AXITINIB

An option in renal cell carcinoma after failure of treatment with sunitinib or pazopanib
NICE approved Feb 2015

Drug/Dosage: **Axitinib** initiate at 5mg po bd continuous therapy

*Patients **not** on anti-hypertensives when axitinib is started:*

After 4 weeks, for patients who tolerate this dose with no severe adverse reactions and whose blood pressure remains ≤ 150/90 mmHg without the need for anti-hypertensives, the dose may be increased to 7mg twice daily.

Subsequently, using the same criteria above, patients who tolerate the 7 mg bd dose without the need for an antihypertensive may have their dose increased to a maximum of 10 mg twice daily.

Patients on anti-hypertensive therapy before axitinib is started:

After 4 weeks, for patients who tolerate the 5mg bd dose with no severe adverse reactions and whose blood pressure remains stable and ≤ 150/90 mmHg without the need for an increase in anti-hypertensive therapy, the dose may be increased to 7mg twice daily. If in doubt, discuss with Consultant.

Subsequently, using the same criteria above, patients who tolerate the 7 mg bd dose without the need for an increase in antihypertensive therapy may have their dose increased to a maximum of 10 mg twice daily.

Administration: Axitinib is available as 5mg and 1mg tablets, which may be taken with or without food, swallowed whole with a glass of water.
Grapefruit and grapefruit juice should be avoided while on axitinib.

Frequency: clinical review 2 weeks after starting, then every 4 weeks
continue for as long as there is clinical benefit, or unacceptable toxicity.

Main Toxicities: hand-foot syndrome; diarrhoea; hypertension; proteinuria; fatigue; hypothyroidism; dysphonia (hoarseness)

Anti- emetics: mildly emetogenic – anti-emetics not routinely needed

Regular: Investigations:	FBC	every 4 weeks
	LFTs	every 4 weeks
	U&Es	every 4 weeks
	Blood pressure	weekly for 1st cycle (ideally via GP, with patient making a record of the readings for the next oncology appointment), then every 4 weeks
	Thyroid function	baseline, then every 3 months
	Urinalysis for proteinuria	baseline, then every 3 months

Comments: Diarrhoea is common, so provide loperamide for new patients, and ask them to report to hot bleep an increase of 4-6 stools per day over baseline.

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Version: 2	Approved by Lead Chemotherapy Nurse: P Deery
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Prepared by: S Taylor	Checked by: C Tucker

	Patients should be advised to apply moisturiser to their hands and feet regularly throughout treatment, and to minimise activities that put pressure on feet or hands if they start to develop sore hands or feet. Recommended moisturisers are Udderly Smooth or urea-containing moisturisers eg Eucerin.
Interactions:	Axitinib is metabolised primarily in the liver by CYP3A4/5. Concomitant use of enzyme inducers (e.g. dexamethasone, phenytoin, St Johns wort) with axitinib should be avoided, as this may increase the risk of therapeutic failure. Co-administration of axitinib with enzyme inhibitors (eg itraconazole, clarithromycin, erythromycin, grapefruit juice) should also be avoided. If a strong inhibitor must be co-administered, a dose decrease of axitinib to approximately half the dose (e.g. the starting dose should be reduced from 5 mg twice daily to 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 inhibitor should be considered.
Dose Modifications	Management of some adverse drug reactions may require temporary interruption or dose reduction of therapy. When dose reduction is necessary, axitinib may be reduced to 3mg twice daily, and further to 2mg twice daily.
Haematological Toxicity:	Temporarily interrupt axitinib if any bleeding event requires medical intervention.
Hypertension:	Blood pressure should be well controlled before starting axitinib. If hypertension develops, it should be treated (usually by GP) and monitored closely until stabilised. If the hypertension is persistent despite the use of anti-hypertensives, the axitinib dose should be reduced. If the patient develops severe hypertension, axitinib should be stopped until the patient is normotensive. Axitinib may then be re-started, with close monitoring, at a lower dose.
Hypothyroidism:	Manage according to standard medical practice. Axitinib treatment may continue.
Proteinuria:	For patients who develop moderate to severe proteinuria (≥ 2+ on dipstick, or > 1g/24 hours), reduce the dose or temporarily interrupt axitinib.
Dysphonia:	Includes sensation of lump in throat, difficulty swallowing, sore throat, hoarse voice and chronic throat clearing. This can be intermittent, but usually resolves after a 1-2 day treatment interruption. Consider a dose reduction if symptoms are severe or troublesome.
Skin Toxicity:	Grade 3 hand-foot syndrome may require a break in treatment until resolved to Grade ≤ 1. The patient should be advised to moisturise their hands and feet regularly, and to keep them cool. Once symptoms have resolved to ≤ Grade 1, axitinib may be re-introduced at a reduced dose.
Hepatic Impairment:	In clinical studies, the systemic exposure to axitinib was approximately two-fold higher in subjects with moderate hepatic impairment (Child-Pugh class B), so a dose decrease is recommended when administering axitinib to these patients. e.g. the start dose should be 2mg bd. Axitinib is not recommended in patients with severe hepatic impairment.
Renal Impairment:	No dose adjustment is required in renal impairment.
References:	Rini, B et al; Lancet 2011; 378: 1931 - 1939