HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use INLYTA safely and effectively. See full prescribing information for INLYTA.

INLYTA® (axitinib) tablets for oral administration
Initial U.S. Approval: 2012

----------INDICATIONS AND USAGE----------

INLYTA is a kinase inhibitor indicated for the treatment of advanced renal cell carcinoma after failure of one prior systemic therapy. (1)

----------DOSAGE AND ADMINISTRATION----------

- The starting dose is 5 mg orally twice daily. Dose adjustments can be made based on individual safety and tolerability. (2.1, 2.2)
- Administer INLYTA dose approximately 12 hours apart with or without food. (2.1)
- INLYTA should be swallowed whole with a glass of water. (2.1)
- If a strong CYP3A4/5 inhibitor is required, decrease the INLYTA dose by approximately half. (2.2)
- For patients with moderate hepatic impairment, decrease the starting dose by approximately half. (2.2)

----------DOSAGE FORMS AND STRENGTHS----------

1 mg and 5 mg tablets (3)

----------CONTRAINDICATIONS----------

None (4)

----------WARNINGS AND PRECAUTIONS----------

- Hypertension including hypertensive crisis has been observed. Blood pressure should be well-controlled prior to initiating INLYTA. Monitor for hypertension and treat as needed. For persistent hypertension despite use of anti-hypertensive medications, reduce the INLYTA dose. (5.1)
- Arterial and venous thrombotic events have been observed and can be fatal. Use with caution in patients who are at increased risk for these events. (5.2, 5.3)
- Hemorrhagic events, including fatal events, have been reported. INLYTA has not been studied in patients with evidence of untreated brain metastasis or recent active gastrointestinal bleeding and should not be used in those patients. (5.4)
- Gastrointestinal perforation and fistula, including death, have occurred. Use with caution in patients at risk for gastrointestinal perforation or fistula. (5.5)
- Hypothyroidism requiring thyroid hormone replacement has been reported. Monitor thyroid function before initiation of, and periodically throughout, treatment with INLYTA. (5.6)
- Stop INLYTA at least 24 hours prior to scheduled surgery. (5.7)
- Reversible Posterior Leukoencephalopathy Syndrome (RPLS) has been observed. Permanently discontinue INLYTA if signs or symptoms of RPLS occur. (5.8)
- Monitor for proteinuria before initiation of, and periodically throughout, treatment with INLYTA. For moderate to severe proteinuria, reduce the dose or temporarily interrupt treatment with INLYTA. (5.9)
- Liver enzyme elevation has been observed during treatment with INLYTA. Monitor ALT, AST and bilirubin before initiation of, and periodically throughout, treatment with INLYTA. (5.10)
- The starting dose of INLYTA should be decreased if used in patients with moderate hepatic impairment. INLYTA has not been studied in patients with severe hepatic impairment. (2.2, 5.11)
- INLYTA can cause fetal harm when administered to a pregnant woman based on its mechanism of action. Women of childbearing potential should be advised of the potential hazard to the fetus and to avoid becoming pregnant while receiving INLYTA. (5.12, 8.1)

----------ADVERSE REACTIONS----------

The most common (≥20%) adverse reactions are diarrhea, hypertension, fatigue, decreased appetite, nausea, dysphonia, palmar-plantar erythrodysesthesia (hand-foot) syndrome, weight decreased, vomiting, asthenia, and constipation. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer, Inc at 1-800-438-1985 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- Avoid strong CYP3A4/5 inhibitors. If unavoidable, reduce the INLYTA dose. (2.2, 7.1)
- Avoid strong CYP3A4/5 inducers. (7.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the Full Prescribing Information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

INLYTA is indicated for the treatment of advanced renal cell carcinoma (RCC) after failure of one prior systemic therapy.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosing

The recommended starting oral dose of INLYTA is 5 mg twice daily. Administer INLYTA doses approximately 12 hours apart with or without food *[see Clinical Pharmacology (12.3)]*. INLYTA should be swallowed whole with a glass of water.

If the patient vomits or misses a dose, an additional dose should not be taken. The next prescribed dose should be taken at the usual time.

2.2 Dose Modification Guidelines

Dose increase or reduction is recommended based on individual safety and tolerability.

Over the course of treatment, patients who tolerate INLYTA for at least two consecutive weeks with no adverse reactions >Grade 2 (according to the Common Toxicity Criteria for Adverse Events [CTCAE]), are normotensive, and are not receiving anti-hypertension medication, may have their dose increased. When a dose increase from 5 mg twice daily is recommended, the INLYTA dose may be increased to 7 mg twice daily, and further to 10 mg twice daily using the same criteria.

Over the course of treatment, management of some adverse drug reactions may require temporary interruption or permanent discontinuation and/or dose reduction of INLYTA therapy *[see Warnings and Precautions (5)]*. If dose reduction from 5 mg twice daily is required, the recommended dose is 3 mg twice daily. If additional dose reduction is required, the recommended dose is 2 mg twice daily.

Strong CYP3A4/5 Inhibitors: 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 recommended. Although INLYTA dose adjustment has not been studied in patients receiving strong CYP3A4/5 inhibitors, if a strong CYP3A4/5 inhibitor must be co-administered, a dose decrease of INLYTA by approximately half is recommended, as this dose reduction is predicted to adjust the axitinib area under the plasma concentration vs time curve (AUC) to the range observed without inhibitors. The subsequent doses can be increased or decreased based on individual safety and tolerability. If co-administration of the strong inhibitor is discontinued, the INLYTA dose should be returned (after 3 – 5 half-lives of the inhibitor) to that used prior to initiation of the strong CYP3A4/5 inhibitor *[see Drug Interactions (7.1) and Clinical Pharmacology (12.3)]*.

Hepatic Impairment: No starting dose adjustment is required when administering INLYTA to patients with mild hepatic impairment (Child-Pugh class A). Based on the pharmacokinetic data,

the INLYTA starting dose should be reduced by approximately half in patients with baseline moderate hepatic impairment (Child-Pugh class B). The subsequent doses can be increased or decreased based on individual safety and tolerability. INLYTA has not been studied in patients with severe hepatic impairment (Child-Pugh class C) *[see Warnings and Precautions (5.11), Use in Specific Populations (8.6), and Clinical Pharmacology (12.3)]*.

3 DOSAGE FORMS AND STRENGTHS

1 mg tablets of INLYTA: red, film-coated, oval tablets, debossed with “Pfizer” on one side and “1 XNB” on the other side.

5 mg tablets of INLYTA: red, film-coated, triangular tablets, debossed with “Pfizer” on one side and “5 XNB” on the other side.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Hypertension and Hypertensive Crisis

In a controlled clinical study with INLYTA for the treatment of patients with RCC, hypertension was reported in 145/359 patients (40%) receiving INLYTA and 103/355 patients (29%) receiving sorafenib. Grade 3/4 hypertension was observed in 56/359 patients (16%) receiving INLYTA and 39/355 patients (11%) receiving sorafenib. Hypertensive crisis was reported in 2/359 patients (<1%) receiving INLYTA and none of the patients receiving sorafenib. The median onset time for hypertension (systolic blood pressure >150 mmHg or diastolic blood pressure >100 mmHg) was within the first month of the start of INLYTA treatment and blood pressure increases have been observed as early as 4 days after starting INLYTA. Hypertension was managed with standard antihypertensive therapy. Discontinuation of INLYTA treatment due to hypertension occurred in 1/359 patients (<1%) receiving INLYTA and none of the patients receiving sorafenib *[see Adverse Reactions (6.1)]*.

Blood pressure should be well-controlled prior to initiating INLYTA. Patients should be monitored for hypertension and treated as needed with standard anti-hypertensive therapy. In the case of persistent hypertension despite use of anti-hypertensive medications, reduce the INLYTA dose. Discontinue INLYTA if hypertension is severe and persistent despite anti-hypertensive therapy and dose reduction of INLYTA, and discontinuation should be considered if there is evidence of hypertensive crisis. If INLYTA is interrupted, patients receiving antihypertensive medications should be monitored for hypotension *[see Dosage and Administration (2.2)]*.

5.2 Arterial Thromboembolic Events

In clinical trials, arterial thromboembolic events have been reported, including deaths. In a controlled clinical study with INLYTA for the treatment of patients with RCC, Grade 3/4 arterial thromboembolic events were reported in 4/359 patients (1%) receiving INLYTA and 4/355 patients (1%) receiving sorafenib. Fatal cerebrovascular accident was reported in 1/359 patients

(<1%) receiving INLYTA and none of the patients receiving sorafenib *[see Adverse Reactions (6.1)]*.

In clinical trials with INLYTA, arterial thromboembolic events (including transient ischemic attack, cerebrovascular accident, myocardial infarction, and retinal artery occlusion) were reported in 17/715 patients (2%), with two deaths secondary to cerebrovascular accident.

Use INLYTA with caution in patients who are at risk for, or who have a history of, these events. INLYTA has not been studied in patients who had an arterial thromboembolic event within the previous 12 months.

5.3 Venous Thromboembolic Events

In clinical trials, venous thromboembolic events have been reported, including deaths. In a controlled clinical study with INLYTA for the treatment of patients with RCC, venous thromboembolic events were reported in 11/359 patients (3%) receiving INLYTA and 2/355 patients (1%) receiving sorafenib. Grade 3/4 venous thromboembolic events were reported in 9/359 patients (3%) receiving INLYTA (including pulmonary embolism, deep vein thrombosis, retinal vein occlusion and retinal vein thrombosis) and 2/355 patients (1%) receiving sorafenib. Fatal pulmonary embolism was reported in 1/359 patients (<1%) receiving INLYTA and none of the patients receiving sorafenib. In clinical trials with INLYTA, venous thromboembolic events were reported in 22/715 patients (3%), with two deaths secondary to pulmonary embolism.

Use INLYTA with caution in patients who are at risk for, or who have a history of, these events. INLYTA has not been studied in patients who had a venous thromboembolic event within the previous 6 months.

5.4 Hemorrhage

In a controlled clinical study with INLYTA for the treatment of patients with RCC, hemorrhagic events were reported in 58/359 patients (16%) receiving INLYTA and 64/355 patients (18%) receiving sorafenib. Grade 3/4 hemorrhagic events were reported in 5/359 (1%) patients receiving INLYTA (including cerebral hemorrhage, hematuria, hemoptysis, lower gastrointestinal hemorrhage, and melena) and 11/355 (3%) patients receiving sorafenib. Fatal hemorrhage was reported in 1/359 patients (<1%) receiving INLYTA (gastric hemorrhage) and 3/355 patients (1%) receiving sorafenib.

INLYTA has not been studied in patients who have evidence of untreated brain metastasis or recent active gastrointestinal bleeding and should not be used in those patients. If any bleeding requires medical intervention, temporarily interrupt the INLYTA dose.

5.5 Gastrointestinal Perforation and Fistula Formation

In a controlled clinical study with INLYTA for the treatment of patients with RCC, gastrointestinal perforation was reported in 1/359 patients (<1%) receiving INLYTA and none of the patients receiving sorafenib. In clinical trials with INLYTA, gastrointestinal perforation was reported in 5/715 patients (1%), including one death. In addition to cases of gastrointestinal perforation, fistulas were reported in 4/715 patients (1%).

Monitor for symptoms of gastrointestinal perforation or fistula periodically throughout treatment with INLYTA.

5.6 Thyroid Dysfunction

In a controlled clinical study with INLYTA for the treatment of patients with RCC, hypothyroidism was reported in 69/359 patients (19%) receiving INLYTA and 29/355 patients (8%) receiving sorafenib. Hyperthyroidism was reported in 4/359 patients (1%) receiving INLYTA and 4/355 patients (1%) receiving sorafenib. In patients who had thyroid stimulating hormone (TSH) <5 μU/mL before treatment, elevations of TSH to ≥10 μU/mL occurred in 79/245 patients (32%) receiving INLYTA and 25/232 patients (11%) receiving sorafenib *[see Adverse Reactions (6.1)]*.

Monitor thyroid function before initiation of, and periodically throughout, treatment with INLYTA. Treat hypothyroidism and hyperthyroidism according to standard medical practice to maintain euthyroid state.

5.7 Wound Healing Complications

No formal studies of the effect of INLYTA on wound healing have been conducted.

Stop treatment with INLYTA at least 24 hours prior to scheduled surgery. The decision to resume INLYTA therapy after surgery should be based on clinical judgment of adequate wound healing.

5.8 Reversible Posterior Leukoencephalopathy Syndrome

In a controlled clinical study with INLYTA for the treatment of patients with RCC, reversible posterior leukoencephalopathy syndrome (RPLS) was reported in 1/359 patients (<1%) receiving INLYTA and none of the patients receiving sorafenib *[see Adverse Reactions (6.1)]*. There were two additional reports of RPLS in other clinical trials with INLYTA.

RPLS is a neurological disorder which can present with headache, seizure, lethargy, confusion, blindness and other visual and neurologic disturbances. Mild to severe hypertension may be present. Magnetic resonance imaging is necessary to confirm the diagnosis of RPLS. Discontinue INLYTA in patients developing RPLS. The safety of reinitiating INLYTA therapy in patients previously experiencing RPLS is not known.

5.9 Proteinuria

In a controlled clinical study with INLYTA for the treatment of patients with RCC, proteinuria was reported in 39/359 patients (11%) receiving INLYTA and 26/355 patients (7%) receiving sorafenib. Grade 3 proteinuria was reported in 11/359 patients (3%) receiving INLYTA and 6/355 patients (2%) receiving sorafenib *[see Adverse Reactions (6.1)]*.

Monitoring for proteinuria before initiation of, and periodically throughout, treatment with INLYTA is recommended. For patients who develop moderate to severe proteinuria, reduce the dose or temporarily interrupt INLYTA treatment.

5.10 Elevation of Liver Enzymes

In a controlled clinical study with INLYTA for the treatment of patients with RCC, alanine aminotransferase (ALT) elevations of all grades occurred in 22% of patients on both arms, with Grade 3/4 events in <1% of patients on the INLYTA arm and 2% of patients on the sorafenib arm.

Monitor ALT, aspartate aminotransferase (AST) and bilirubin before initiation of and periodically throughout treatment with INLYTA.

5.11 Hepatic Impairment

The systemic exposure to axitinib was higher in subjects with moderate hepatic impairment (Child-Pugh class B) compared to subjects with normal hepatic function. A dose decrease is recommended when administering INLYTA to patients with moderate hepatic impairment (Child-Pugh class B). INLYTA has not been studied in patients with severe hepatic impairment (Child-Pugh class C) *[see Dosage and Administration (2.2), Use in Specific Populations (8.6), and Clinical Pharmacology (12.3)]*.

5.12 Pregnancy

INLYTA can cause fetal harm when administered to a pregnant woman based on its mechanism of action. There are no adequate and well-controlled studies in pregnant women using INLYTA. In developmental toxicity studies in mice, axitinib was teratogenic, embryotoxic and fetotoxic at maternal exposures that were lower than human exposures at the recommended clinical dose.

Women of childbearing potential should be advised to avoid becoming pregnant while receiving INLYTA. If this drug is used during pregnancy, or if a patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to the fetus *[see Use in Specific Populations (8.1)]*.

6 ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The safety of INLYTA has been evaluated in 715 patients in monotherapy studies, which included 537 patients with advanced RCC. The data described *[see Adverse Reactions (6.1)]* reflect exposure to INLYTA in 359 patients with advanced RCC who participated in a randomized clinical study versus sorafenib *[see Clinical Studies (14)]*.

The following risks, including appropriate action to be taken, are discussed in greater detail in other sections of the label *[see Warnings and Precautions (5.1-5.10 and 5.12)]*: hypertension, arterial thromboembolic events, venous thromboembolic events, hemorrhage, gastrointestinal perforation and fistula formation, thyroid dysfunction, wound healing complications, RPLS, proteinuria, elevation of liver enzymes, and fetal development.

6.1 Clinical Trials Experience

The median duration of treatment was 6.4 months (range 0.03 to 22.0) for patients who received INLYTA and 5.0 months (range 0.03 to 20.1) for patients who received sorafenib. Dose modifications or temporary delay of treatment due to an adverse reaction occurred in 199/359 patients (55%) receiving INLYTA and 220/355 patients (62%) receiving sorafenib. Permanent discontinuation due to an adverse reaction occurred in 34/359 patients (9%) receiving INLYTA and 46/355 patients (13%) receiving sorafenib.

The most common (≥20%) adverse reactions observed following treatment with INLYTA were diarrhea, hypertension, fatigue, decreased appetite, nausea, dysphonia, palmar-plantar

erythrodysesthesia (hand-foot) syndrome, weight decreased, vomiting, asthenia, and constipation. Table 1 presents adverse reactions reported in ≥10% patients who received INLYTA or sorafenib.

Table 1. Adverse Reactions Occurring in ≥10% of Patients Who Received INLYTA or Sorafenib

Adverse Reaction[a]	INLYTA (N=359)		Sorafenib (N=355)	
	All Grades[b]	Grade 3/4	All Grades[b]	Grade 3/4
	%	%	%	%
Diarrhea	55	11	53	7
Hypertension	40	16	29	11
Fatigue	39	11	32	5
Decreased appetite	34	5	29	4
Nausea	32	3	22	1
Dysphonia	31	0	14	0
Palmar-plantar erythrodysesthesia syndrome	27	5	51	16
Weight decreased	25	2	21	1
Vomiting	24	3	17	1
Asthenia	21	5	14	3
Constipation	20	1	20	1
Hypothyroidism	19	<1	8	0
Cough	15	1	17	1
Mucosal inflammation	15	1	12	1
Arthralgia	15	2	11	1
Stomatitis	15	1	12	<1
Dyspnea	15	3	12	3
Abdominal pain	14	2	11	1
Headache	14	1	11	0
Pain in extremity	13	1	14	1
Rash	13	<1	32	4
Proteinuria	11	3	7	2
Dysgeusia	11	0	8	0
Dry skin	10	0	11	0
Dyspepsia	10	0	2	0
Pruritus	7	0	12	0
Alopecia	4	0	32	0
Erythema	2	0	10	<1

[a] Percentages are treatment-emergent, all-causality events
[b] National Cancer Institute Common Terminology Criteria for Adverse Events, Version 3.0

Selected adverse reactions (all grades) that were reported in <10% of patients treated with INLYTA included dizziness (9%), upper abdominal pain (8%), myalgia (7%), dehydration (6%), epistaxis (6%), anemia (4%), hemorrhoids (4%), hematuria (3%), tinnitus (3%), lipase increased (3%), pulmonary embolism (2%), rectal hemorrhage (2%), hemoptysis (2%), deep vein

thrombosis (1%), retinal-vein occlusion/thrombosis (1%), polycythemia (1%), transient ischemic attack (1%), and RPLS (<1%).

Table 2 presents the most common laboratory abnormalities reported in ≥10% patients who received INLYTA or sorafenib.

Table 2. Laboratory Abnormalities Occurring in ≥10% of Patients Who Received INLYTA or Sorafenib

Laboratory Abnormality	N	INLYTA		N	Sorafenib	
		All Grades[a]	Grade 3/4		All Grades[a]	Grade 3/4
		%	%		%	%
Hematology						
Hemoglobin decreased	320	35	<1	316	52	4
Lymphocytes (absolute) decreased	317	33	3	309	36	4
Platelets decreased	312	15	<1	310	14	0
White blood cells decreased	320	11	0	315	16	<1
Chemistry						
Creatinine increased	336	55	0	318	41	<1
Bicarbonate decreased	314	44	<1	291	43	0
Hypocalcemia	336	39	1	319	59	2
ALP increased	336	30	1	319	34	1
Hyperglycemia	336	28	2	319	23	2
Lipase increased	338	27	5	319	46	15
Amylase increased	338	25	2	319	33	2
ALT increased	331	22	<1	313	22	2
AST increased	331	20	<1	311	25	1
Hypernatremia	338	17	1	319	13	1
Hypoalbuminemia	337	15	<1	319	18	1
Hyperkalemia	333	15	3	314	10	3
Hypoglycemia	336	11	<1	319	8	<1
Hyponatremia	338	13	4	319	11	2
Hypophosphatemia	336	13	2	318	49	16

[a] National Cancer Institute Common Terminology Criteria for Adverse Events, Version 3.0
ALP: alkaline phosphatase; ALT: alanine aminotransferase; AST: aspartate aminotransferase

Selected laboratory abnormalities (all grades) that were reported in <10% of patients treated with INLYTA included hemoglobin increased (above the upper limit of normal) (9% for INLYTA versus 1% for sorafenib).

7 DRUG INTERACTIONS

In vitro data indicate that axitinib is metabolized primarily by CYP3A4/5 and, to a lesser extent, CYP1A2, CYP2C19, and uridine diphosphate-glucuronosyltransferase (UGT) 1A1.

7.1 CYP3A4/5 Inhibitors

Co-administration of ketoconazole, a strong inhibitor of CYP3A4/5, increased the plasma exposure of axitinib in healthy volunteers. Co-administration of INLYTA with strong CYP3A4/5

inhibitors should be avoided. Grapefruit or grapefruit juice may also increase axitinib plasma concentrations and should be avoided. Selection of concomitant medication with no or minimal CYP3A4/5 inhibition potential is recommended. If a strong CYP3A4/5 inhibitor must be co-administered, the INLYTA dose should be reduced *[see Dosage and Administration (2.2) and Clinical Pharmacology (12.3)]*.

7.2 CYP3A4/5 Inducers

Co-administration of rifampin, a strong inducer of CYP3A4/5, reduced the plasma exposure of axitinib in healthy volunteers. Co-administration of INLYTA with strong CYP3A4/5 inducers (e.g., rifampin, dexamethasone, phenytoin, carbamazepine, rifabutin, rifapentin, phenobarbital, and St. John's wort) should be avoided. Selection of concomitant medication with no or minimal CYP3A4/5 induction potential is recommended *[see Dosage and Administration (2.2) and Clinical Pharmacology (12.3)]*. Moderate CYP3A4/5 inducers (e.g., bosentan, efavirenz, etravirine, modafinil, and nafcillin) may also reduce the plasma exposure of axitinib and should be avoided if possible.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category D *[see Warnings and Precautions (5.12)]*.

There are no adequate and well-controlled studies with INLYTA in pregnant women. INLYTA can cause fetal harm when administered to a pregnant woman based on its mechanism of action. Axitinib was teratogenic, embryotoxic and fetotoxic in mice at exposures lower than human exposures at the recommended starting dose. If this drug is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to the fetus.

Oral axitinib administered twice daily to female mice prior to mating and through the first week of pregnancy caused an increase in post-implantation loss at all doses tested (≥15 mg/kg/dose, approximately 10 times the systemic exposure (AUC) in patients at the recommended starting dose). In an embryo-fetal developmental toxicity study, pregnant mice received oral doses of 0.15, 0.5 and 1.5 mg/kg/dose axitinib twice daily during the period of organogenesis. Embryo-fetal toxicities observed in the absence of maternal toxicity included malformation (cleft palate) at 1.5 mg/kg/dose (approximately 0.5 times the AUC in patients at the recommended starting dose) and variation in skeletal ossification at ≥0.5 mg/kg/dose (approximately 0.15 times the AUC in patients at the recommended starting dose).

8.3 Nursing Mothers

It is not known whether axitinib is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from INLYTA, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

The safety and efficacy of INLYTA in pediatric patients have not been studied.

Toxicities in bone and teeth were observed in immature mice and dogs administered oral axitinib twice daily for 1 month or longer. Effects in bone consisted of thickened growth plates in mice and dogs at ≥15 mg/kg/dose (approximately 6 and 15 times, respectively, the systemic exposure (AUC) in patients at the recommended starting dose). Abnormalities in growing incisor teeth (including dental caries, malocclusions and broken and/or missing teeth) were observed in mice administered oral axitinib twice daily at ≥5 mg/kg/dose (approximately 1.5 times the AUC in patients at the recommended starting dose). Other toxicities of potential concern to pediatric patients have not been evaluated in juvenile animals.

8.5 Geriatric Use

In a controlled clinical study with INLYTA for the treatment of patients with RCC, 123/359 patients (34%) treated with INLYTA were ≥65 years of age. Although greater sensitivity in some older individuals cannot be ruled out, no overall differences were observed in the safety and effectiveness of INLYTA between patients who were ≥65 years of age and younger.

No dosage adjustment is required in elderly patients *[see Dosage and Administration (2.2) and Clinical Pharmacology (12.3)]*.

8.6 Hepatic Impairment

In a dedicated hepatic impairment trial, compared to subjects with normal hepatic function, systemic exposure following a single dose of INLYTA was similar in subjects with baseline mild hepatic impairment (Child-Pugh class A) and higher in subjects with baseline moderate hepatic impairment (Child-Pugh class B).

No starting dose adjustment is required when administering INLYTA to patients with mild hepatic impairment (Child-Pugh class A). A starting dose decrease is recommended when administering INLYTA to patients with moderate hepatic impairment (Child-Pugh class B) *[see Dosage and Administration (2.2), Warnings and Precautions (5.11), and Clinical Pharmacology (12.3)]*.

INLYTA has not been studied in subjects with severe hepatic impairment (Child-Pugh class C).

8.7 Renal Impairment

No dedicated renal impairment trial for axitinib has been conducted. Based on the population pharmacokinetic analyses, no significant difference in axitinib clearance was observed in patients with pre-existing mild to severe renal impairment (15 mL/min ≤creatinine clearance [CLcr] <89 mL/min) *[see Clinical Pharmacology (12.3)]*. No starting dose adjustment is needed for patients with pre-existing mild to severe renal impairment. Caution should be used in patients with end-stage renal disease (CLcr <15 mL/min).

10 OVERDOSAGE

There is no specific treatment for INLYTA overdose.

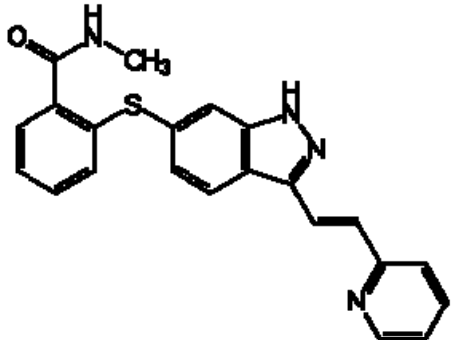
In a controlled clinical study with INLYTA for the treatment of patients with RCC, 1 patient inadvertently received a dose of 20 mg twice daily for 4 days and experienced dizziness (Grade 1).

In a clinical dose finding study with INLYTA, subjects who received starting doses of 10 mg twice daily or 20 mg twice daily experienced adverse reactions which included hypertension, seizures associated with hypertension, and fatal hemoptysis.

In cases of suspected overdose, INLYTA should be withheld and supportive care instituted.

11 DESCRIPTION

INLYTA (axitinib) is a kinase inhibitor. Axitinib has the chemical name *N*-methyl-2-[3-((*E*)-2-pyridin-2-yl-vinyl)-1*H*-indazol-6-ylsulfanyl]-benzamide. The molecular formula is $C_{22}H_{18}N_4OS$ and the molecular weight is 386.47 Daltons. The chemical structure is:



Axitinib is a white to light-yellow powder with a pKa of 4.8. The solubility of axitinib in aqueous media over the range pH 1.1 to pH 7.8 is in excess of 0.2 μg/mL. The partition coefficient (n-octanol/water) is 3.5.

INLYTA is supplied as red, film-coated tablets containing either 1 mg or 5 mg of axitinib together with microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, magnesium stearate, and Opadry® II red 32K15441 as inactive ingredients. The Opadry II red 32K15441 film coating contains lactose monohydrate, HPMC 2910/Hypromellose 15cP, titanium dioxide, triacetin (glycerol triacetate), and red iron oxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

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.

12.2 Pharmacodynamics

The effect of a single oral dose of INLYTA (5 mg) in the absence and presence of 400 mg ketoconazole on the QTc interval was evaluated in a randomized, single-blinded, two-way crossover study in 35 healthy subjects. No large changes in mean QTc interval (i.e., >20 ms) from

placebo were detected up to 3 hours post-dose. However, small increases in mean QTc interval (i.e., <10 ms) cannot be ruled out.

12.3 Pharmacokinetics

The population pharmacokinetic analysis pooled data from 17 trials in healthy subjects and patients with cancer. A two-compartment disposition model with first-order absorption and lag-time adequately describes the axitinib concentration-time profile.

Absorption and Distribution: Following single oral 5-mg dose administration, the median T_{max} ranged from 2.5 to 4.1 hours. Based on the plasma half-life, steady state is expected within 2 to 3 days of dosing. Dosing of axitinib at 5 mg twice daily resulted in approximately 1.4-fold accumulation compared to administration of a single dose. At steady state, axitinib exhibits approximately linear pharmacokinetics within the 1-mg to 20-mg dose range. The mean absolute bioavailability of axitinib after an oral 5 mg dose is 58%.

Compared to overnight fasting, administration of INLYTA with a moderate fat meal resulted in 10% lower AUC and a high fat, high-calorie meal resulted in 19% higher AUC. INLYTA can be administered with or without food *[see Dosage and Administration (2.1)]*.

Axitinib is highly bound (>99%) to human plasma proteins with preferential binding to albumin and moderate binding to α_1-acid glycoprotein. In patients with advanced RCC (n=20), at the 5 mg twice daily dose in the fed state, the geometric mean (CV%) C_{max} and AUC_{0-24} were 27.8 (79%) ng/mL and 265 (77%) ng.h/mL, respectively. The geometric mean (CV%) clearance and apparent volume of distribution were 38 (80%) L/h and 160 (105%) L, respectively.

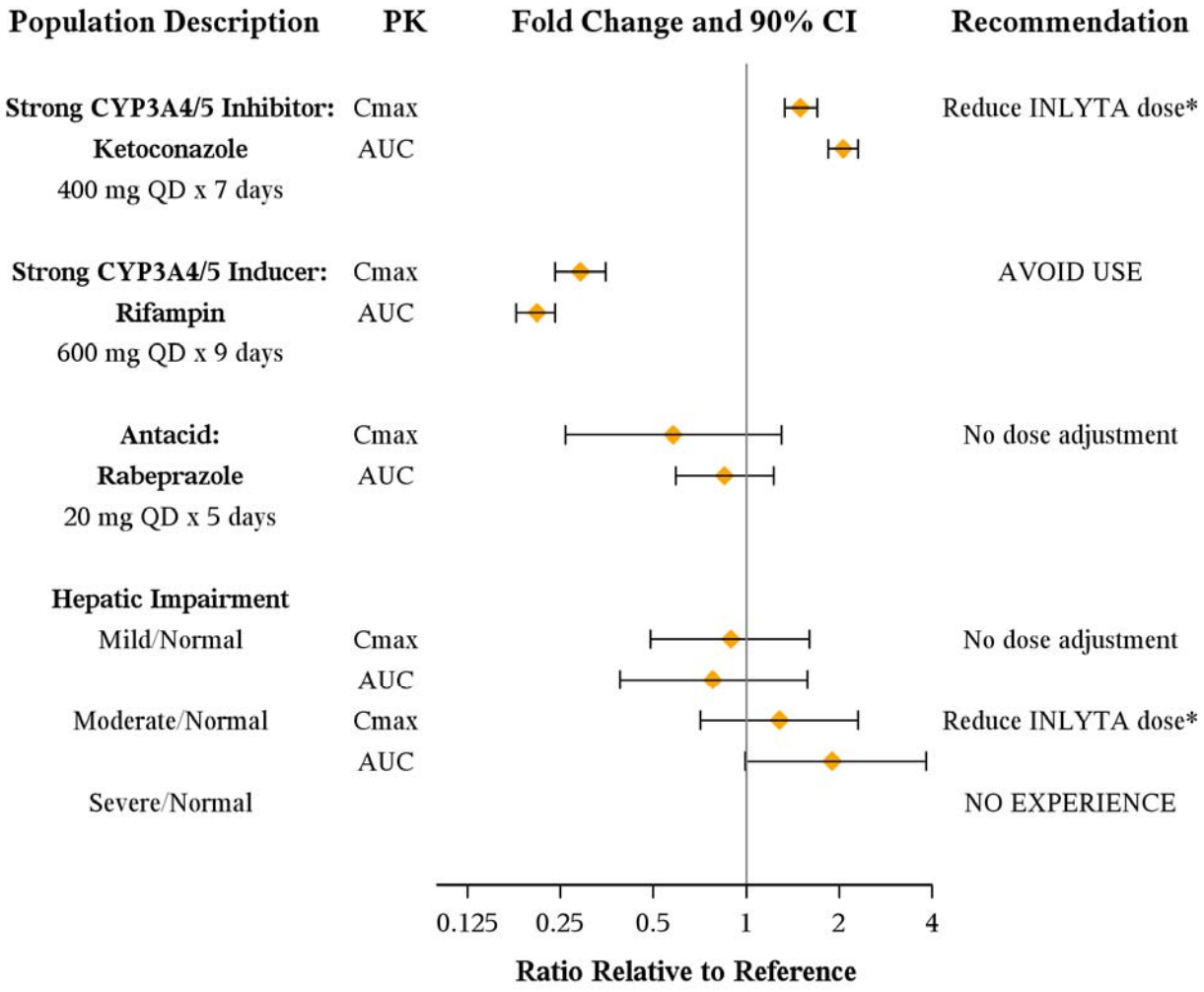
Metabolism and Elimination: The plasma half life of INLYTA ranges from 2.5 to 6.1 hours. Axitinib is metabolized primarily in the liver by CYP3A4/5 and to a lesser extent by CYP1A2, CYP2C19, and UGT1A1. Following oral administration of a 5-mg radioactive dose of axitinib, approximately 41% of the radioactivity was recovered in feces and approximately 23% was recovered in urine. Unchanged axitinib, accounting for 12% of the dose, was the major component identified in feces. Unchanged axitinib was not detected in urine; the carboxylic acid and sulfoxide metabolites accounted for the majority of radioactivity in urine. In plasma, the N-glucuronide metabolite represented the predominant radioactive component (50% of circulating radioactivity) and unchanged axitinib and the sulfoxide metabolite each accounted for approximately 20% of the circulating radioactivity.

The sulfoxide and N-glucuronide metabolites show approximately ≥400-fold less *in vitro* potency against VEGFR-2 compared to axitinib.

Drug-Drug Interactions

Effects of Other Drugs on INLYTA: Axitinib is metabolized primarily in the liver by CYP3A4/5. Additionally, the aqueous solubility of axitinib is pH dependent, with higher pH resulting in lower solubility. The effects of a strong CYP3A4/5 inhibitor, a strong CYP3A4/5 inducer, and an antacid on the pharmacokinetics of axitinib are presented in Figure 1 *[see Dosage and Administration (2.2) and Drug Interactions (7.1, 7.2)]*.

Figure 1. Impact of Co-administered Drugs and Hepatic Impairment on Axitinib Pharmacokinetics



AUC: area under the curve; Cmax: maximum concentration. *See Dosage and Administration (2).

Effects of INLYTA on Other Drugs: *In vitro* studies demonstrated that axitinib has the potential to inhibit CYP1A2 and CYP2C8. However, co-administration of axitinib with paclitaxel, a CYP2C8 substrate, did not increase plasma concentrations of paclitaxel in patients.

In vitro studies indicated that axitinib does not inhibit CYP2A6, CYP2C9, CYP2C19, CYP2D6, CYP2E1, CYP3A4/5, or UGT1A1 at therapeutic plasma concentrations. *In vitro* studies in human hepatocytes indicated that axitinib does not induce CYP1A1, CYP1A2, or CYP3A4/5.

Axitinib is an inhibitor of the efflux transporter P-glycoprotein (P-gp) *in vitro*. However, INLYTA is not expected to inhibit P-gp at therapeutic plasma concentrations.

Pharmacokinetics in Specific Populations

Pediatric Use: INLYTA has not been studied in patients <18 years of age.

Hepatic Impairment: The effects of hepatic impairment on the pharmacokinetics of axitinib are presented in Figure 1 *[see Dosage and Administration (2.2), Warnings and Precautions (5.11), and Use in Specific Populations (8.6)]*.

Renal Impairment: Population pharmacokinetic analysis (based on pre-existing renal function) was carried out in 590 healthy volunteers and patients, including five with severe renal impairment (15 mL/min ≤CLcr <29 mL/min), 64 with moderate renal impairment (30 mL/min ≤CLcr <59 mL/min), and 139 with mild renal impairment (60 mL/min ≤CLcr <89 mL/min). Mild to severe renal impairment did not have meaningful effects on the pharmacokinetics of axitinib. Data from only one patient with end-stage renal disease are available *[see Use in Specific Populations (8.7)]*.

Other Intrinsic Factors: Population pharmacokinetic analyses indicate that there are no clinically relevant effects of age, gender, race, body weight, body surface area, UGT1A1 genotype, or CYP2C19 genotype on the clearance of axitinib.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies have not been conducted with axitinib.

Axitinib was not mutagenic in an *in vitro* bacterial reverse mutation (Ames) assay and was not clastogenic in the *in vitro* human lymphocyte chromosome aberration assay. Axitinib was genotoxic in the *in vivo* mouse bone marrow micronucleus assay.

INLYTA has the potential to impair reproductive function and fertility in humans. In repeat-dose toxicology studies, findings in the male reproductive tract were observed in the testes/epididymis (decreased organ weight, atrophy or degeneration, decreased numbers of germinal cells, hypospermia or abnormal sperm forms, reduced sperm density and count) at ≥15 mg/kg/dose administered orally twice daily in mice (approximately 7 times the systemic exposure (AUC) in patients at the recommended starting dose) and ≥1.5 mg/kg/dose administered orally twice daily in dogs (approximately 0.1 times the AUC in patients at the recommended starting dose). Findings in the female reproductive tract in mice and dogs included signs of delayed sexual maturity, reduced or absent corpora lutea, decreased uterine weights and uterine atrophy at ≥5 mg/kg/dose (approximately 1.5 or 0.3 times the AUC in patients at the recommended starting dose compared to mice and dogs, respectively).

In a fertility study in mice, axitinib did not affect mating or fertility rate when administered orally twice daily to males at any dose tested up to 50 mg/kg/dose following at least 70 days of administration (approximately 57 times the AUC in patients at the recommended starting dose). In female mice, reduced fertility and embryonic viability were observed at all doses tested (≥15 mg/kg/dose administered orally twice daily) following at least 15 days of treatment with axitinib (approximately 10 times the AUC in patients at the recommended starting dose).

14 CLINICAL STUDIES

The safety and efficacy of INLYTA were evaluated in a randomized, open-label, multicenter Phase 3 study. Patients (N=723) with advanced RCC whose disease had progressed on or after

treatment with 1 prior systemic therapy, including sunitinib-, bevacizumab-, temsirolimus-, or cytokine-containing regimens were randomized (1:1) to receive INLYTA (N=361) or sorafenib (N=362). Progression-free survival (PFS) was assessed by a blinded independent central review committee. Other endpoints included objective response rate (ORR) and overall survival (OS).

Of the patients enrolled in this study, 389 patients (54%) had received 1 prior sunitinib-based therapy, 251 patients (35%) had received 1 prior cytokine-based therapy (interleukin-2 or interferon-alfa), 59 patients (8%) had received 1 prior bevacizumab-based therapy, and 24 patients (3%) had received 1 prior temsirolimus-based therapy. The baseline demographic and disease characteristics were similar between the INLYTA and sorafenib groups with regard to age (median 61 years), gender (72% male), race (75% white, 21% Asian), Eastern Cooperative Oncology Group (ECOG) performance status (55% 0, 45% 1), and histology (99% clear cell).

There was a statistically significant advantage for INLYTA over sorafenib for the endpoint of PFS (see Table 3 and Figure 2). There was no statistically significant difference between the arms in OS.

Table 3. Efficacy Results

Endpoint/Study Population	INLYTA	Sorafenib	HR (95% CI)	P-value
Overall ITT	N= 361	N = 362		
Median PFS[a,b] in months (95% CI)	6.7 (6.3, 8.6)	4.7 (4.6, 5.6)	0.67 (0.54, 0.81)	<0.0001[c]
Median OS in months (95% CI)	20.1 (16.7, 23.4)	19.2 (17.5, 22.3)	0.97 (0.80, 1.17)	NS
ORR % (95% CI)	19.4 (15.4, 23.9)	9.4 (6.6, 12.9)	2.06[d] (1.41, 3.00)	-[e]
PFS by prior treatment				
Sunitinib-refractory subgroup	N=194	N=195		
Median, months (95% CI)	4.8 (4.5, 6.4)	3.4 (2.8, 4.7)	0.74 (0.57, 0.96)	-[e]
Cytokine-refractory subgroup	N=126	N=125		
Median, months (95% CI)	12.1 (10.1, 13.9)	6.5 (6.3, 8.3)	0.46 (0.32, 0.68)	-[e]

CI: Confidence interval; HR: Hazard ratio (INLYTA/sorafenib); ITT: Intent to treat; ORR: Objective response rate; NS: Not significant; OS: Overall survival; PFS: Progression-free survival

[a] Time from randomization to progression or death due to any cause, whichever occurs first.

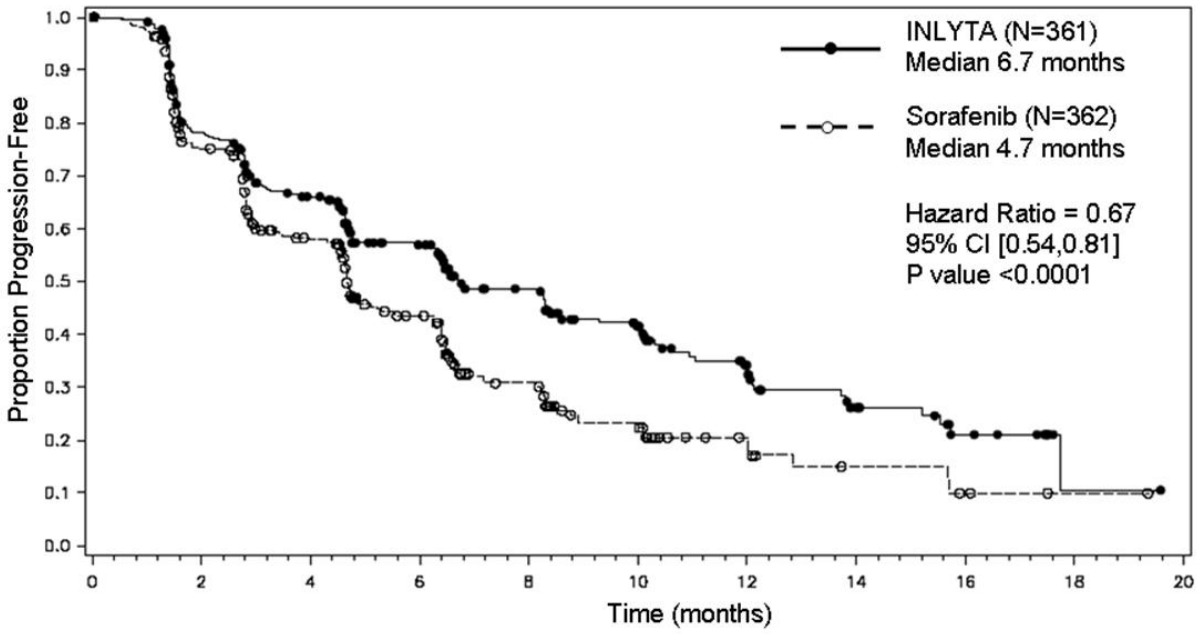
[b] Assessed by independent radiology review according to RECIST.

[c] One-sided p-value from a log-rank test of treatment stratified by ECOG performance status and prior therapy (comparison is considered statistically significant if the one-sided p-value is <0.023).

[d] Risk ratio is used for ORR. A risk ratio >1 indicated a higher likelihood of responding in the axitinib arm; a risk ratio <1 indicated a higher likelihood of responding in the sorafenib arm.

[e] P-value not included since it was not adjusted for multiple testing.

Figure 2. Kaplan-Meier Curve for Progression Free Survival by Independent Assessment (Intent-to-Treat Population)



16 HOW SUPPLIED/STORAGE AND HANDLING

INLYTA tablets are supplied as follows:

1 mg tablets are red film-coated, oval tablets debossed with “Pfizer” on one side and “1 XNB” on the other; available in bottles of 180: NDC 0069-0145-01.

5 mg tablets are red film-coated, triangular tablets debossed with “Pfizer” on one side and “5 XNB” on the other; available in bottles of 60: NDC 0069-0151-11.

Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

See FDA Approved Patient Labeling

17.1 Hypertension

Advise patients that hypertension may develop during INLYTA treatment and that blood pressure should be monitored regularly during treatment *[see Warnings and Precautions (5.1)]*.

17.2 Arterial/Venous Thromboembolic Events

Advise patients that arterial and venous thromboembolic events have been observed during INLYTA treatment and to inform their doctor if they experience symptoms suggestive of thromboembolic events *[see Warnings and Precautions (5.2, 5.3)]*.

17.3 Hemorrhage

Advise patients that INLYTA may increase the risk of bleeding and to promptly inform their doctor of any bleeding episodes *[see Warnings and Precautions (5.4)]*.

17.4 Gastrointestinal Disorders

Advise patients that gastrointestinal disorders such as diarrhea, nausea, vomiting, and constipation may develop during INLYTA treatment and to seek immediate medical attention if they experience persistent or severe abdominal pain because cases of gastrointestinal perforation and fistula have been reported in patients taking INLYTA *[see Warnings and Precautions (5.5) and Adverse Reactions (6.1)]*.

17.5 Abnormal Thyroid Function

Advise patients that abnormal thyroid function may develop during INLYTA treatment and to inform their doctor if symptoms of abnormal thyroid function occur *[see Warnings and Precautions (5.6)]*.

17.6 Wound Healing Complications

Advise patients to inform their doctor if they have an unhealed wound or if they have surgery scheduled *[see Warnings and Precautions (5.7)]*.

17.7 Reversible Posterior Leukoencephalopathy Syndrome

Advise patients to inform their doctor if they have worsening of neurological function consistent with RPLS (headache, seizure, lethargy, confusion, blindness and other visual and neurologic disturbances) *[see Warnings and Precautions (5.8)]*.

17.8 Pregnancy

Advise patients that INLYTA may cause birth defects or fetal loss and that they should not become pregnant during treatment with INLYTA. Both male and female patients should be counseled to use effective birth control during treatment with INLYTA. Female patients should also be advised against breast-feeding while receiving INLYTA *[see Warnings and Precautions (5.12) and Use in Specific Populations (8.3)]*.

17.9 Concomitant Medications

Advise patients to inform their doctor of all concomitant medications, vitamins, or dietary and herbal supplements.

FDA-Approved Patient Labeling

LAB- 0561-1.0

Issued January 2012

PATIENT INFORMATION

INLYTA® (in-ly-ta)
(axitinib)
Tablets

Read this Patient Information before you start taking INLYTA and each time you get a refill. There may be new information. This information does not take the place of talking with your doctor about your medical condition or your treatment.

What is INLYTA?

INLYTA is a prescription medicine used to treat advanced kidney cancer (advanced renal cell carcinoma or RCC) when one prior drug treatment for this disease has not worked.

It is not known if INLYTA is safe or effective in children.

What should I tell my doctor before taking INLYTA?

Before you take INLYTA, tell your doctor if you:

- have high blood pressure
- have thyroid problems
- have liver problems
- have a history of blood clots in your veins or arteries (types of blood vessels), including stroke, heart attack, or change in vision
- have any bleeding problems
- have an unhealed wound
- plan to have surgery. You should stop taking INLYTA at least 24 hours before planned surgery.
- have any other medical conditions

For females, tell your doctor if you:

- are pregnant or plan to become pregnant. Taking INLYTA during pregnancy may cause the death of an unborn baby or birth defects. You should not become pregnant while taking INLYTA. Talk to your doctor if you are pregnant or plan to become pregnant.
- are able to become pregnant. You should use effective birth control during your treatment with INLYTA. Talk to your doctor about birth control methods to prevent pregnancy while you are taking INLYTA.
- are breastfeeding or plan to breastfeed. It is not known if INLYTA passes into your breast milk. You and your doctor should decide if you will take INLYTA or breastfeed. You should not do both.

For males:

- use effective birth control during your treatment with INLYTA. Talk to your doctor about birth control methods.
- if your female partner becomes pregnant while you are taking INLYTA, tell your doctor right away.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. INLYTA and certain other medicines can affect each other causing serious side effects.

Especially tell your doctor if you take:

- dexamethasone
- St. John's Wort (Hypericum perforatum)
- Medicine for:
  - asthma
  - tuberculosis
  - seizures
  - bacterial infections
  - fungal infections
  - depression
  - HIV or AIDS

Ask your doctor or pharmacist if you are not sure if your medicine is one listed above. If you are taking any medicines for the conditions listed above, your doctor might need to prescribe a different medicine or your dose of INLYTA may need to be changed. Talk with your doctor before you start taking any new medicine.

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How should I take INLYTA?

- Take INLYTA exactly as prescribed by your doctor.
- Your doctor may change your dose if needed.
- INLYTA can be taken with or without food.
- Take INLYTA 2 times a day approximately 12 hours apart.
- Swallow INLYTA tablets whole with a glass of water.
- Your doctor should check your blood pressure regularly during treatment with INLYTA.
- If you vomit or miss a dose of INLYTA, take your next dose at your regular time. Do not take two doses at the same time.
- If you take too much INLYTA, call your doctor or go to the nearest hospital emergency room right away.

What should I avoid while taking INLYTA?

- Do not drink grapefruit juice or eat grapefruit. Grapefruit may increase the amount of INLYTA in your blood.

What are the possible side effects of INLYTA?

INLYTA may cause serious side effects, including:

- **High blood pressure (hypertension).** Your doctor should check your blood pressure regularly during treatment with INLYTA. If you develop blood pressure problems, your doctor may prescribe medicine to treat your high blood pressure, lower your dose, or stop your treatment with INLYTA.
- **Thyroid gland problems.** Your doctor should do blood tests to check your thyroid gland function before and during your treatment with INLYTA. Tell your

doctor if you have any of the following symptoms during your treatment with INLYTA:

- tiredness that worsens or that does not go away
- feeling hot or cold
- your voice deepens
- weight gain or weight loss
- hair loss
- muscle cramps and aches

- **Problem with blood clots in your veins or arteries.** Get emergency help and call your doctor if you get any of the following symptoms:
  - chest pain or pressure
  - pain in your arms, back, neck or jaw
  - shortness of breath
  - numbness or weakness on one side of your body
  - trouble talking
  - headache
  - vision changes
- **Bleeding.** INLYTA can cause bleeding which can be serious, and sometimes lead to death. Call your doctor or get medical help if you develop any bleeding, including:
  - unexpected bleeding or bleeding that lasts a long time, such as:
  - unusual bleeding from the gums
  - menstrual bleeding or vaginal bleeding that is heavier than normal
  - bleeding that is severe or you cannot control
  - pink or brown urine
  - red or black stools (looks like tar)
  - bruises that happen without a known cause or get larger
  - cough up blood or blood clots
  - vomit blood or your vomit looks like “coffee grounds”
  - unexpected pain, swelling, or joint pain
  - headaches, feeling dizzy or weak
- **Tear in your stomach or intestinal wall (perforation).** Get medical help right away if you get the following symptoms:
  - severe stomach (abdominal) pain or stomach pain that does not go away
  - vomit blood
  - red or black stools
- **Reversible Posterior Leukoencephalopathy Syndrome (RPLS).** A condition called reversible posterior leukoencephalopathy syndrome (RPLS) can happen while taking INLYTA. Call your doctor right away if you get:
  - headache
  - seizures
  - weakness
  - confusion
  - high blood pressure
  - blindness or change in vision
  - problems thinking
- **Increased protein in your urine.** Your doctor should check your urine for protein before and during your treatment with INLYTA. If you develop protein

in your urine, your doctor may decrease your dose of INLYTA or stop your treatment.
- **Change in liver function.** Your doctor should do blood tests before and during your treatment with INLYTA to check your liver function.

The most common side effects of INLYTA include:
- diarrhea (frequent or loose bowel movements)
- high blood pressure
- tiredness or feeling weak
- decreased appetite
- nausea
- hoarseness
- rash, redness, itching or peeling of your skin on your hands and feet
- decreased weight
- vomiting
- constipation

Tell your doctor if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of INLYTA. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store INLYTA?
- Store INLYTA at room temperature between 68°F to 77°F (20°C to 25°C).

Keep INLYTA and all medicines out of the reach of children.

General information about INLYTA.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use INLYTA for a condition for which it was not prescribed. Do not give INLYTA to other people, even if they have the same symptoms you have. It may harm them.

This Patient Information leaflet summarizes the most important information about INLYTA. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about INLYTA that is written for healthcare professionals.

For more information, go to www.inlyta.com or call 877-744-5675.

What are the ingredients in INLYTA?

Active ingredient: axitinib

Inactive ingredients: microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, magnesium stearate, and Opadry® II red 32K15441. The Opadry II red 32K15441 film coating contains: lactose monohydrate, HPMC 2910/Hypromellose 15cp, titanium dioxide, triacetin (glycerol triacetate), and red iron oxide.

This Patient Information has been approved by the U.S. Food and Drug Administration.

LAB-0438-1.0

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