

## Axitinib: Drug information

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(For additional information [see "Axitinib: Patient drug information"](#))

For abbreviations and symbols that may be used in Lexicomp ([show table](#))

**Brand Names: US** Inlyta

**Brand Names: Canada** Inlyta

**Pharmacologic Category** Antineoplastic Agent, Tyrosine Kinase Inhibitor; Antineoplastic Agent, Vascular Endothelial Growth Factor (VEGF) Inhibitor

### Dosing: Adult

**Renal cell cancer, advanced:** Oral: Initial: 5 mg twice daily (approximately every 12 hours)

*Dose increases:* If dose is tolerated (no adverse events above grade 2, blood pressure is normal and no antihypertensive use) for at least 2 consecutive weeks, may increase the dose to 7 mg twice daily, and then further increase (using the same tolerance criteria) to 10 mg twice daily.

*Dose decreases:* For adverse events, reduce dose from 5 mg twice daily to 3 mg twice daily; further reduce to 2 mg twice daily if adverse events persist.

*Dosage adjustment for strong CYP3A4 inhibitors:* Avoid concomitant administration with strong CYP3A4 inhibitors (eg, clarithromycin, itraconazole, ketoconazole, nefazodone, protease inhibitors, telithromycin, voriconazole, grapefruit juice); if concomitant administration with a strong CYP3A4 inhibitor cannot be avoided, ~50% dosage reduction is recommended; adjust dose based on individual tolerance and safety. When the strong CYP3A4 inhibitor is discontinued, resume previous axitinib dose after 3 to 5 half-lives of the inhibitor have passed.

**Thyroid cancer, differentiated, advanced (off-label use):** Oral: Initial: 5 mg twice daily on an empty stomach; increase or decrease dose in 20% increments based on response or toxicity; continue until disease progression or unacceptable toxicity (Cohen 2014) **or** Initial: 5 mg twice daily with food; if tolerated for 2 consecutive weeks, may increase to 7 mg twice daily, and then to 10 mg twice daily (unless receiving antihypertensive medication or blood pressure >150/90 mm Hg); for grade 3 or higher toxicity, interrupt therapy and/or reduce dose to 3 mg twice daily, if further dose reduction necessary, reduce to 2 mg twice daily; continue until disease progression or unacceptable toxicity (Locati 2014).

**Dosing: Geriatric** Refer to adult dosing. No adjustment necessary.

**Dosing: Renal Impairment**

Mild to severe renal impairment (CrCl 15 to <89 mL/minute): No initial dosage adjustment necessary.

End-stage renal disease (ESRD): There are no dosage adjustments provided in the manufacturer's labeling; use with caution.

## Dosing: Hepatic Impairment

Mild impairment (Child-Pugh class A): No starting dosage adjustment necessary.

Moderate impairment (Child-Pugh class B): Reduce starting dose by ~50%; increase or decrease based on individual tolerance.

Severe impairment (Child-Pugh class C): There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

## Dosing: Adjustment for Toxicity

**Adverse events:** May require temporary interruption, dose decreases (reduce dose from 5 mg twice daily to 3 mg twice daily; further reduce to 2 mg twice daily) or discontinuation

**Cardiac failure:** May require permanent discontinuation

**Hypertension:** Treat with standard antihypertensive therapy.

Persistent hypertension: May require dose reduction

Severe, persistent (despite antihypertensives and dose reduction), or evidence of hypertensive crisis: Discontinue treatment

**Hemorrhage:** Any bleeding requiring medical intervention: Temporarily interrupt treatment.

**Proteinuria (moderate-to-severe):** Reduce dose or temporarily interrupt treatment.

**Dosage Forms** Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Tablet, Oral:

Inlyta: 1 mg, 5 mg

**Generic Equivalent Available (US)** No

**Prescribing and Access Restrictions** Available from select specialty pharmacies. Further information may be obtained at 877-744-5675 or [www.inlytahcp.com](http://www.inlytahcp.com).

**Administration** Oral: Swallow tablet whole with a glass of water. May be taken with or without food. If a dose is missed or vomited, do not make up; resume dosing with the next scheduled dose. A suspension may be prepared for nasogastric administration (refer to Extemporaneously Prepared information).

## Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage.

NIOSH recommends single gloving for administration of intact tablets or capsules. If manipulating tablets/capsules (eg, to prepare an oral suspension), NIOSH recommends double gloving, a protective gown, and preparation in a controlled device; if not prepared in a controlled device, respiratory and eye/face protection as well as ventilated engineering controls are recommended. NIOSH recommends double gloving, a protective gown, and (if there is a potential for vomit or spit up) eye/face protection for administration of an oral liquid/feeding tube administration (NIOSH 2016).

**Use Renal cell carcinoma, advanced:** Treatment of advanced renal cell carcinoma after failure of one prior systemic therapy.

### **Use: Off-Label**

Thyroid cancer (differentiated, advanced)

## **Medication Safety Issues**

### **Sound-alike/look-alike issues:**

Axitinib may be confused with afatinib, alectinib, apixaban, gefitinib, imatinib, PAZOPanib, PONATinib, SORAFenib, SUNItinib, vandetanib, vemurafenib

### **High alert medication:**

This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

## **Adverse Reactions**

>10%:

Cardiovascular: Hypertension (40%; grades 3/4: 16%)

Central nervous system: Fatigue (39%), voice disorder (31%), headache (14%)

Dermatologic: Palmar-plantar erythrodysesthesia (27%; grades 3/4: 5%), skin rash (13%; grades 3/4: <1%)

Endocrine & metabolic: Decreased serum bicarbonate (44%), hypocalcemia (39%), hyperglycemia (28%), weight loss (25%), hypothyroidism (19%; grades 3/4: <1%), hypernatremia (17%), hyperkalemia (15%), hypoalbuminemia (15%), hyponatremia (13%), hypophosphatemia (13%), hypoglycemia (11%)

Gastrointestinal: Diarrhea (55%; grades 3/4: 11%), decreased appetite (34%), nausea (32%; grades 3/4: 3%), increased serum lipase (3% to 27%), increased serum amylase (25%), vomiting (24%; grades 3/4: 3%), constipation (20%), mucosal inflammation (15%), stomatitis (15%), abdominal pain

(8% to 14%), dysgeusia (11%)

Genitourinary: Proteinuria (11%; grade 3: 3%)

Hematologic and oncologic: Anemia (4% to 35%; grades 3/4: <1%), lymphocytopenia (33%; grades 3/4: 3%), hemorrhage (16%; grades 3/4 1%), thrombocytopenia (15%; grades 3/4: <1%), leukopenia (11%)

Hepatic: Increased serum alkaline phosphatase (30%), increased serum ALT (22%; grades 3/4: <1%), increased serum AST (20%; grades 3/4: <1%)

Neuromuscular & skeletal: Weakness (21%), arthralgia (15%), limb pain (13%)

Renal: Increased serum creatinine (55%)

Respiratory: Cough (15%), dyspnea (15%)

1% to 10%:

Cardiovascular: Venous thrombosis (grades 3/4: 3%), arterial thrombosis (2%; grade 3/4: 1%), pulmonary embolism (2%) deep vein thrombosis (1%), transient ischemic attack (1%), retinal vein occlusion ( $\leq 1\%$ ), retinal thrombosis ( $\leq 1\%$ )

Central nervous system: Dizziness (9%)

Dermatologic: Xeroderma (10%), pruritus (7%), alopecia (4%), erythema (2%)

Endocrine & metabolic: Dehydration (6%), hyperthyroidism (1%)

Gastrointestinal: Dyspepsia (10%), hemorrhoids (4%), gastrointestinal fistula (1%), gastrointestinal perforation ( $\leq 1\%$ )

Genitourinary: Hematuria (3%)

Hematologic and Oncologic: Increased hemoglobin (9%), rectal hemorrhage (2%), polycythemia (1%)

Neuromuscular & skeletal: Myalgia (7%)

Otic: Tinnitus (3%)

Respiratory: Epistaxis (6%), hemoptysis (2%)

<1%, postmarketing, and/or case reports: Cardiac failure, cerebral hemorrhage, cerebrovascular accident, fever, hypertensive crisis, neutropenia, reversible posterior leukoencephalopathy syndrome

## Contraindications

There are no contraindications listed within the manufacturer's US labeling.

*Canadian labeling:* Hypersensitivity to axitinib or any component of the formulation.

## Warnings/Precautions

**Concerns related to adverse effects:**

- **Cardiac effects:** Cardiac failure, including fatal events, has been observed rarely. Monitor for signs/symptoms of cardiac failure throughout therapy; management may require permanent therapy discontinuation.
- **Gastrointestinal events:** Gastrointestinal perforation and fistulas (including a fatality) have been reported. Monitor for signs/symptoms throughout treatment.
- **Hemorrhage:** Hemorrhagic events (cerebral hemorrhage, gastrointestinal hemorrhage, hematuria, hemoptysis, and melena) have been reported (with some fatalities). Temporarily interrupt treatment with any hemorrhage requiring medical intervention.
- **Hypertension:** May cause hypertension; the median onset is within the first month, and has been observed as early as 4 days after treatment initiation. Hypertensive crisis has been reported. Blood pressure should be well-controlled prior to treatment initiation. Monitor blood pressure and treat with standard antihypertensive therapy. Persistent hypertension (despite antihypertensive therapy) may require dose reduction; discontinue if severe and persistent despite concomitant antihypertensives (or dose reduction), or with evidence of hypertensive crisis. Monitor for hypotension if on antihypertensive therapy and axitinib is withheld or discontinued.
- **Proteinuria:** Proteinuria is associated with use. Monitor for proteinuria at baseline and periodically throughout therapy. If moderate or severe proteinuria occurs, reduce dose or temporarily withhold treatment.
- **Reversible posterior leukoencephalopathy syndrome (RPLS):** Cases of RPLS have been reported. Symptoms of RPLS include confusion, headache, hypertension (mild-to-severe), lethargy, seizure, blindness and/or other vision or neurologic disturbances; interrupt treatment and manage hypertension. MRI is recommended to confirm RPLS diagnosis. Discontinue axitinib if RPLS is confirmed. The safety of reinitiating axitinib in patients previously experiencing RPLS is unknown.
- **Thrombotic events:** Arterial thrombotic events (cerebrovascular accident, MI, retinal artery occlusion, and transient ischemic attack), with fatalities, have been reported. Venous thrombotic events, including pulmonary embolism, deep vein thrombosis, retinal vein occlusion and retinal vein thrombosis, have been observed (with some fatalities). Use with caution in patients with a history of or risks for arterial or venous thrombotic events; has not been studied in patients within 12 months of an arterial thrombotic event or within 6 months of a venous thrombotic event.
- **Thyroid dysfunction:** Hypothyroidism occurs commonly with tyrosine kinase inhibitors, including axitinib. Hyperthyroidism has also been reported. Monitor thyroid function at baseline and periodically throughout therapy. Thyroid disorders should be treated according to standard practice to achieve/maintain euthyroid state.
- **Wound healing complications:** Although the effect on wound healing has not been studied with axitinib, vascular endothelial growth factor (VEGF) receptor inhibitors are associated with impaired wound healing. Discontinue treatment at least 24 hours prior to scheduled surgery; treatment reinitiation should be guided by clinical judgment and wound assessment.

***Disease-related concerns:***

- **Brain metastases:** Has not been studied in patients with evidence of untreated brain metastases; use is not recommended.
- **Gastrointestinal bleeding:** Has not been studied in patients with recent active gastrointestinal

bleeding; use is not recommended.

- Hepatic impairment: Systemic exposure to axitinib is increased in patients with moderate impairment (Child-Pugh class B); dose reductions are recommended. Has not been studied in patients with severe impairment (Child-Pugh class C). Increases in ALT have been observed; monitor liver function tests prior to therapy initiation and periodically throughout treatment.

#### **Concurrent drug therapy issues:**

- Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

**Metabolism/Transport Effects** Substrate of CYP1A2 (minor), CYP2C19 (minor), CYP3A4 (major), UGT1A1; **Note:** Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential

## **Drug Interactions**

(For additional information: [Launch drug interactions program](#)) Lexicomp®

Aprepitant: May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors). *Risk C: Monitor therapy*

Bisphosphonate Derivatives: Angiogenesis Inhibitors (Systemic) may enhance the adverse/toxic effect of Bisphosphonate Derivatives. Specifically, the risk for osteonecrosis of the jaw may be increased. *Risk C: Monitor therapy*

Conivaptan: May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors). *Risk X: Avoid combination*

CYP3A4 Inducers (Moderate): May decrease the serum concentration of Axitinib. *Risk X: Avoid combination*

CYP3A4 Inducers (Strong): May decrease the serum concentration of Axitinib. *Risk X: Avoid combination*

CYP3A4 Inhibitors (Moderate): May decrease the metabolism of CYP3A4 Substrates (High risk with Inhibitors). *Risk C: Monitor therapy*

CYP3A4 Inhibitors (Strong): May increase the serum concentration of Axitinib. Management: Avoid concurrent use of axitinib with any strong CYP3A inhibitor whenever possible. If a strong CYP3A inhibitor must be used with axitinib, a 50% axitinib dose reduction is recommended. *Risk X: Avoid combination*

Dasatinib: May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors). *Risk C: Monitor therapy*

Deferasirox: May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers). *Risk C: Monitor therapy*

Fosaprepitant: May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors). *Risk C: Monitor therapy*

Fusidic Acid (Systemic): May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors). *Risk X: Avoid combination*

Grapefruit Juice: May increase the serum concentration of Axitinib. *Risk X: Avoid combination*

Idelalisib: May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors). *Risk X: Avoid combination*

Netupitant: May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors). *Risk C: Monitor therapy*

Palbociclib: May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors). *Risk C: Monitor therapy*

Pitolisant: May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers).  
Management: Combined use of pitolisant with a CYP3A4 substrate that has a narrow therapeutic index should be avoided. Other CYP3A4 substrates should be monitored more closely when used with pitolisant. *Risk D: Consider therapy modification*

Sarilumab: May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers). *Risk C: Monitor therapy*

Siltuximab: May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers). *Risk C: Monitor therapy*

Simeprevir: May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors). *Risk C: Monitor therapy*

St John's Wort: May decrease the serum concentration of Axitinib. *Risk X: Avoid combination*

Stiripentol: May increase the serum concentration of CYP3A4 Substrates (High risk with Inhibitors).  
Management: Use of stiripentol with CYP3A4 substrates that are considered to have a narrow therapeutic index should be avoided due to the increased risk for adverse effects and toxicity. Any CYP3A4 substrate used with stiripentol requires closer monitoring. *Risk D: Consider therapy modification*

Tocilizumab: May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers).  
*Risk C: Monitor therapy*

**Food Interactions** Axitinib serum concentrations may be increased when taken with grapefruit or grapefruit juice. Management: Avoid concurrent use.

**Pregnancy Risk Factor** D ([show table](#))

**Pregnancy Implications** Teratogenic, embryotoxic, and fetotoxic events were observed in animal reproduction studies when administered in doses less than the normal human dose. Based on its mechanism of action and because axitinib inhibits angiogenesis (a critical component of fetal development), adverse effects on pregnancy would be expected. Women of childbearing potential should be advised to avoid pregnancy during therapy.

**Breast-Feeding Considerations** It is not known if axitinib is excreted in breast milk. Due to the potential for serious adverse reactions in the nursing infant, the manufacturer recommends a decision be made to discontinue nursing or to discontinue the drug, taking into account the importance of treatment to the mother.

**Dietary Considerations** Avoid grapefruit and grapefruit juice.

**Monitoring Parameters** Hepatic function (ALT, AST, and bilirubin; baseline and periodic), thyroid function (baseline and periodic), urinalysis (for proteinuria; baseline and periodically); blood pressure, signs/symptoms of RPLS, gastrointestinal bleeding/perforation/fistula, signs/symptoms cardiac failure

Thyroid function testing recommendations (Hamnvik, 2011):

Preexisting levothyroxine therapy: Obtain baseline TSH levels, then monitor every 4 weeks until levels and levothyroxine dose are stable, then monitor every 2 months

Without preexisting thyroid hormone replacement: TSH at baseline, then monthly for 4 months, then every 2-3 months

**Mechanism of Action** Axitinib is a selective second generation tyrosine kinase inhibitor which blocks angiogenesis and tumor growth by inhibiting vascular endothelial growth factor receptors (VEGFR-1, VEGFR-2, and VEGFR-3).

## Pharmacodynamics/Kinetics

Absorption: Rapid (Rugo 2005)

Distribution:  $V_d$ : 160 L

Protein binding: >99%; to albumin (primarily) and to  $\alpha_1$  acid glycoprotein (AAG)

Metabolism: Hepatic; primarily via CYP3A4/5 and to a lesser extent via CYP1A2, CYP2C19 and UGT1A1

Bioavailability: 58%

Half-life elimination: 2.5 to 6.1 hours

Time to peak: 2.5 to 4 hours

Excretion: Feces (~41%; 12% as unchanged drug); urine (~23%; as metabolites)

## Pricing: US

**Tablets** (Inlyta Oral)

1 mg (180): \$16416.28

5 mg (60): \$16416.28

**Disclaimer:** The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

**Brand Names: International** Inlita (UA); Inlyta (IS); Inlyta (AE, AR, AT, AU, BE, CH, CL, CN, CY, CZ, DE, DK, EE, ES, FR, GB, HK, HR, HU, IE, JP, KR, LB, LT, LU, MT, MY, NL, NO, NZ, PE, PL, PT, QA, RO,



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