PT. PFIZER INDONESIA
Local Product Document

Generic Name: Axitinib
Trade Name: INLYTA
CDS Effective Date: May 22, 2025
Supersedes: December 11, 2019

1 NAME OF THE MEDICINAL PRODUCT
INLYTA

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each film-coated tablet contains 1 mg or 5 mg axitinib.

For the full list of excipients, see Section **6.1**.

3 PHARMACEUTICAL FORM
Film-coated tablet.

INLYTA 1 mg film-coated tablets
Red oval film-coated tablet debossed with “Pfizer” on one side and “1 XNB” on the other.

INLYTA 5 mg film-coated tablets
Red triangular film-coated tablet debossed with “Pfizer” on one side and “5 XNB” on the other.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Axitinib is indicated for the treatment of patients with advanced renal cell carcinoma (RCC) of clear cell histology after failure of one prior systemic therapy with sunitinib, cytokine or sorafenib (see also Section **5.1**).

Axitinib should be prescribed by a qualified healthcare professional who is experienced in the use of anti-neoplastic therapy.

4.2 Posology and method of administration
Posology
Treatment with axitinib should be initiated by a physician experienced in the use of anticancer therapies.

The recommended starting oral dose of axitinib is 5 mg twice daily. Administer axitinib doses approximately 12 hours apart with or without food (see Section **5.2**). Axitinib should be swallowed whole with a glass of water.

Treatment should continue as long as clinical benefit is observed or until unacceptable toxicity occurs, that cannot be managed by concomitant medications or dose adjustments.

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.

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

Patients who tolerate the axitinib starting dose of 5 mg twice daily with no adverse reactions >Grade 2 (according to the Common Toxicity Criteria for Adverse Events [CTCAE]) for two consecutive weeks, are normotensive, and are not receiving antihypertensive medication, may have their dose increased to 7 mg twice daily. Subsequently, using the same criteria, patients who tolerate the axitinib dose of 7 mg twice daily, may have their dose increased to a maximum of 10 mg twice daily.

Management of some adverse drug reactions may require temporary or permanent discontinuation and/or dose reduction of axitinib therapy. When dose reduction is necessary, the axitinib dose may be reduced to 3 mg twice daily and further to 2 mg twice daily.

Dose adjustment is not required on the basis of patient age, race, gender, or body weight.

Concomitant strong CYP3A4/5 inhibitors
Co-administration of axitinib with strong CYP3A4/5 inhibitors should be avoided (e.g., ketoconazole, itraconazole, clarithromycin, atazanavir, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, and telithromycin) as they may increase axitinib plasma concentrations. Grapefruit may also increase axitinib plasma concentrations. Selection of an alternate concomitant medication with no or minimal CYP3A4/5 inhibition potential is recommended.

Although axitinib 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 axitinib to approximately half the dose (e.g., from a starting dose of 5 mg twice daily to a reduced dose of 2 mg twice daily) is recommended. If co-administration of the strong inhibitor is discontinued, a return to the axitinib dose used prior to initiation of the strong CYP3A4/5 inhibitor should be considered (after 3-5 half-lives of the inhibitor).

Concomitant strong CYP3A4/5 inducers
Co-administration of axitinib with strong CYP3A4/5 inducers (e.g., rifampin, dexamethasone, phenytoin, carbamazepine, rifabutin, rifapentine, phenobarbital, and *Hypericum perforatum* [also known as St. John's wort]) may decrease axitinib plasma concentrations. Selection of an alternate concomitant medication with no or minimal CYP3A4/5 induction potential is recommended.

Although axitinib dose adjustment has not been studied in patients receiving strong CYP3A4/5 inducers, if a strong CYP3A4/5 inducer must be co-administered, a gradual dose increase of axitinib is recommended. If the dose of axitinib is increased, the patient should be monitored carefully for toxicity. If co-administration of the strong inducer is

discontinued, the axitinib dose should be immediately returned to the dose used prior to initiation of the strong CYP3A4/5 inducer.

Use in pediatrics
The safety and efficacy of axitinib in children (<18 years) have not been established. No data are available.

Use in the elderly (≥65 years)
No dose adjustment is required (see Section **5.2**).

Hepatic impairment
No dose adjustment is required when administering axitinib to patients with mild hepatic impairment (Child-Pugh class A). A dose decrease is recommended when administering axitinib to patients with moderate hepatic impairment (Child-Pugh class B) [e.g., the starting dose should be reduced from 5 mg twice daily to 2 mg twice daily]. Axitinib has not been studied in patients with severe hepatic impairment (Child-Pugh class C) and should not be used in this population (see Sections **4.4** and **5.2**).

Renal impairment
No dose adjustment is required (see Section **5.2**).

Virtually no data are available regarding axitinib treatment in patients with a creatinine clearance of <15 mL/min.

4.3 Contraindications
Hypersensitivity to axitinib or to any of the excipients.

4.4 Special warnings and precautions for use
Specific safety events should be monitored before initiation of, and periodically throughout, treatment with axitinib as described below.

Cardiac failure events
In a controlled clinical study with axitinib for the treatment of patients with RCC, cardiac failure events (including cardiac failure, cardiopulmonary failure, left ventricular dysfunction, and right ventricular failure) were reported in 6/359 patients (1.7%) receiving axitinib and 3/355 patients (0.8%) receiving sorafenib. Grade 3/4 cardiac failure events were observed in 2/359 patients (0.6%) receiving axitinib and 1/355 patients (0.3%) receiving sorafenib. Fatal cardiac failure was reported in 2/359 patients (0.6%) receiving axitinib and 1/355 patients (0.3%) receiving sorafenib.

In clinical studies with axitinib for the treatment of patients with RCC, cardiac failure events (including cardiac failure, cardiac failure congestive, cardiopulmonary failure, left ventricular dysfunction, ejection fraction decreased, and right ventricular failure) were reported in 12/672 patients (1.8%) receiving axitinib. Grade 3/4 cardiac failure events were reported in 7/672 patients (1.0%) and fatal cardiac failure events were reported in 2/672 patients (0.3%) receiving axitinib.

Monitor for signs or symptoms of cardiac failure periodically throughout treatment with axitinib. Management of cardiac failure events may require temporary interruption or permanent discontinuation and/or dose reduction of axitinib therapy.

Hypertension
In a controlled clinical study with axitinib for the treatment of patients with RCC, hypertension was reported in 145/359 patients (40%) receiving axitinib and 103/355 patients (29%) receiving sorafenib. Grade 3 hypertension was observed in 55/359 patients (15%) receiving axitinib and 38/355 patients (11%) receiving sorafenib and Grade 4 hypertension was observed in 1/359 patients (<1%) receiving axitinib and 1/355 patients (<1%) receiving sorafenib. Hypertensive crisis was reported in 2/359 patients (<1%) receiving axitinib and none of the patients (0%) 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 axitinib or sorafenib treatment and blood pressure increases have been observed as early as 4 days after starting axitinib. Hypertension was managed with standard antihypertensive therapy. Discontinuation of axitinib treatment due to hypertension occurred in 1/359 patients (<1%) receiving axitinib and none of the patients (0%) receiving sorafenib.

In pooled clinical studies with axitinib for the treatment of patients with RCC, hypertension was reported in 344/672 patients (51%) receiving axitinib. Grade 3 hypertension was reported in 148/672 patients (22%) receiving axitinib. Grade 4 hypertension was reported in 7/672 patients (1%) receiving axitinib.

Blood pressure should be well-controlled prior to initiating axitinib. Patients should be monitored for hypertension and treated as needed with standard antihypertensive therapy. In the case of persistent hypertension despite use of antihypertensive medications, the axitinib dose should be reduced. For patients who develop severe hypertension, temporarily interrupt axitinib treatment and restart at a lower dose once the patient is normotensive (see Section **4.2**). If axitinib is interrupted, patients receiving antihypertensive medications should be monitored for hypotension.

In case of severe or persistent arterial hypertension and symptoms suggestive of posterior reversible encephalopathy syndrome (see below), a diagnostic brain magnetic resonance image (MRI) should be considered.

Aneurysms and artery dissections
The use of Vascular Endothelial Growth Factor (VEGF) pathway inhibitors in patients with or without hypertension may promote the formation of aneurysms and/or artery dissections. Before initiating axitinib, this risk should be carefully considered in patients with risk factors such as hypertension or history of aneurysm.

In pooled clinical studies with axitinib for the treatment of patients with RCC, aneurysms and artery dissections were not reported in patients receiving axitinib.

Thyroid dysfunction
In a controlled clinical study with axitinib for the treatment of patients with RCC, hypothyroidism was reported in 69/359 patients (19%) receiving axitinib and 29/355 patients (8%) receiving sorafenib. Hyperthyroidism was reported in 4/359 patients (1%) receiving axitinib 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 axitinib and 25/232 patients (11%) receiving sorafenib.

In pooled clinical studies with axitinib for the treatment of patients with RCC, hypothyroidism was reported in 165/672 patients (25%) receiving axitinib. Hyperthyroidism was reported in 11/672 patients (2%) receiving axitinib.

Monitor thyroid function before initiation of, and periodically throughout, treatment with axitinib. Hypothyroidism and hyperthyroidism should be treated according to standard medical practice to maintain euthyroid state.

Arterial thromboembolic events
In a controlled clinical study with axitinib for the treatment of patients with RCC, Grade 3/4 arterial thromboembolic events were reported in 4/359 patients (1%) receiving axitinib and 4/355 patients (1%) receiving sorafenib. The most frequent arterial thromboembolic event was transient ischemic attack (1%). Fatal cerebrovascular accident was reported in 1/359 patients (<1%) receiving axitinib.

In pooled clinical studies with axitinib for the treatment of patients with RCC, arterial thromboembolic events were reported in 19/672 patients (3%) receiving axitinib. Grade 3 arterial thromboembolic events were reported in 8/672 patients (1%). Grade 4 arterial thromboembolic events were reported in 9/672 patients (1%). Fatal arterial thromboembolic events were reported in 2 patients (<1%) receiving axitinib.

In monotherapy studies with axitinib, arterial thromboembolic events (including transient ischemic attack, cerebrovascular accident, myocardial infarction, and retinal artery occlusion) were reported in 16/699 patients (2%).

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

Venous thromboembolic events
In a controlled clinical study with axitinib for the treatment of patients with RCC, venous thromboembolic events were reported in 11/359 patients (3%) receiving axitinib and 2/355 patients (1%) receiving sorafenib. Grade 3/4 venous thromboembolic events were reported in 9/359 patients (3%) receiving axitinib (including pulmonary embolism, deep vein thrombosis, and retinal-vein occlusion/thrombosis) and 2/355 patients (1%) receiving sorafenib. Fatal pulmonary embolism was reported in 1/359 patients (<1%) receiving axitinib and none of the patients (0%) receiving sorafenib.

In pooled clinical studies with axitinib for the treatment of patients with RCC, venous thromboembolic events were reported in 19/672 patients (3%) receiving axitinib. Grade 3 venous thromboembolic events were reported in 6/672 patients (1%). Grade 4 venous thromboembolic events were reported in 8/672 patients (1%). Fatal venous thromboembolic events were reported in 1/672 patients (<1%) receiving axitinib.

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

Elevation of hemoglobin or hematocrit
Increases in hemoglobin or hematocrit, reflective of increases in red blood cell mass, may occur during treatment with axitinib. An increase in red blood cell mass may increase the risk of thromboembolic events.

Elevated hemoglobin above the upper limit of normal (ULN) was observed in 31/320 patients (10%) receiving axitinib and 3/316 patients (1%) receiving sorafenib.

Monitor hemoglobin or hematocrit before initiation of, and periodically throughout, treatment with axitinib. If hemoglobin or hematocrit becomes elevated above the normal level, patients should be treated according to standard medical practice to decrease hemoglobin or hematocrit to an acceptable level.

Hemorrhage
In a controlled clinical study with axitinib for the treatment of patients with RCC, in which patients with untreated brain metastasis were excluded, hemorrhagic events were reported in 58/359 patients (16%) receiving axitinib and 64/355 patients (18%) receiving sorafenib. The most common hemorrhagic events in patients treated with axitinib were epistaxis (6%), hematuria (3%), hemoptysis (2%), and rectal hemorrhage (2%). Grade 3/4 hemorrhagic events were reported in 5/359 patients (1%) receiving axitinib (including cerebral hemorrhage, hematuria, hemoptysis, lower gastrointestinal hemorrhage, and melaena) and 11/355 (3%) patients receiving sorafenib. Fatal hemorrhage was reported in 1/359 patients (<1%) receiving axitinib (gastric hemorrhage) and 3/355 patients (1%) receiving sorafenib.

In pooled clinical studies with axitinib for the treatment of patients with RCC, hemorrhagic events were reported in 173/672 patients (26%) receiving axitinib. Grade 3 hemorrhagic events were reported in 20/672 patients (3%). Grade 4 hemorrhagic events were reported in 7/672 patients (1%) and fatal hemorrhagic events were reported in 3/672 patients (<1%) receiving axitinib.

Axitinib 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 axitinib dose.

Gastrointestinal perforation and fistula formation
In a controlled clinical study with axitinib for the treatment of patients with RCC, gastrointestinal perforation was reported in 1/359 patients (<1%) receiving axitinib and none of the patients (0%) receiving sorafenib. In addition to cases of gastrointestinal perforation, fistulas were reported in 2/359 patients (1%) receiving axitinib and 1/355 patients (<1%) receiving sorafenib. In pooled clinical studies with axitinib for the treatment of patients with RCC, gastrointestinal perforation and fistula were reported in 13/672 patients (2%) receiving axitinib. In monotherapy studies with axitinib (N=699), fatal gastrointestinal perforation was reported in 1/699 patient (<1%). 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 axitinib.

Wound healing complications
No formal studies of the effect of axitinib on wound healing have been conducted.

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

Reversible posterior leukoencephalopathy syndrome
In a controlled clinical study with axitinib for the treatment of patients with RCC, reversible posterior leukoencephalopathy syndrome (RPLS) was reported in 1/359 patients (<1%) receiving axitinib and none of the patients (0%) receiving sorafenib.

In pooled clinical studies with axitinib for the treatment of patients with RCC, RPLS was reported in 2/672 patients (<1%) receiving axitinib.

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. In patients with signs/symptoms of RPLS, temporarily interrupt or permanently discontinue axitinib. The safety of reinitiating axitinib therapy in patients previously experiencing RPLS is not known.

Proteinuria
In a controlled clinical study with axitinib for the treatment of patients with RCC, proteinuria was reported in 39/359 patients (11%) receiving axitinib and 26/355 patients (7%) receiving sorafenib. Grade 3 proteinuria was reported in 11/359 patients (3%) receiving axitinib and 6/355 patients (2%) receiving sorafenib.

In pooled clinical studies with axitinib for the treatment of patients with RCC, proteinuria was reported in 142/672 patients (21%) receiving axitinib. Grade 3 proteinuria was reported in 32/672 patients (5%) receiving axitinib. Grade 4 proteinuria was reported in 1/672 patients (<1%) receiving axitinib.

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

Elevation of liver enzymes
In a clinical dose-finding study, concurrent elevations of alanine aminotransferase [ALT] (12 times the ULN) and bilirubin (2.3 times the ULN), considered to be drug-related hepatotoxicity, were observed in 1 patient who received axitinib at a starting dose of 20 mg twice daily (4 times the recommended starting dose). In a controlled clinical study with axitinib for the treatment of patients with RCC, no concurrent elevations of ALT (>3 times the ULN) and bilirubin (>2 times the ULN) were observed for axitinib (N=359) or sorafenib (N=355).

Monitor liver function tests before initiation of, and periodically throughout, treatment with axitinib.

Hepatic impairment
In clinical studies with axitinib, the systemic exposure to axitinib was approximately 2-fold 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 axitinib to patients with moderate hepatic impairment (Child-Pugh class B). Axitinib has not been studied in patients with severe hepatic impairment (Child-Pugh class C).

4.5 Interaction with other medicinal products and other forms of interaction

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.

CYP3A4/5 inhibitors
Ketoconazole, a strong inhibitor of CYP3A4/5, administered at a dose of 400 mg once daily for 7 days, increased the mean area under the curve (AUC) 2-fold and C_{max} 1.5-fold of a single 5-mg oral dose of axitinib in healthy volunteers. Co-administration of axitinib with strong CYP3A4/5 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, atazanavir, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, and telithromycin) should be avoided. Grapefruit may also increase axitinib plasma concentrations. 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 axitinib dose should be reduced (see Section **4.2**).

CYP3A4/5 inducers
Rifampin, a strong inducer of CYP3A4/5, administered at a dose of 600 mg once daily for 9 days, reduced the mean AUC by 79% and C_{max} by 71% of a single 5-mg dose of axitinib in healthy volunteers. Co-administration of axitinib with strong CYP3A4/5 inducers (e.g., rifampin, dexamethasone, phenytoin, carbamazepine, rifabutin, rifapentine, phenobarbital, and *Hypericum perforatum* [also known as St. John's wort]) should be avoided. Selection of concomitant medication with no or minimal CYP3A4/5

induction potential is recommended. 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 (see Section **4.2**).

CYP1A2 and CYP2C19 inhibitors
CYP1A2 and CYP2C19 constitute minor (<10%) pathways in axitinib metabolism. The effect of strong inhibitors of these isozymes on axitinib pharmacokinetics has not been studied. Caution should be exercised due to the risk of increased axitinib plasma concentrations in patients taking strong inhibitors of these isozymes.

CYP1A2 induction by smoking
CYP1A2 constitutes a minor (<10%) pathway in axitinib metabolism. The effect of smoking related CYP1A2 induction on axitinib pharmacokinetics has not been fully characterised. The risk of decreased axitinib plasma concentrations should be considered when administering axitinib to smokers.

***In vitro* studies of CYP and UGT inhibition and induction**
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 indicated that axitinib has a potential to inhibit CYP1A2. Therefore, co-administration of axitinib with CYP1A2 substrates may result in increased plasma concentrations of CYP1A2 substrates (e.g., theophylline).

In vitro studies also indicated that axitinib has the potential to inhibit CYP2C8. However, co-administration of axitinib with paclitaxel, a known CYP2C8 substrate, did not result in increased plasma concentrations of paclitaxel in patients with advanced cancer, indicating lack of clinical CYP2C8 inhibition.

In vitro studies in human hepatocytes also indicated that axitinib does not induce CYP1A1, CYP1A2, or CYP3A4/5. Therefore co-administration of axitinib is not expected to reduce the plasma concentration of co-administered CYP1A1, CYP1A2, or CYP3A4/5 substrates *in vivo*.

***In vitro* studies with P-glycoprotein**
In vitro studies indicated that axitinib inhibits P-glycoprotein. However, axitinib is not expected to inhibit P-glycoprotein at therapeutic plasma concentrations. Therefore, co-administration of axitinib is not expected to increase the plasma concentration of digoxin, or other P-glycoprotein substrates, *in vivo*.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential
Women of childbearing potential must use effective contraception during and up to 1 week after treatment.

Pregnancy
Axitinib may cause fetal harm when administered to a pregnant woman. Axitinib was teratogenic, embryotoxic and fetotoxic in mice at exposures lower than human exposure at the recommended starting dose. 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 dose 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) (see Section **5.3**).

There are no adequate and well-controlled studies in pregnant women using axitinib. Women of childbearing potential should be advised to avoid becoming pregnant while receiving axitinib. Axitinib should not be used during pregnancy unless the clinical condition of the woman requires treatment with this medicinal product. 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.

Lactation
No studies have been conducted in humans to assess the effect of axitinib on milk production, its presence in breast milk, or its effects on the breast-fed child. It is unknown whether axitinib is excreted in human milk. A risk to suckling child cannot be excluded.

Since many drugs are commonly excreted in human milk, and because of the potential for serious adverse reactions in nursing infants due to exposure to axitinib, a decision should be made whether to discontinue nursing or to discontinue axitinib, taking into account the benefit of breast feeding for child and the benefit of therapy for the woman.

Fertility
Based on non-clinical findings, axitinib has the potential to impair reproductive function and fertility in humans (see Section **5.3**).

4.7 Effects on ability to drive and use machines
No studies on the effect of axitinib on the ability to drive and use machines have been performed. Patients should be advised that they may experience events such as dizziness and/or fatigue during treatment with axitinib.

4.8 Undesirable effects
The data described below reflect exposure to axitinib in 672 patients with advanced RCC who participated in the pivotal randomized clinical study or 4 additional studies with axitinib in patients with advanced RCC and from post-marketing experience.

The median duration of treatment was 6.4 months (range 0.03 to 22.0) for patients who received axitinib 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 event occurred in 199/359 patients (55%) receiving axitinib and 220/355 patients (62%) receiving sorafenib. Permanent discontinuation due to an adverse event occurred in 33/359 patients (9%) receiving axitinib and 46/355 patients (13%) receiving sorafenib.

The most common (≥20%) adverse reactions observed following treatment with axitinib were diarrhea, hypertension, fatigue, decreased appetite, nausea, weight decreased, dysphonia, palmar-plantar erythrodysesthesia (hand-foot) syndrome, haemorrhage, hypothyroidism, vomiting, proteinuria, cough, and constipation.

The following risks, including appropriate action to be taken, are discussed in greater detail in Section **4.4** cardiac failure events, hypertension, aneurysms and artery dissections, thyroid dysfunction, arterial thromboembolic events, venous thromboembolic events, elevation of hemoglobin or hematocrit, haemorrhage, gastrointestinal perforation and fistula formation, wound healing complications, RPLS, proteinuria, and elevation of liver enzymes.

Table 1 presents adverse reactions reported in patients who received axitinib

The adverse reactions are listed by system organ class, frequency category and grade of severity. Frequency categories are defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

Table 1. Adverse Reactions Reported in Patients with Advanced RCC who Received Axitinib

System Organ Class	ADR Term[a,b]	Axitinib (N=672) Frequency			Category[c]
		All Grades (%)	Grade 3 (%)	Grade 4 (%)	
Blood and Lymphatic System Disorders	Anaemia	6.3	1.2	0.4	Common
	Thrombocytopenia	1.6	0.1	0.0	
	Polycythaemia	1.5	0.1	0.0	
	Neutropenia	0.3	0.1	0.0	Uncommon
	Leukopenia	0.4	0.0	0.0	
Endocrine Disorders	Hypothyroidism	24.6	0.3	0.0	Very Common
	Hyperthyroidism	1.6	0.1	0.1	Common
Metabolism and Nutrition Disorders	Decreased appetite	39.0	3.6	0.3	Very Common
	Dehydration	6.7	3.1	0.3	Common
	Hyperkalaemia	2.7	1.2	0.1	
	Hypercalcaemia	2.2	0.1	0.3	
Nervous System Disorders	Headache	16.2	0.7	0.0	Very Common
	Dysgeusia	11.5	0.0	0.0	
	Dizziness	9.1	0.6	0.0	Common

	Reversible posterior leukoencephalopathy syndrome[d]	0.3	0.1	0.0	Uncommon
Ear and Labyrinth Disorders	Tinnitus	3.1	0.0	0.0	Common
Cardiac Disorders	Cardiac failure events[e*]	1.8	0.3	0.7	Common
Vascular Disorders	Aneurysms and artery dissections[m*]	-	-	-	Not Known
	Hypertension[f]	51.2	22.0	1.0	Very Common
	Haemorrhage[g*]	25.7	3.0	1.0	
	Venous thromboembolic events[h*]	2.8	0.9	1.2	Common
	Arterial thrombotic events[i*]	2.8	1.2	1.3	
	Hypertensive crisis	0.3	0.1	0.1	Uncommon
Respiratory, Thoracic and Mediastinal Disorders	Dyspnoea[*]	17.1	3.6	0.6	Very Common
	Cough	20.4	0.6	0.0	
	Dysphonia	32.7	0.0	0.1	
	Oropharyngeal pain	7.4	0.0	0.0	Common
Gastrointestinal Disorders	Pancreatitis[l,m*]	-	-	-	Not Known
	Diarrhoea	55.4	10.1	0.1	Very Common
	Vomiting	23.7	2.7	0.1	
	Nausea	33.0	2.2	0.1	
	Abdominal pain	14.7	2.5	0.3	
	Stomatitis	15.5	1.8	0.0	
	Constipation	20.2	1.0	0.0	
	Dyspepsia	11.2	0.1	0.0	
	Upper abdominal pain	9.4	0.9	0.0	Common
	Haemorrhoids	3.3	0.0	0.0	
	Glossodynia	2.8	0.0	0.0	
	Gastrointestinal perforation and fistula[j]	1.9	0.9	0.3	
	Flatulence	4.5	0.0	0.0	
Hepatobiliary Disorders	Hyperbilirubinaemia	1.3	0.1	0.1	Common
Skin & Subcutaneous Tissue Disorders	Palmar-plantar erythrodysaesthesia (hand-foot syndrome)	32.1	7.6	0.0	Very Common
	Rash	14.3	0.1	0.0	
	Dry skin	10.1	0.1	0.0	
	Erythema	3.7	0.0	0.0	Common
	Pruritus	6.0	0.0	0.0	
	Alopecia	5.7	0.0	0.0	
Musculoskeletal, Connective Tissue and Bone Disorders	Arthralgia	17.7	1.9	0.3	Very Common
	Pain in extremity	14.1	1.0	0.3	
	Myalgia	8.2	0.6	0.1	Common
Renal and Urinary Disorders	Proteinuria[k]	21.1	4.8	0.1	Very Common
	Renal failure	1.6	0.9	0.1	Common
	Fatigue	45.1	10.6	0.3	Very Common

General Disorders and Administration Site Conditions	Asthenia*	13.8	2.8	0.3	
	Mucosal inflammation	13.7	1.0	0.0	
Investigations	Weight decreased	32.7	4.9	0.0	Very Common
	Thyroid stimulating hormone increased	7.9	0.0	0.0	Common
	Lipase increased	3.7	0.7	0.7	
	Blood creatinine increased	5.7	0.4	0.0	
	Alanine aminotransferase increased	6.5	1.2	0.0	
	Blood alkaline phosphatase increased	4.8	0.3	0.0	
	Aspartate aminotransferase increased	6.1	1.0	0.0	
	Amylase increased	3.4	0.6	0.4	

*Includes fatal events.
[a] Adverse reactions are listed according to treatment-emergent, all-causality frequency.
[b] National Cancer Institute Common Terminology Criteria for Adverse Events, Version 3.0.
[c] Frequency categories are based on the "all grades" values.
[d] Reversible posterior leukoencephalopathy syndrome includes the following preferred term: Leukoencephalopathy.
[e] Cardiac failure events includes the following preferred terms: cardiac failure, cardiac failure congestive, cardiopulmonary failure, ejection fraction decreased, left ventricular dysfunction and right ventricular failure.
[f] Hypertension includes the following preferred terms: accelerated hypertension, blood pressure increased, hypertension and hypertensive crisis.
[g] Haemorrhage includes the following preferred terms: activated partial thromboplastin time prolonged, anal haemorrhage, arterial haemorrhage, blood urine present, central nervous system haemorrhage, cerebral haemorrhage, coagulation time prolonged, conjunctival haemorrhage, contusion, diarrhea haemorrhagic, dysfunctional uterine bleeding, epistaxis, gastric haemorrhage, gastrointestinal haemorrhage, gingival bleeding, haematemesis, haematochezia, haematocrit decreased, haematoma, haematuria, haemoglobin decreased, haemoptysis, haemorrhage, haemorrhage coronary artery, haemorrhage urinary tract, haemorrhoidal haemorrhage, haemostasis, increased tendency to bruise, international normalized ratio increased, lower gastrointestinal haemorrhage, melaena, petechiae, pharyngeal haemorrhage, prothrombin time prolonged, pulmonary haemorrhage, purpura, rectal haemorrhage, red blood cell count decreased, renal haemorrhage, scleral haemorrhage, scrotal haematocoele, splenic haematoma, splinter haemorrhage, subarachnoid haemorrhage, tongue haemorrhage, upper gastrointestinal haemorrhage and vaginal haemorrhage.
[h] Venous thromboembolic events includes the following preferred terms: Budd-Chiari syndrome, deep vein thrombosis, jugular vein thrombosis, pelvic venous thrombosis, pulmonary embolism, retinal vein occlusion, retinal vein thrombosis, subclavian vein thrombosis, venous thrombosis, and venous thrombosis limb.
[i] Arterial thrombotic events includes the following preferred terms: acute myocardial infarction, embolism, myocardial infarction, retinal artery occlusion and transient ischaemic attack.
[j] Gastrointestinal perforation and fistula includes the following preferred terms: abdominal abscess, anal abscess, anal fistula, fistula, gastrointestinal anastomotic leak, gastrointestinal perforation, large intestine perforation, oesophagobronchial fistula and peritonitis.
[k] Proteinuria includes the following preferred terms: protein urine, protein urine present and proteinuria.
[l] Pancreatitis includes the following preferred terms: pancreatitis and pancreatitis acute.
[m] Identified during post-marketing use of axitinib; no cases were identified in the clinical study pool presented in the table.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:
Pusat Farmakovigilans/MESO Nasional
Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif
Badan Pengawas Obat dan Makanan
Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560
Email: pv-center@pom.go.id
Phone: +62-21-4244691 Ext.1079

Website: https://e-meso.pom.go.id/ADR

PT Pfizer Indonesia
Email: IDN.AEReporting@pfizer.com
Website: www.pfizersafetyreporting.com

4.9 Overdose

There is no specific treatment for axitinib overdose.

In a controlled clinical study with axitinib 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 axitinib, 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, axitinib should be withheld and supportive care instituted.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antineoplastic agents, protein kinase inhibitors, ATC code: L01EK01

Mechanism of action

Axitinib is a potent and selective tyrosine kinase inhibitor of vascular endothelial growth factor receptor (VEGFR)-1, VEGFR-2, and VEGFR-3. These receptors are implicated in pathologic angiogenesis, tumor growth, and metastatic progression of cancer. Axitinib has been shown to potently inhibit VEGF-mediated endothelial cell proliferation and survival. Axitinib inhibited the phosphorylation of VEGFR-2 in xenograft tumor vasculature that expressed the target *in vivo* and produced tumor growth delay, regression, and inhibition of metastases in many experimental models of cancer.

Pharmacodynamics effects

In a randomized, 2-way crossover study, 35 healthy subjects were administered a single oral dose of axitinib (5 mg) in the absence and presence of 400 mg ketoconazole for 7 days. Results of this study indicated that axitinib plasma exposures up to 2-fold greater than the therapeutic levels expected following a 5 mg dose did not produce clinically-significant QT interval prolongation.

Clinical efficacy

The safety and efficacy of axitinib 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 axitinib (n=361) or sorafenib (n=362). The primary endpoint, progression-free

survival (PFS), was assessed using a blinded independent central review. Secondary 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 axitinib and sorafenib groups with regard to age, gender, race, Eastern Cooperative Oncology Group (ECOG) performance status, geographic region, and prior treatment.

In the overall patient population and the two main subgroups (prior sunitinib treatment and prior cytokine treatment), there was a statistically significant advantage for axitinib over sorafenib for the primary endpoint of PFS (see Table 2 and Figures 1, 2 and 3). The magnitude of median PFS effect was different in the subgroups by prior therapy. Two of the subgroups were too small to give reliable results (prior temsirolimus treatment or prior bevacizumab treatment). There were no statistically significant differences between the arms in OS in the overall population or in the subgroups by prior therapy.

Table 2. Efficacy Results

Endpoint/Study Population	Axitinib	Sorafenib	HR (95% CI)	p-value
Overall ITT	**N = 361**	**N = 362**		
Median PFS[a,b] in months (95% CI)	6.8 (6.4, 8.3)	4.7 (4.6, 6.3)	0.67 (0.56, 0.81)	<0.0001[c]
Median OS[d] in months (95% CI)	20.1 (16.7, 23.4)	19.2 (17.5, 22.3)	0.97 (0.80, 1.17)	0.374[c]
ORR[b,e] % (95% CI)	19.4 (15.4, 23.9)	9.4 (6.6, 12.9)	2.06[f] (1.41, 3.00)	0.0001[g]
Prior sunitinib treatment	**N = 194**	**N = 195**		
Median PFS[a,b] in months (95% CI)	4.8 (4.5, 6.5)	3.4 (2.8, 4.7)	0.74 (0.58, 0.94)	0.0063[h]
Median OS[d] in months (95% CI)	15.2 (12.8, 18.3)	16.5 (13.7, 19.2)	1.00 (0.78, 1.27)	NS
ORR [b,e] % (95% CI)	11.3 (7.2, 16.7)	7.7 (4.4, 12.4)	1.48[f] (0.79, 2.75)	NS
Prior cytokine treatment	**N = 126**	**N = 125**		
Median PFS[a,b] in months (95% CI)	12.0 (10.1, 13.9)	6.6 (6.4, 8.3)	0.52 (0.38, 0.72)	<0.0001[h]
Median OS[d] in months (95% CI)	29.4 (24.5, NE)	27.8 (23.1, 34.5)	0.81 (0.56, 1.19)	NS
ORR[b,e] % (95% CI)	32.5 (24.5, 41.5)	13.6 (8.1, 20.9)	2.39[f] (1.43-3.99)	0.0002[i]

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

[a] Time from randomization to progression or death due to any cause, whichever occurs first. Cutoff date: 03 June 2011.

[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.

[d] Cutoff date: 01 November 2011.

[e] Cutoff date: 31 August 2010.

[f] 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.

[g] One-sided p-value from Cochran-Mantel-Haenszel test of treatment stratified by ECOG performance status and prior therapy.

[h] One-sided p-value from a log-rank test of treatment stratified by ECOG performance status.

[i] One-sided p-value from Cochran-Mantel-Haenszel test of treatment stratified by ECOG performance status.

Figure 1: Kaplan-Meier curve for progression-free survival by independent assessment for the overall population

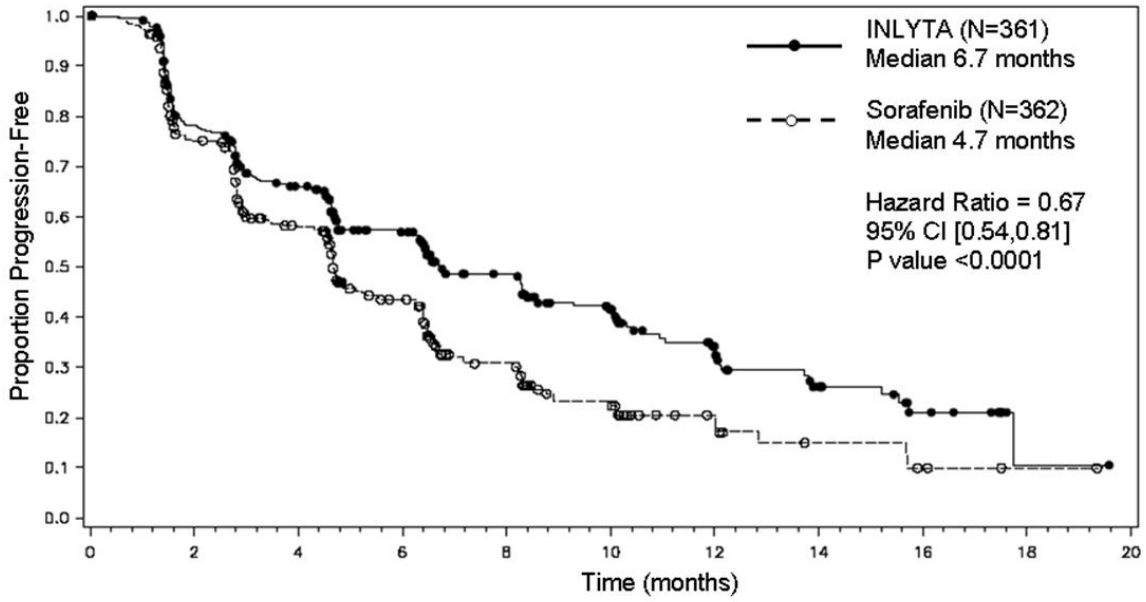


Figure 2: Kaplan-Meier curve of progression-free survival by independent assessment for the prior sunitinib subgroup

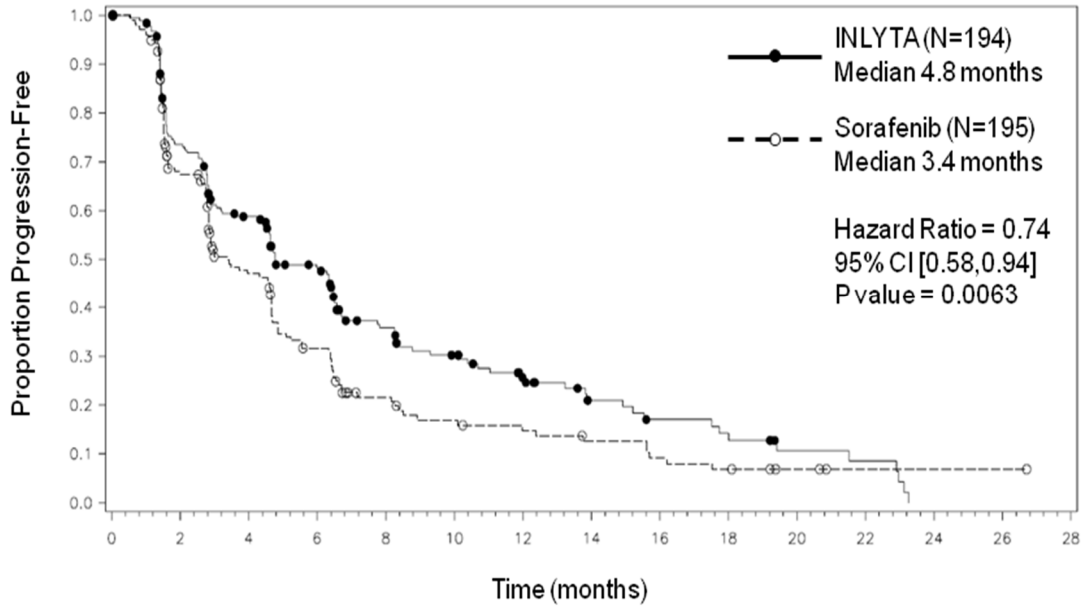
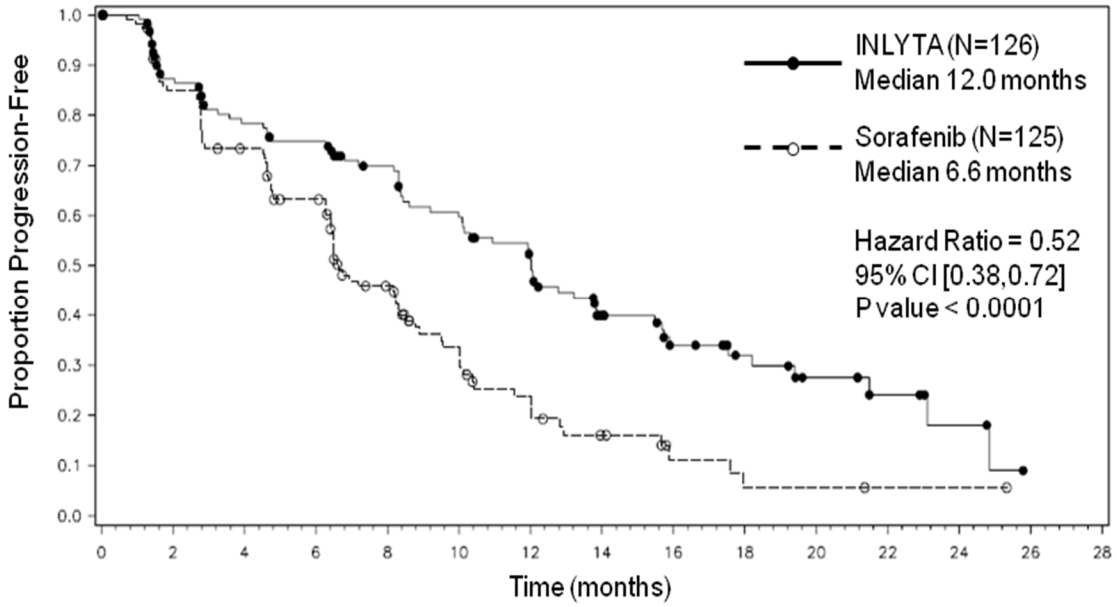


Figure 3: Kaplan-Meier curve of progression-free survival by independent assessment for the prior cytokine subgroup



Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with axitinib in all subsets of the paediatric population for treatment of kidney and renal pelvis carcinoma (excluding nephroblastoma, nephroblastomatosis, clear cell sarcoma, mesoblastic nephroma, renal medullary carcinoma and rhabdoid tumour of the kidney) (see Section **4.2** for information on paediatric use).

5.2 Pharmacokinetic properties

After oral administration of axitinib tablets, the mean absolute bioavailability is 58% compared to intravenous administration. The plasma half-life of axitinib ranges from 2.5 to 6.1 hours. Dosing of axitinib at 5 mg twice daily resulted in <2-fold accumulation compared to administration of a single dose. Based on the short half-life of axitinib, steady state is expected within 2 to 3 days of the initial dose.

Absorption and distribution

Peak axitinib concentrations in plasma are generally reached within 4 hours following oral administration of axitinib with the median T_{max} ranging from 2.5 to 4.1 hours. Administration of axitinib with a moderate fat meal resulted in 10% lower exposure compared to overnight fasting. A high fat, high-calorie meal resulted in 19% higher exposure compared to overnight fasting. Axitinib may be administered with or without food.

The average C_{max} and AUC increased proportionally over an axitinib dosing range of 5 to 10 mg. *In vitro* binding of axitinib to human plasma proteins is >99% with preferential binding to albumin and moderate binding to α_1-acid glycoprotein. At the 5 mg twice daily

dose in the fed state, the geometric mean peak plasma concentration and 24-hour AUC were 27.8 ng/mL and 265 ng h/mL, respectively in patients with advanced RCC. The geometric mean oral clearance and apparent volume of distribution were 38 L/h and 160 L, respectively.

Metabolism and elimination
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, 30%-60% of the radioactivity was recovered in feces and 23% of the radioactivity 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 and 8000-fold less *in vitro* potency, respectively, against VEGFR-2 compared to axitinib.

Special populations
Gender, race and age
Population pharmacokinetic analyses in patients with advanced cancer (including advanced RCC) and healthy volunteers indicate that there are no clinically relevant effects of age, gender, body weight, race, renal function, UGT1A1 genotype, or CYP2C19 genotype.

Pediatric population
Axitinib has not been studied in patients <18 years of age.

Hepatic impairment
In vitro and *in vivo* data indicate that axitinib is primarily metabolized by the liver. Compared to subjects with normal hepatic function, systemic exposure following a single dose of axitinib was similar in subjects with mild hepatic impairment (Child-Pugh class A) and higher (approximately 2-fold) in subjects with moderate hepatic impairment (Child-Pugh class B). Axitinib has not been studied in subjects with severe hepatic impairment (Child-Pugh class C).

Renal impairment
Unchanged axitinib is not detected in the urine.

Axitinib has not been studied in subjects with renal impairment. In clinical studies with axitinib for the treatment of patients with RCC, patients with serum creatinine >1.5 times the ULN or calculated creatinine clearance <60 mL/min were excluded. Population pharmacokinetic analyses have shown that axitinib clearance was not altered in subjects with renal impairment and no dose adjustment of axitinib is required.

5.3 Preclinical safety data

Repeat dose toxicity

Major toxicity findings in mice and dogs following repeated dosing for up to 9 months were the gastrointestinal, haematopoietic, reproductive, skeletal and dental systems, with No Observed Adverse Effect Levels (NOAEL) approximately equivalent to or below expected human exposure at the recommended clinical starting dose (based on AUC levels).

Carcinogenicity

Carcinogenicity studies have not been performed with axitinib.

Genotoxicity

Axitinib was tested using a series of genetic toxicology assays consisting of *in vitro* bacterial reverse mutation (Ames), human lymphocyte chromosome aberration, and *in vivo* mouse bone marrow micronucleus assays. Axitinib was not mutagenic or clastogenic in these assays.

Impairment of fertility

Axitinib has the potential to impair reproductive function and fertility in humans. 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) at ≥100 mg/kg/day in mice (approximately 306 times the AUC at the recommended starting dose in humans) and ≥3 mg/kg/day in dogs (approximately 0.5 times the AUC at the recommended starting dose in humans). 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 ≥10 mg/kg/day (approximately equivalent to the AUC at the recommended starting dose in humans).

Axitinib did not affect mating or fertility in male mice at any dose tested up to 100 mg/kg/day. However, reduced testicular weights, sperm density and count were noted at ≥30 mg/kg/day (approximately 72 times the AUC at the recommended starting dose in humans) following at least 70 days of treatment with axitinib. No adverse male reproductive effects in mice were noted at 10 mg/kg/day (approximately 21 times the AUC at the recommended starting dose in humans). In female mice, reduced fertility and embryonic viability were observed at all doses tested (≥30 mg/kg/day) following at least 15 days of treatment with axitinib (approximately 64 times the AUC at the recommended starting dose in humans).

Developmental toxicity

Pregnant mice exposed to axitinib at an oral dose level of 3 mg/kg/day (approximately 3 times the AUC at the recommended starting dose in humans), showed an increased occurrence of cleft palate and common variations in skeletal ossification. No fetal alterations were observed in mice at a dose level of 1 mg/kg/day (approximately equivalent to the AUC at the recommended starting dose in humans).

Toxicity studies in juvenile animals
Physeal dysplasia was observed in immature mice and dogs given axitinib at doses of ≥30 mg/kg/day for at least 1 month (approximately 37 times the AUC at the recommended starting dose in humans); the incidence and severity was dose-related and the effects were reversible when treatment stopped. Dental caries were observed in mice treated for more than 1 month at axitinib doses of ≥10 mg/kg/day (approximately 9 times the AUC at the recommended starting dose in humans); residual findings, indicative of partial reversibility, were observed when treatment stopped. For physeal dysplasia, no effect levels of 10 mg/kg/day in mouse (approximately 8 times the AUC at the recommended starting dose in humans) and 10 mg/kg/day in dogs (approximately equivalent to the AUC at the recommended starting dose in humans) were determined in animals given axitinib for 1 month. A no effect level was not defined for caries of the incisors in mice. Other toxicities of potential concern to pediatric patients have not been evaluated in juvenile animals.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core
Microcrystalline cellulose
Lactose monohydrate
Croscarmellose sodium
Magnesium stearate

Tablet film-coating
Hypromellose 2910 (15 mPa·s)
Titanium dioxide (E171)
Lactose monohydrate
Triacetin (E1518)
Iron oxide red (E172)

6.2 Incompatibilities

Not applicable.

6.3 Storage condition

Store below 30°C.

6.4 Nature and contents of container

INLYTA 1-mg film-coated tablets
Packs containing 28 tablets: 2 blisters @ 14 film-coated tablets, Reg. No. DKI1390701417A1
INLYTA 5-mg film-coated tablets
Packs containing 28 tablets: 2 blisters @ 14 film-coated tablets, Reg. No. DKI1390701417B1

6.5 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

HARUS DENGAN RESEP DOKTER

Manufactured by
Pfizer Manufacturing Deutschland GmbH
Freiburg Im Breisgau
Germany

Imported by
PT. Pfizer Indonesia
Jakarta, Indonesia

Nama Generik: Axitinib
Merek Dagang: INLYTA
Tanggal CDS Efektif: 22 Mei 2025
Menggantikan: 11 Desember 2019
Disetujui oleh BPOM:

Leaflet kemasan: Informasi untuk pasien

Inlyta 1 mg tablet salut selaput
Inlyta 5 mg tablet salut selaput
Axitinib

Baca semua isi leaflet ini dengan teliti sebelum Anda mulai meminum obat ini karena terdapat informasi yang penting bagi Anda.
- Simpan leaflet ini. Anda mungkin perlu membacanya kembali.
- Jika Anda memiliki pertanyaan lebih lanjut, hubungi dokter, apoteker atau perawat Anda.
- Obat ini hanya diresepkan untuk Anda. Jangan berikan kepada orang lain. Obat ini dapat membahayakan mereka, meskipun gejala penyakitnya sama dengan Anda.
- Jika Anda merasakan efek samping apa pun, hubungi dokter, apoteker, atau perawat Anda. Termasuk segala bentuk kemungkinan efek samping yang tidak tercantum di dalam leaflet ini.

Isi leaflet ini

1. Penjelasan tentang Inlyta dan kegunaannya

Inlyta adalah obat yang mengandung zat aktif axitinib. Axitinib menekan pasokan darah ke tumor dan memperlambat pertumbuhan kanker.

Inlyta diindikasikan untuk mengobati pasien dengan kanker ginjal stadium lanjut (karsinoma sel ginjal stadium lanjut) pada orang dewasa, ketika obat lain (yaitu sunitinib, sitokin atau sorafenib) tidak lagi mampu menghentikan perkembangan penyakit ini.

Inlyta harus diberikan oleh tenaga medis berkompeten yang ahli dalam penggunaan terapi anti kanker.

Jika Anda memiliki pertanyaan mengenai cara kerja obat ini atau alasan obat ini diresepkan untuk Anda, hubungi dokter Anda.

2. Yang perlu Anda ketahui sebelum meminum Inlyta

Jangan meminum Inlyta:
Jika Anda alergi terhadap axitinib atau bahan lain yang terkandung di dalam obat ini (tercantum di bagian 6). Jika Anda merasa memiliki alergi, mintalah saran dari dokter Anda.

Peringatan dan langkah-langkah pencegahan

Konsultasikan dengan dokter atau perawat Anda sebelum meminum Inlyta:

- **Jika Anda memiliki tekanan darah tinggi.**
  Inlyta dapat meningkatkan tekanan darah Anda. Penting kiranya memeriksa tekanan darah Anda sebelum meminum obat ini, dan memeriksa secara berkala selama Anda meminumnya. Jika Anda memiliki tekanan darah tinggi (hipertensi) Anda dapat dirawat dengan obat yang mampu menurunkan tekanan darah. Dokter Anda harus memastikan bahwa tekanan darah Anda aman sebelum memulai perawatan dengan Inlyta, dan selama menjalani perawatan dengan obat ini.

- **Jika Anda memiliki masalah dengan kelenjar tiroid.**
  Inlyta dapat menimbulkan masalah kelenjar tiroid. Laporkan kepada dokter Anda jika Anda merasa mudah lelah, secara umum merasa lebih dingin dibandingkan orang lain, atau suara Anda semakin berat selama meminum obat ini. Fungsi tiroid Anda sebaiknya diperiksa sebelum Anda meminum Inlyta dan memeriksa secara berkala selama Anda meminumnya. Jika kelenjar tiroid Anda tidak memproduksi hormon tiroid yang cukup sebelumnya, atau selama Anda dalam perawatan dengan obat ini, maka Anda harus diterapi dengan terapi pengganti hormon tiroid.

- **Jika Anda baru saja mengalami masalah penggumpalan darah pada vena dan arteri Anda (jenis-jenis pembuluh darah), termasuk stroke, serangan jantung, embolisme, atau trombosis.**
  Dapatkan pertolongan darurat secepatnya dan hubungi dokter Anda jika Anda mendapatkan gejala-gejala seperti nyeri atau tekanan dada; nyeri pada lengan, punggung, leher atau rahang Anda; sesak napas; salah satu sisi tubuh Anda terasa kebas atau lemah; kesulitan berbicara; sakit kepala; perubahan penglihatan; atau pening selama menjalani perawatan dengan obat ini.

- **Jika Anda mengalami masalah pendarahan.**
  Inlyta dapat meningkatkan peluang Anda mengalami pendarahan. Konsultasikan dengan dokter jika Anda mengalami pendarahan apa pun, batuk darah atau dahak berdarah selama menjalani perawatan dengan obat ini.

- **Jika Anda menderita atau pernah menderita aneurisma (pembesaran dan pelemahan dinding pembuluh darah) atau sobekan pada dinding pembuluh darah.**

- **Jika selama perawatan dengan obat ini Anda mengalami nyeri lambung (perut) parah atau nyeri lambung menetap.**
  Inlyta dapat meningkatkan risiko terbentuknya lubang pada lambung atau usus atau terbentuknya fistula (saluran menyerupai tabung yang abnormal dari satu rongga tubuh normal ke rongga tubuh lainnya atau kulit). Konsultasikan dengan dokter Anda jika Anda mengalami nyeri perut selama menjalani perawatan dengan obat ini.

- **Jika Anda akan menjalani operasi atau jika Anda memiliki luka yang belum sembuh.**
  Dokter Anda harus menghentikan Inlyta setidaknya 24 jam sebelum Anda menjalani operasi sebab dapat memengaruhi penyembuhan luka. Perawatan Anda dengan obat ini harus dimulai kembali setelah luka dinyatakan cukup sembuh.

- **Jika selama perawatan dengan obat ini, Anda mengalami beberapa gejala seperti sakit kepala, kebingungan, kejang (serangan mendadak), atau perubahan penglihatan dengan atau tanpa tekanan darah tinggi.**
  Mintalah pertolongan darurat secepatnya dan hubungi dokter Anda. Hal ini bisa jadi merupakan efek samping neurologis langka yang disebut sindrom ensefalopati reversibel posterior.

- **Jika Anda memiliki masalah dengan hati.**
  Dokter Anda harus melakukan tes untuk memeriksa fungsi hati Anda sebelum dan selama perawatan dengan Inlyta.

Penggunaan pada anak-anak dan remaja
Inlyta tidak direkomendasikan untuk pasien berusia di bawah 18 tahun. Obat ini belum diteliti pada anak-anak dan remaja.

Obat lain dan Inlyta
Beberapa obat mungkin memengaruhi Inlyta, atau dipengaruhi olehnya. Harap konsultasikan dengan dokter, apoteker atau perawat Anda mengenai semua obat yang baru-baru ini Anda minum, yang sedang Anda minum, atau berencana Anda minum, termasuk obat yang diperoleh tanpa resep, seperti vitamin dan obat-obatan herbal. Obat-obatan yang tercantum di dalam leaflet ini mungkin bukan satu-satunya obat yang dapat berinteraksi dengan Inlyta.

Obat-obatan berikut dapat meningkatkan risiko efek samping Inlyta:
- ketokonazol atau itrakonazol, digunakan untuk mengobati infeksi jamur;
- klaritromisin, eritromisin atau telitromisin, antibiotik yang digunakan untuk mengobati infeksi bakteri;
- atazanavir, indinavir, nelfinavir, ritonavir atau sakuinavir, digunakan untuk mengobati infeksi HIV/AIDS;
- nefazodon, digunakan untuk mengobati depresi.

Obat-obatan berikut dapat mengurangi efektivitas Inlyta:
- rifampisin, rifabutin atau rifapentine, digunakan untuk mengobati tuberkulosis (TB);
- deksametason, obat steroid yang diresepkan untuk banyak kondisi yang berbeda, termasuk penyakit serius;
- fenitoin, karbamazepin atau fenobarbital, anti-epilepsi yang digunakan untuk menghentikan kejang atau serangan mendadak;
- *St. John's wort* (*Hypericum perforatum*), sebuah produk herbal yang digunakan untuk terapi depresi.

Obat-obatan ini **harus dihindari** selama Anda menjalani perawatan dengan Inlyta. Jika Anda sedang meminum salah satunya, konsultasikan dengan dokter, apoteker atau perawat Anda. Dokter Anda dapat mengubah dosis obat ini, mengubah dosis Inlyta, atau mengalihkan Anda ke obat lain.

Inlyta dapat meningkatkan efek samping yang terkait dengan teofilin, yang digunakan untuk mengobati asma atau penyakit paru lainnya.

Inlyta dengan makanan dan minuman
Anda dapat meminum obat ini baik setelah atau sebelum makan.
Jangan meminum obat ini dengan *grapefruit* atau *grapefruit juice*, sebab dapat meningkatkan peluang timbulnya efek samping.

Hamil dan menyusui
- Inlyta dapat membahayakan janin atau bayi yang sedang menyusui.
- Jangan meminum obat ini selama masa kehamilan. Konsultasikan dengan dokter Anda sebelum meminumnya jika Anda sedang hamil atau berpeluang untuk hamil.
- Gunakan metode kontrasepsi yang handal selama Anda meminum Inlyta dan hingga 1 minggu setelah dosis terakhir obat ini, guna mencegah kehamilan.
- Jangan menyusui selama menjalani perawatan dengan Inlyta. Jika Anda sedang menyusui, dokter Anda dapat merundingkan dengan Anda apakah sebaiknya menghentikan pemberian ASI atau menghentikan perawatan dengan Inlyta.

Jika Anda sedang hamil atau menyusui, atau mungkin sedang hamil atau berencana untuk hamil, konsultasikan dengan dokter, apoteker atau perawat Anda sebelum meminum obat ini.

Mengemudi dan menjalankan mesin
Jika Anda mengalami rasa pening dan/atau lelah selama menjalani perawatan dengan Inlyta, berhati-hatilah saat mengemudi atau menjalankan mesin.

Inlyta mengandung laktosa (gula susu)
Jika Anda telah dinyatakan oleh dokter mengalami intoleransi terhadap beberapa jenis gula, hubungi dokter Anda sebelum meminum obat ini.

3. Cara meminum Inlyta
Selalu minum obat ini dengan tepat sesuai anjuran dokter. Anda harus berkonsultasi dengan dokter, apoteker atau perawat Anda jika merasa tidak yakin.

Dosis awal yang direkomendasikan adalah 5 mg dua kali sehari. Selanjutnya dokter Anda mungkin dapat meningkatkan atau menurunkan dosis tergantung toleransi Anda terhadap terapi dengan Inlyta.

Telan tablet utuh dengan air, sesudah atau sebelum makan. Jarak antara setiap dosis Inlyta kurang lebih adalah 12 jam.

Jika Anda meminum Inlyta melebihi yang dianjurkan
Jika tanpa sengaja Anda meminum terlalu banyak tablet atau dosis melebihi yang dianjurkan, segera hubungi dokter Anda. Bila memungkinkan, perlihatkan kemasan, atau leaflet ini kepada dokter. Anda mungkin memerlukan penanganan medis.

Jika Anda lupa meminum Inlyta
Minum dosis berikutnya sesuai jadwal yang biasa. Jangan meminum dosis ganda untuk mengganti tablet yang terlupa.

Jika Anda berhenti meminum Inlyta
Jika Anda tidak dapat/sanggup meminum obat ini sebagaimana yang diresepkan oleh dokter Anda atau Anda merasa tidak memerlukannya lagi, segera hubungi dokter Anda.

Jika Anda memiliki pertanyaan lebih lanjut mengenai penggunaan obat ini, konsultasikan dengan dokter, apoteker atau perawat Anda.

4. Kemungkinan efek samping

Seperti semua obat-obatan yang ada, obat ini dapat menimbulkan efek samping, sekali pun tidak dirasakan semua orang.

Jika Anda merasakan efek samping apa pun, hubungi dokter, apoteker atau perawat Anda. Termasuk segala bentuk kemungkinan efek samping yang tidak tercantum di dalam leaflet ini.

Beberapa efek samping dapat bersifat serius. Anda harus segera menghubungi dokter Anda jika mengalami efek samping serius mana pun di bawah ini (lihat juga bagian 2 "Apa yang perlu Anda ketahui sebelum meminum Inlyta"):

- **Penggumpalan darah pada vena dan arteri Anda (jenis-jenis pembuluh darah), termasuk stroke, serangan jantung, embolisme, atau trombosis.** Dapatkan pertolongan darurat secepatnya dan hubungi dokter Anda jika Anda mendapatkan gejala-gejala seperti nyeri atau tekanan dada; nyeri pada lengan, punggung, leher atau rahang Anda; sesak napas; salah satu sisi tubuh Anda terasa kebas atau lemah; kesulitan berbicara; sakit kepala; perubahan penglihatan; atau pening.

- **Pendarahan.** Segera laporkan ke dokter Anda jika Anda mengalami gejala mana pun atau masalah pendarahan serius selama perawatan dengan Inlyta: feses kehitaman, batuk darah atau dahak berdarah, atau perubahan status mental.

- **Lubang pada lambung atau usus atau terbentuknya fistula (saluran menyerupai tabung yang abnormal dari satu rongga tubuh normal ke**

rongga tubuh lainnya atau kulit). Laporkan ke dokter Anda jika Anda mengalami nyeri perut parah.

- **Peningkatan tekanan darah yang parah.** Laporkan ke dokter Anda jika Anda mengalami tekanan darah yang sangat tinggi, sakit kepala parah, atau nyeri dada parah.

- **Pembengkakan otak reversibel (sindrom ensefalopati reversibel posterior).** Dapatkan pertolongan darurat secepatnya dan hubungi dokter Anda jika Anda mengalami beberapa gejala seperti sakit kepala, kebingungan, kejang (serangan mendadak), atau perubahan penglihatan dengan atau tanpa tekanan darah tinggi.

Efek samping lain dengan Inlyta di antaranya:

Efek samping yang sangat umum (dapat memengaruhi lebih dari 1 dalam 10 orang):
- Tekanan darah tinggi, atau peningkatan tekanan darah
- Diare, perasaan mual atau mengalami mual (mual atau muntah), nyeri mulut, lidah atau tenggorok, konstipasi
- Kurang energi, merasa lemah atau letih
- Kelenjar tiroid yang kurang aktif (tampak dari hasil tes darah Anda)
- Kemerahan dan pembengkakan telapak tangan atau telapak kaki (sindrom tangan-kaki) ruam kulit, kulit terasa kering
- Hilangnya nafsu makan
- Terdapat protein di dalam urin (tampak dari hasil tes urin Anda)
- Penurunan berat badan
- Sakit kepala, gangguan atau berkurangnya indra pengecap
- Suara parau
- Perdarahan
- Sesak napas, batuk, nyeri tenggorokan, atau iritasi hidung dan tenggorokan
- Gangguan pencernaan
- Dispepsia
- Nyeri abdomen
- Stomatitis
- Ruam
- Kulit kering
- Nyeri sendi, nyeri di tangan atau kaki
- Inflamasi mukosa

Efek samping yang umum (dapat memengaruhi hingga 1-10 dari 100 orang):
- Dehidrasi (hilangnya cairan tubuh)
- Gagal ginjal
- Nyeri abdomen bagian atas, wasir, gusi berdarah, darah keluar dari rektum
- Nyeri otot
- Glosodinia (nyeri lidah)

- Pening
- Kulit gatal, kulit kemerahan, rambut rontok
- Telinga berdenging (tinitus)
- Menurunnya jumlah sel darah merah (tampak dari hasil tes darah Anda)
- Menurunnya jumlah sel trombosit (sel yang membantu penggumpalan darah) (tampak dari hasil tes darah Anda)
- Perubahan kadar kimiawi/enzim yang berbeda dalam darah (tampak dari hasil tes darah Anda)
- Kelenjar tiroid yang hiperaktif (tampak dari hasil tes darah Anda)
- Peningkatan jumlah sel darah merah (tampak dari hasil tes darah Anda)
- Anemia
- Polisitemia
- Hiperkalemia
- Hiperkalsemia
- Kejadian gagal jantung
- Kejadian tromboemboli vena
- Kejadian trombosis arteri
- Fistula (saluran menyerupai tabung yang abnormal dari satu rongga tubuh normal ke rongga tubuh lainnya atau kulit)
- Nyeri orofaringeal
- Kembung

Efek samping yang tidak umum (dapat memengaruhi hingga 1-10 dari 1.000 orang):

- Sindrom leukoensefalopati reversibel posterior
- Menurunnya jumlah sel darah putih (tampak dari hasil tes darah Anda)
- Neutropenia
- Krisis hipertensi

Tidak diketahui: frekuensi tidak dapat diperkirakan dari data yang tersedia

- Pembesaran dan pelemahan dinding pembuluh darah atau sobekan pada dinding pembuluh darah (aneurisma dan diseksi arteri).
- Nyeri di perut (abdomen) yang disebabkan oleh inflamasi pankreas.

Melaporkan efek samping

Jika Anda mengalami efek samping apa pun, bicarakan dengan dokter, apoteker, atau perawat Anda. Termasuk segala kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Dengan melaporkan efek samping, Anda dapat membantu memberikan informasi lebih banyak tentang keamanan obat ini.

Untuk melaporkan efek samping, hubungi www.pfizersafetyreporting.com atau email di IDN.AEReporting@pfizer.com.

5. Cara menyimpan Inlyta

Simpan obat ini jauh dari penglihatan dan jangkauan anak-anak.

Jangan gunakan obat ini melebihi tanggal kedaluwarsa yang tertera pada karton dan pada blister atau label botol yang disebutkan setelah tanda "EXP". Tanggal kedaluwarsa mengacu pada hari terakhir di setiap bulan.

Obat ini perlu disimpan di bawah suhu 30°C.

Jangan gunakan kemasan yang rusak atau memperlihatkan tanda-tanda kerusakan.

Jangan membuang obat melalui saluran pembuangan air atau bersama sampah rumah tangga. Konsultasikan dengan apoteker Anda mengenai cara membuang obat yang tidak lagi digunakan. Langkah-langkah ini akan membantu memelihara kelestarian lingkungan.

6. Isi kemasan dan informasi lain

Apa kandungan Inlyta

- Zat aktifnya adalah axitinib. Tablet Inlyta tersedia dalam beberapa kekuatan.
  Inlyta 1 mg: masing-masing tablet mengandung 1 mg axitinib
  Inlyta 5 mg: masing-masing tablet mengandung 5 mg axitinib

- Bahan lainnya adalah selulosa mikrokristal, laktosa monohidrat, natrium kroskarmelosa, magnesium stearat, hipromelosa 2910 (15 mPa·s), titanium dioksida (E171), triasetin (E1518), besi oksida merah (E172).

Bentuk tampilan Inlyta dan isi kemasannya

Inlyta 1 mg tablet salut selaput berwarna merah, berbentuk oval dan bertuliskan "Pfizer" pada satu sisi dan "1 XNB" pada sisi lainnya. Inlyta 1 mg tersedia dalam kemasan blister berisi 28 tablet ; No. Reg.: DKI1390701417A1.

Inlyta 5 mg tablet salut selaput berwarna merah, berbentuk oval dan bertuliskan "Pfizer" pada satu sisi dan "5 XNB" pada sisi lainnya. Inlyta 5 mg tersedia dalam kemasan blister berisi 28 tablet ; No. Reg.: DKI1390701417B1.

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HARUS DENGAN RESEP DOKTER

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