BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

INLYTA® (axitinib)
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:** Inlyta (axitinib) and/or generic equivalent (if available) is 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. First-line treatment of advanced renal cell carcinoma (RCC) in combination with Bavencio (avelumab) or Keytruda (pembrolizumab)

b. Treatment of advanced renal cell carcinoma (RCC) after failure of one prior systemic therapy as a single agent

c. 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 completed **ALL** the following **baseline tests** before initiation of treatment and will have continued monitoring as clinically appropriate:
   a. Thyroid function test
   b. Blood pressure, with hypertensive individuals showing good control on standard antihypertensive therapy
   c. Urinalysis for evidence of proteinuria
   d. Negative pregnancy test in a woman of reproductive potential
   e. Eastern Cooperative Oncology Group (ECOG) performance score 0 or 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 use with strong CYP3A4/5 inducers (e.g., rifampin, dexamethasone, phenytoin, carbamazepine, rifabutin, rifapentine, phenobarbital, and St. John's wort, others)

7. Individual does not have severe hepatic impairment (Child-Pugh Class C)

8. Individual does not have untreated brain metastasis

9. There is no recent history of active gastrointestinal bleeding

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Inlyta (axitinib) and/or generic equivalent (if available) is 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 has documentation of positive clinical response to therapy defined as there is no evidence of disease progression and there is no evidence of unacceptable toxicity

3. Individual has been adherent with the medication

4. **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)

5. Individual has not developed any significant adverse drug effects that may exclude continued use such as:
    a. Arterial thromboembolic events
    b. Cardiovascular event such as congestive heart failure or myocardial infarction
    c. Gastrointestinal perforation and fistula formation
    d. Hemorrhage
    e. Hepatotoxicity
    f. Hypertensive crisis and hypertension that is severe and persistent despite therapy
    g. Reversible Posterior Leukoencephalopathy Syndrome
    h. Venous thromboembolic events

6. Individual is not currently taking any other drugs which cause severe adverse reactions or any significant drug interactions requiring discontinuation such as use with strong CYP3A4/5 inducers (e.g., rifampin, dexamethasone, phenytoin, carbamazepine, rifabutin, rifapentine, phenobarbital, and St. John's wort, others)

7. Individual does not have severe hepatic impairment (Child-Pugh Class C)

8. Individual does not have untreated brain metastasis

9. There is no recent history of active gastrointestinal bleeding

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:

Inlyta (axitinib), a tyrosine kinase inhibitor, is indicated for the treatment of advanced renal cell carcinoma (RCC) in combination with avelumab or pembrolizumab as first-line therapy or as a single agent after failure of one prior systemic therapy.

Inlyta (axitinib) has been shown to inhibit receptor tyrosine kinases including vascular endothelial growth factor receptors (VEGFR)-1, VEGFR-2, and VEGFR-3 at therapeutic plasma concentrations. These receptors are implicated in pathologic angiogenesis, tumor growth, and cancer progression. VEGF-mediated endothelial cell proliferation and survival were inhibited by axitinib *in vitro* and in animal models. Inlyta (axitinib) was shown to

inhibit tumor growth and phosphorylation of VEGFR-2 in animal tumor models.

RCCs, which originate within the renal cortex, constitute 80-85% of primary renal neoplasms. Urothelial (or transitional cell) carcinomas of the renal pelvis account for about 8% of kidney tumors, and other parenchymal epithelial tumors, such as oncocytomas, collecting duct tumors, and renal sarcomas, are rare. RCC can be classified as localized RCC or advanced RCC. There are several subtypes of RCCs: clear cell, papillary (or chromophilic), chromophobe, oncocyte, and collecting duct. The most common histologic pattern of RCC is clear cell which accounts for 75-85% of tumors. Non-clear cell RCC includes papillary, chromophobe, collecting duct, translocation carcinomas, and unclassified types. Medullary renal carcinoma is a variant of collecting duct carcinoma.

Surgery, either radical nephrectomy or partial nephrectomy, is curative in the majority of patients with localized RCC who do not have metastases and for those with resectable primary tumor and a single metastasis. Cryotherapy, radiofrequency ablation may be an alternative for patients with small renal masses who are not surgical candidates.

Many RCCs are clinically silent, and the diagnosis is frequently not made until disease is locally advanced (and unresectable) or has metastasized. Many patients who initially are resectable will eventually have a recurrence. Systemic therapy involving immunotherapy, molecularly targeted agents, surgery, and radiation may have a role depending upon the extent of disease, sites of involvement, and patient-specific comorbidities.

Definitions:

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

ECOG Performance status:

Eastern Co-operative Oncology Group (ECOG) Performance Status	
Grade	ECOG description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, 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, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: 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:

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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

Resources:

Inlyta (axitinib) product information, revised by Pfizer Laboratories Div Pfizer, Inc. 07-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 24, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Kidney Cancer Version 1.2026 – Updated July 24, 2025. Available at https://www.nccn.org. Accessed October 08, 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.