CENTENE Corporation	
CLINICAL POLICY	
Department: Medical Management	**Document Name:** Inlyta®
Page: 1 of 5	**Reference Number:** NH.PHAR.100
Effective Date: 05/12	**Replaces Document:**
Retired:	**Reviewed:** 06/13, 08/16, 07/17
Specialist Review: No	**Revised:** 06/14
Product Type: All	**Committee Approval**: 05/12, 06/13, 06/14

IMPORTANT REMINDER

This Clinical Policy has been developed by appropriately experienced and licensed health care professionals based on a thorough review and consideration of generally accepted standards of medical practice, peer-reviewed medical literature, government agency/program approval status, and other indicia of medical necessity.

The purpose of this Clinical Policy is to provide a guide to medical necessity. Benefit determinations should be based in all cases on the applicable contract provisions governing plan benefits ("Benefit Plan Contract") and applicable state and federal requirements, as well as applicable plan-level administrative policies and procedures. To the extent there are any conflicts between this Clinical Policy and the Benefit Plan Contract provisions, the Benefit Plan Contract provisions will control.

Clinical policies are intended to be reflective of current scientific research and clinical thinking. This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

Subject:

Medical necessity criteria for Inlyta® (axitinib)

Description:

The intent of the criteria is to ensure that patients follow selection elements established by Centene® medical policy.

FDA-Approved Indication

Inlyta is a kinase inhibitor indicated for the treatment of advanced renal cell carcinoma (RCC) after failure of one prior systemic therapy.[1] Coverage for other cancer diagnoses may be authorized provided effective treatment with such drug is recognized for treatment of such indication in one of the standard reference compendia

Policy/Criteria:

It is the policy of Health Plans affiliated with Centene Corporation® that Inlyta is **medically necessary** for members when meeting the following algorithm criteria:

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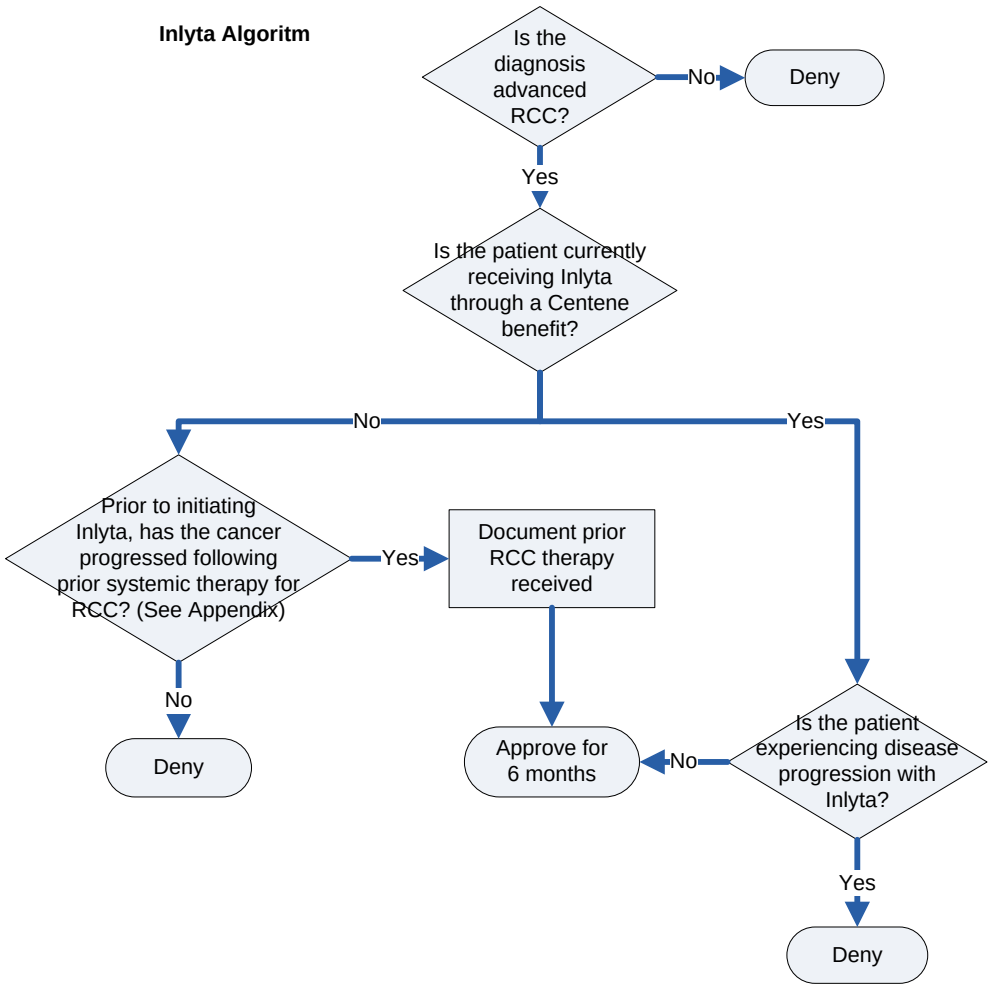

Background

RCC is the most common type of kidney cancer and comprises approximately 2% to 3% of all malignancies.[2] The rate of RCC has increased by 2% per year for the past 65 years.[2] Previously, systemic treatment of advanced RCC was limited to cytokines, such as interleukin-2 and interferon alpha which were associated with modest clinical benefit and significant toxicity.[2,3] Today, targeted therapies are widely used as first- and second-line agents for advanced RCC.[2] These new agents act by inhibiting vascular endothelial growth factor (VEGF) or mammalian target of rapamycin (mTOR).[2,3] Through these actions, the targeted therapies have extended the time in which the tumor does not grow or progress for a disease that is mostly incurable.[3] In the absence of a curative therapy, sequential therapy with targeted therapies is the current standard

of care for advanced RCC.[3] However, a challenge remains in determining the best sequence of therapies for advanced RCC. The approved targeted therapies for RCC are sunitinib, sorafenib, pazopanib, temsirolimus, everolimus, bevacizumab in combination with interferon, and Inlyta (axitinib).[1-3]

Inlyta is indicated for the treatment of advanced RCC after failure of one prior systemic therapy which consists of Avastin® (bevacizumab) + cytokine therapy (interferon-alpha or interleukin-2) + Sutent ® (sunitinib) and Votrient® (pazopanib) Inlyta is a potent, second-generation tyrosine kinase inhibitor that selectively inhibits VEGF receptors (VEGFR)-1, -2 and -3.[1,4] These receptors are implicated in pathologic angiogenesis, tumor growth, and cancer progression.[1] Inhibition of angiogenesis is an important strategy in the treatment of solid tumors such as RCC.[5] Inlyta was approved based on a pivotal phase 3 trial comparing Inlyta to sorafenib in the second-line treatment of advanced RCC.[1,4] First-line treatments for patients enrolled in the trial were sunitinib, bevacizumab, temsirolimus, and cytokines.[1,4] Patients receiving Inlyta had a median progression free survival (PFS) of 6.7 months compared with 4.7 months for those treated with sorafenib.[1,4] The PFS for Inlyta was greatest for the subset of patients who received cytokines as initial therapy.[1,4] In patients treated initially with sunitinib, the difference in median PFS was 1.4 months.[4] Therapy was discontinued due to adverse events in 4% of Inlyta patients and 8% of sorafenib patients.[4] The most common adverse events for Inlyta were hypertension, diarrhea, and fatigue.[4]

Safety

There are no contraindications or boxed warnings for Inlyta.[1] Warnings and precautions address potential adverse events with Inlyta. Hypertension and hypertensive crisis have occurred. Blood pressure should be well-controlled prior to starting Inlyta. Patients should receive antihypertensive medications as indicated.

The recommended starting oral dose of Inlyta is 5 mg twice daily administer approximately 12 hours apart. Patients should actively monitor blood pressure throughout treatment with more frequent assessments during the first cycle of treatment, the first 6 weeks, and periodically thereafter. Patients should be treated with antihypertensive therapy if required. Blood pressure should be managed according to JNC8 guidelines. However, if persistent hypertension occurs despite antihypertensive therapy, a dose-reduction may be necessary (to 3 mg twice daily). If additional dose reduction is required, the recommended dose is 2 mg twice daily.

The concomitant use of strong CYP3A4/ 5 inhibitors should be avoided (e.g., ketoconazole, itraconazole, clarithromycin, atazanavir, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, and voriconazole). Selection of an alternate concomitant medication with no or minimal CYP3A4/5 inhibition potential is highly recommended [1]. Inlyta should be used with

caution in patients at increased risk for arterial and venous thrombotic events as events have been observed and can be fatal. Hemorrhagic events, gastrointestinal perforation and fistula have also occurred; caution is recommended in patients at risk for these events. Patients with untreated brain metastasis or active gastrointestinal bleeding should not use Inlyta. Inlyta should be stopped at least 24 hours prior to scheduled surgery. Patients should be monitored for hypothyroidism, proteinuria and liver enzyme elevations before initiation of and periodically throughout treatment with Inlyta. Permanently discontinue Inlyta if reversible posterior leukoencephalopathy syndrome occurs.

Appendix

Examples of first-line systemic therapies for RCC:[1-3,6]

- Avastin® (bevacizumab)
- Cytokine therapy (interferon-alpha, interleukin-2)
- Votrient® (pazopanib)
- Sutent® (sorafenib)
- Torisel (temsirolimus)

Bibliography

1. Inlyta [package insert]. New York, NY: Pfizer Inc.; January 2012.
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4. Rini BI, Escudier B, Tomczak P, et al. Comparative effectiveness of axitinib versus sorafenib in advanced renal cell carcinoma (AXIS): a randomised phase 3 trial. *Lancet*. 2011;378(9807):1931-1939.
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Revision Log	Date
Converted to Centene policy template	06/13
Updated background and safety sections. Removed duplicate questioning within algorithm regarding prior use of inlyta.	06/14
Added Coverage for other cancer diagnoses may be authorized provided effective treatment with such drug is recognized for treatment of such indication in one of the standard reference compendia	07/15

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Annual Review. No Changes	08/16
Annual Review, No Changes	07/17