Clinical Policy Title:	axitinib
Policy Number:	RxA.167
Drug(s) Applied:	Inlyta®
Original Policy Date:	03/06/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of busines

Background

Axitinib (Inlyta®) is a kinase inhibitor indicated:

- In combination with avelumab, for the first-line treatment of patients with advanced renal cell carcinoma (RCC).
- In combination with pembrolizumab, for the first-line treatment of patients with advanced RCC.
- As a single agent, for the treatment of advanced renal cell carcinoma (RCC) after failure of one prior systemic therapy.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
axitinib (Inlyta®)	Advanced RCC	5 mg by mouth twice daily	20 mg/day
axitinib (Inlyta®) with avelumab	Advanced RCC	5 mg by mouth twice daily with avelumab 800 mg every 2 weeks.	20 mg/day axitinib
axitinib (Inlyta®) with pembrolizumab	Advanced RCC	5 mg by mouth twice daily with pembrolizumab 200 mg every 3 weeks or 400 mg every 6 weeks.	20 mg/day axitinib

Dosage Forms

- Tablets: 1 mg, 5 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Renal Cell Carcinoma (must meet all):

1. Diagnosis of relapsed or stage IV RCC;
2. For clear cell histology, prescribed as (must meet one of the following):
   a. First-line single agent therapy, useful in certain circumstances;

b. Subsequent single agent therapy (failure of previous therapy, see *Appendix B*) ;
c. Combination therapy with pembrolizumab or avelumab as (must meet I or ii):
   i. First line therapy for favorable risk, poor/intermediate risk
   ii. Subsequent therapy

3. For non-clear cell histology, prescribed as single agent systemic therapy, useful in certain circumstances;
4. Prescribed by or in consultation with an oncologist;
5. Age ≥ 18 years;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 20 mg per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval Duration
Commercial: 6 months
Medicaid: 6 months

B. Thyroid Carcinoma (off-label) (must meet all):

1. Diagnosis of differentiated thyroid carcinoma (i.e., follicular, Hurthle cell or papillary thyroid carcinoma);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is unresectable, locally advanced, or metastatic;
5. Failure of lenvatinib (Lenvima®)* or sorafenib (Nexavar®)* unless contraindicated or clinically adverse effects are experienced;
   *Prior authorization may be required.
6. Request meets one of the following (a or b):
   a. Dose does not exceed 5 mg twice daily;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or documentation supports that member has met initial approval criteria for the covered indications and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   c. New dose does not exceed 20 mg per day;
   d. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

DTC: Differentiated thyroid carcinoma
FDA: Food and Drug Association
RCC: Renal cell carcinoma

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
• Votrient® (pazopanib) • Sutent® (sunitinib) • Opdivo® (nivolumab) ± Yervoy® (ipilimumab) Avastin® (bevacizumab) ± (Intron A (interferon alfa-2b), Tarceva (erlotinib) or Afinitor®/Afinitor® Disperz (everolimus)) • Proleukin® (aldesleukin) • Cabometyx® (cabozantinib) • Torisel® (temsirolimus) • Afinitor®/Afinitor® Disperz (everolimus) ± Lenvima® (lenvatinib) • Tarceva® (erlotinib)	Varies	Varies
Lenvima® (lenvatinib)	24 mg by mouth once daily	24 mg/day
Nexavar®(sorafenib)	400 mg by mouth once daily	400 mg/day

Therapeutic alternatives are listed as Brand name (generic) when the drug is available by brand name only and generic (Brand name) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported

- Boxed Warning(s):
  - None reported

APPENDIX D: General Information

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 mouse models. Axitinib was shown to inhibit tumor growth and phosphorylation of VEGFR-2 in tumor xenograft mouse models.

References

1. Inlyta Prescribing Information. New York, NY: Pfizer Labs, Inc.; June 2020. Available at https://www.inlyta.com/ . Accessed March 19,2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed October 15, 2018; March 19,2021.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/. Accessed February 19,2021
4. National Comprehensive Cancer Network Guidelines. Kidney Cancer Version 2.2021-February 3, 2021. Available at https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf . Accessed March 19, 2021.
5. National Comprehensive Cancer Network Guidelines. Thyroid Carcinoma Version 3.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed March 19, 2021.
6. Axitinib. Lexi-Drugs. Lexicomp. Wolters Kluwer. Hudson, OH. Available at https://online.lexi.com. Accessed February 19,2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	02/2020	03/06/2020
Policy was reviewed: 1. Policy title table was updated. 2. Background was updated to include more specific indications. 3. Dosing information was updated to accompany updated indications. 4. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 5. References were updated.	06/14/2020	09/14/2020
Policy was reviewed: 1. Continuation approval therapy rephrased to :Member is currently receiving medication that has been authorized by RxAdvance or documentation supports that member has met initial approval criteria for the covered indications and has received this medication for at least 30 days.." 2. Dosing Information & Therapeutic Alternatives abbreviated form "PO,BID changed to by mouth, Twice daily respectively. 3. References were updated.Initial therapy criteria was updated to clarify prescribing criteria under section I.A.2 and I.A.3 4. Updated dosing criteria based on NCCN evidence under section I.B.6	03/19/2021	06/10/2021