range: 12 days to 11.8 months).

ILD/pneumonitis led to dose interruption in 1.1% of patients, dose reduction in 0.6% of patients, and permanent discontinuation in 0.6% of patients.

Monitor patients for new or worsening pulmonary symptoms. Advise patients to report symptoms. If ILD/pneumonitis is suspected, immediately withhold; based on severity and resolution, resume at same or reduced dose, or permanently discontinue.

QTc Interval Prolongation: QTc interval prolongation can occur, which can increase the risk for ventricular tachyarrhythmias (e.g., torsades de pointes) or sudden death. IBTROZI prolongs the QTc interval in a concentration-dependent manner.

In patients who received IBTROZI and underwent at least one post baseline ECG, QTcF increase of >60 msec compared to baseline and QTcF >500 msec occurred in 13% and 2.6% of patients, respectively. 3.4% of patients experienced Grade ≥3. Median time from first dose of IBTROZI to onset of ECG QT prolongation was 22 days (range: 1 day to 38.7 months). Dose interruption and dose reduction each occurred in 2.8% of patients.

Monitor ECGs and electrolytes prior to start of therapy, and then periodically thereafter as clinically indicated. Adjust frequency based on risk factors such as known long QT syndromes, clinically significant bradyarrhythmias, severe or uncontrolled heart failure, and concomitant medications.

Significant QTc interval prolongation may occur when IBTROZI is taken with food, strong and moderate CYP3A inhibitors, and/or drugs with a known potential to prolong QTc. Administer IBTROZI on an empty stomach. Avoid concomitant use with strong and moderate CYP3A inhibitors and/or drugs with a known potential to prolong QTc.

Advise patients to immediately report any symptoms of QT interval prolongation. Based on severity and resolution, withhold, then resume at same or reduced dose, or permanently discontinue.

IMPORTANT SAFETY INFORMATION FOR IBTROZI™ (taletrectinib) (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Hyperuricemia: Hyperuricemia can occur and was reported in 14% of patients, with 16% of these requiring urate-lowering medication without pre-existing gout or hyperuricemia. 0.3% of patients experienced Grade ≥3. Median time to first onset was 2.1 months (range: 7 days to 35.8 months). Dose interruption occurred in 0.3% of patients.

Monitor serum uric acid levels prior to initiating and periodically during treatment. Initiate urate-lowering medications as clinically indicated. Advise patients to report symptoms. Based upon severity and resolution, withhold, then resume at same or reduced dose, or permanently discontinue.

Myalgia with Creatine Phosphokinase (CPK) Elevation: Myalgia with or without CPK elevation can occur. Myalgia occurred in 10% of patients. Median time to first onset was 11 days (range: 2 days to 10 months).

Concurrent myalgia with increased CPK within a 7–day time period occurred in 0.9% of patients. Dose interruption occurred in 0.3% of patients with myalgia and concurrent CPK elevation.

Advise patients to report any unexplained muscle pain, tenderness, or weakness. Monitor serum CPK levels during treatment every 2 weeks during the first month, and then as clinically indicated. Based on severity, withhold, then resume at same or reduced dose upon improvement.

Skeletal Fractures: IBTROZI can increase the risk of fractures. ROS1 inhibitors as a class have been associated with skeletal fractures. 3.4% of patients experienced fractures, including 1.4% Grade 3. Some fractures occurred in the setting of a fall or other predisposing factors such as osteoporosis, bone metastasis, and age-related degenerative conditions. Median time to first onset of fracture was 10.7 months (range: 26 days to 29.1 months). Dose interruption occurred in 0.3% of patients.

Advise patients to immediately report symptoms. Promptly evaluate patients with signs or symptoms (e.g., pain, changes in mobility, deformity) of fractures.

There are no data on the effects of IBTROZI on healing of known fractures and risk of future fractures.

Embryo-Fetal Toxicity: Based on literature, animal studies, and its mechanism of action, IBTROZI can cause fetal harm when administered to a pregnant woman. Verify the pregnancy status of females of reproductive potential prior to initiating IBTROZI. Advise females to inform their healthcare provider of a known or suspected pregnancy.

Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential and male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 weeks following the last dose.

ADVERSE REACTIONS

Among patients who received IBTROZI, the most frequently reported adverse reactions (≥20%) were diarrhea (64%), nausea (47%), vomiting (43%), dizziness (22%), rash (22%), constipation (21%), and fatigue (20%).

The most frequently reported Grade 3/4 laboratory abnormalities (≥5%) were increased ALT (13%), increased AST (10%), decreased neutrophils (5%), and increased creatine phosphokinase (5%).

IMPORTANT SAFETY INFORMATION FOR IBTROZI™ (taletrectinib) (cont'd)

DRUG INTERACTIONS

- **Strong and Moderate CYP3A Inhibitors:** Avoid concomitant use.
- **Strong and Moderate CYP3A Inducers:** Avoid concomitant use.
- **Gastric Acid Reducing Agents:** Avoid concomitant use with PPIs and H2 receptor antagonists. If an acid-reducing agent cannot be avoided, administer locally acting antacids at least 2 hours before or 2 hours after taking IBTROZI.
- **Drugs that Prolong the QTc Interval:** Avoid concomitant use. If concomitant use cannot be avoided, adjust the frequency of monitoring as recommended. Withhold IBTROZI if the QTc interval is >500 msec or the change from baseline is >60 msec.

OTHER CONSIDERATIONS

- **Pregnancy:** Please see important information in Warnings and Precautions under Embryo-Fetal Toxicity.
- **Lactation:** Advise women not to breastfeed during treatment and for 3 weeks after the last dose.
- **Effect on Fertility:** Based on findings in animals, IBTROZI may impair fertility in males and females. The effects on animal fertility were reversible.
- **Pediatric Use:** The safety and effectiveness of IBTROZI in pediatric patients has not been established.
- **Photosensitivity:** IBTROZI can cause photosensitivity. Advise patients to minimize sun exposure and to use sun protection, including broad-spectrum sunscreen, during treatment and for at least 5 days after discontinuation.

Please see accompanying full Prescribing Information.

Nuvation Bio®