BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 1/1/2016
LAST REVIEW DATE: 11/19/2020
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INLYTA® (axitinib)

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

INLYTA® (axitinib)

Criteria:

- **Criteria for initial therapy:** Inlyta (axitinib) is considered ***medically necessary*** and will be approved when **ALL** of 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. A confirmed diagnosis of **ONE** of the following:

     a. Therapy for relapse or stage IV kidney cancer in combination with Keytruda (pembrolizumab, preferred) or Bavencio (avelumab) as first-line therapy for clear cell histology

     b. Therapy for relapse or stage IV kidney cancer in combination with Keytruda (pembrolizumab) or Bavencio (avelumab) as subsequent therapy for clear cell histology

     c. As single agent subsequent therapy for relapse or stage IV kidney cancer with clear cell histology

     d. As single agent systemic therapy for relapse or stage IV kidney cancer with non-clear cell histology

     e. Advanced renal cell carcinoma (RCC) after failure of **one** prior systemic therapy

     f. Therapy for Hürthle cell, follicular, or papillary thyroid carcinoma if clinical trials or other systemic therapies are not available or appropriate for treatment of progressive and/or symptomatic iodine-refractory unresectable locoregional recurrent or persistent disease or distant metastatic disease

     g. 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. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     a. Liver function tests
     b. Thyroid function test
     c. Blood pressure, with hypertensive individuals showing good control on standard antihypertensive therapy
     d. Urinalysis for evidence of proteinuria
     e. Negative pregnancy test in a woman of reproductive potential
     f. Eastern Cooperative Oncology Group (ECOG) performance score 0 or 1

  5. Will not be used in an individual with severe hepatic impairment (Child-Pugh Class C)

  Initial approval duration: 6 months

INLYTA® (axitinib)

- **Criteria for continuation of coverage (renewal request):** Inlyta (axitinib) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  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 not worsened while on therapy
     a. Worsening is defined as:
        i. Disease progressed while on Inlyta
        ii. There is no evidence of efficacy, disease stability and/or improvement

  3. Individual has been adherent with the medication

  4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
     a. Significant adverse effect such as:
        i. Hypertension and Hypertensive Crisis
        ii. Arterial thromboembolic events
        iii. Venous thromboembolic events
        iv. Hemorrhage
        v. Cardiac failure
        vi. Reversible Posterior Leukoencephalopathy Syndrome
        vii. Gastrointestinal perforation and fistula formation
        viii. Hepatic impairment

  5. Will not be used in an individual with severe hepatic impairment (Child-Pugh Class C)

  6. There are no significant interacting drugs

  Renewal duration: 12 months

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, oncoyte, 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.

Resources:

Inlyta (axitinib) product information, revised by manufacturer 06-2020, at DailyMed http://dailymed.nlm.nih.gov accessed 08-31-20

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Kidney Cancer Version 1.2021 – July 15, 2020; https://www.nccn.org. Accessed August 31, 2020

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Thyroid Carcinoma Version 2.2020 – July 15, 2020; https://www.nccn.org. Accessed August 31, 2020

George D, Jonasch E. Systemic therapy of advanced clear cell renal carcinoma. In: UpToDate, Atkins MB, Shah S (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com (Accessed on August 31, 2020)

Choueiri TK, Pal SK. The treatmeent of advanced non-clear cell renal carcinoma. In: UpToDate, Atkins MB, Shah S (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com (Accessed on August 31, 2020)

Atkins MB. Overview of the treatment of renal cell carcinoma. In: UpToDate, Richie JP, Shah S (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com (Accessed on August 31, 2020)

Atkins MB. Anti-angiogenic and molecularly targeted therapy for advanced or metastatic clear-cell renal cell carcinoma. In: UpToDate, Richie JP, Shah S (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com (Accessed on August 31, 2020)

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

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