PHARMACY COVERAGE GUIDELINE

LYTGOBI® (futibatinib)
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Lytgobi (futibatinib) and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Unresectable, locally advanced, or metastatic intrahepatic cholangiocarcinoma harboring fibroblast growth factor receptor 2 (FGFR2) gene fusions or other rearrangements that has been previously treated with a platinum-based regimen (e.g., oxaliplatin, cisplatin)

b. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

4. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
   a. Evidence of an FGFR2 gene fusion or other rearrangement
   b. Comprehensive ophthalmological examination including optical coherence tomography (OCT)
   c. Negative pregnancy test in a woman of childbearing potential
   d. Eastern Cooperative Oncology Group status of 0-1

5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual is not currently taking any other drugs which cause severe adverse reactions or any significant drug interactions requiring discontinuation such as:
   a. Dual P-gp and strong CYP3A inhibitors (e.g., clarithromycin, ketoconazole, itraconazole, others)
   b. Dual P-gp and strong CYP3A inducers (e.g., carbamazepine, phenobarbital, phenytoin, rifampin, St. John's wort, rifabutin, others)

7. Individual does not have severe renal impairment (CrCl 15 – 29 mL/min) or renal dialysis in end-stage renal disease (CrCl less than 15 mL/min)

8. Individual does not have moderate or severe hepatic impairment (total bilirubin greater than 1.5 times the upper limit of normal and any AST value).

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Lytgobi (futibatinib) and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

2. Individual's condition has responded while on therapy with response defined as the following:
   a. Documented evidence of efficacy, disease stability and/or improvement
   b. No evidence of disease progression

3. The requested dose is at least 12 mg daily

4. Individual has been adherent with the medication

5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic

should be reported to the FDA] (see Definitions section)

6. Individual has not developed any significant adverse drug effects that may exclude continued use such as:
    a. Retinal pigment epithelial detachment (RPED)
    b. Hyperphosphatemia if serum phosphate is not less than or equal to 7 mg/dL within 2 weeks following 2 dose interruptions and reductions
    c. Soft tissue mineralization, calcinosis, nonuremic calciphylaxis and vascular calcification
    d. Other life-threatening adverse reaction

7. Individual is not currently taking any other drugs which cause severe adverse reactions or any significant drug interactions requiring discontinuation such as:
    a. Dual P-gp and strong CYP3A inhibitors (e.g., clarithromycin, ketoconazole, itraconazole, others)
    b. Dual P-gp and strong CYP3A inducers (e.g., carbamazepine, phenobarbital, phenytoin, rifampin, St. John's wort, rifabutin, others)

8. Individual does not have severe renal impairment (CrCl 15 – 29 mL/min) or renal dialysis in end-stage renal disease (CrCl less than 15 mL/min)

9. Individual does not have moderate or severe hepatic impairment (total bilirubin greater than 1.5 times the upper limit of normal and any AST value).

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Lytgobi (futibatinib) is a kinase inhibitor indicated for the treatment of adult patients with previously treated, unresectable, locally advanced, or metastatic intrahepatic cholangiocarcinoma harboring fibroblast growth factor receptor 2 (FGFR2) gene fusions or other rearrangements.

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). An FDA-approved test for detection of FGFR2 gene fusions or other rearrangements in patients with unresectable, locally advanced, or metastatic intrahepatic cholangiocarcinoma for selecting patients for treatment with LYTGOBI is not available.

Futibatinib is a small molecule kinase inhibitor of FGFR 1, 2, 3, and 4 that covalently binds FGFR. Constitutive FGFR signaling can support the proliferation and survival of malignant cells. Futibatinib inhibited FGFR

phosphorylation and downstream signaling and decreased cell viability in cancer cell lines with FGFR alterations including FGFR fusions/rearrangements, amplifications, and mutations.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Eastern Co-operative Oncology Group (ECGO) Performance Status:

Grade	ECOG description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physical strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities, up and about more than 50% of waking hours
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
4	Completely disabled, cannot carry on any self-care, totally confined to bed or chair
5	Dead
Oken, MM, Creech, RH, Tormey, DC, et al.: Toxicity and Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982	

NCCN recommendation definitions:

Category 1:
Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A:
Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B:
Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3:
Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

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Resources:

Lytgobi (futibatinib) product information, revised by Taiho Pharmaceutical Co., Ltd. 04-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 09, 2024.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Biliary Tract Cancers Version 6.2024 – Updated January 10, 2025. Available at https://www.nccn.org. Accessed January 29, 2025.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.