Indication	Monotherapy treatment of unresectable locally advanced or metastatic urothelial carcinoma (UC), harbouring a susceptible fibroblast growth factor receptor 3 (FGFR3) genetic alteration that has been previously treated with at least one line of therapy containing a PD-1 or PD-L1 inhibitor in the unresectable locally advanced or metastatic treatment setting (neoadjuvant or adjuvant therapy containing a PD-1 or PD-L1 inhibitor with disease progression during or within 12 months of its completion counts as treatment in the advanced or metastatic disease setting). NB the patient must have not previously received any specifically FGFR3-targeted therapy unless the patient has received erdafitinib via a company early access scheme.
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 28 days Continue until disease progression, unacceptable toxicity or patient's choice to discontinue treatment. A formal medical review as to whether treatment with erdafitinib should continue or not should be scheduled to occur at least by the end of the first 8 weeks of treatment.
Monitoring Parameters pre-treatment	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • **Ophthalmological examination** should be performed prior to initiation of therapy, to include an Amsler grid test, fundoscopy, visual acuity and if available optical coherence tomography. Repeat examination, to include an Amsler grid test, should take place every cycle for the first 4 cycles and then every 3rd cycle thereafter, additional monitoring should be performed urgently if clinically indicated. Results of ophthalmology assessment to be reviewed as part of the pre-treatment assessment. • **FBC, U&Es** (including Phosphate) and **LFTs** baseline, and then at every cycle thereafter. In addition, serum phosphate **MUST** be taken 14-21 days after treatment commences and result should be used to dose patient (see Management of adverse reactions and dose adjustments). • Patients should be counselled prior to treatment on the importance of following a low phosphate diet. • The patient should not have untreated or symptomatic brain metastases prior to starting treatment. • **ECG** prior to treatment and as clinically indicated thereafter. • **Hepatic impairment:** No dose adjustment is required in mild or moderate impairment. There are no data in severe hepatic impairment, alternative treatment should be considered. • **Renal impairment:** No dose adjustment is required in mild or moderate impairment (CrCl 30 to 89ml/min). There are no data in severe renal impairment (CrCl <30ml/min), alternative treatment should be considered. • **Management of adverse reactions and dose adjustments:** o The recommended starting dose of erdafitinib is 8mg OD. o This dose should be maintained and serum phosphate level should be assessed between 14 and 21 days after initiating treatment. Up-titrate the dose to 9 mg OD if the serum phosphate level is <9.0 mg/dL (<2.91 mmol/L), and there is no drug-related toxicity. o If the phosphate level is 9.0 mg/dL or higher follow the relevant dose modifications in table 1. o **After day 21 the serum phosphate level should not be used to guide up-titration of dose.** o If a dose reduction is required in patients on **9mg OD** the first dose reduction should be to 8mg OD, second dose reduction to 6mg OD, third dose reduction to 5mg OD and 4th dose reduction to 4mg OD.

	○ If a dose reduction is required in patients on **8mg OD** the first dose reduction should be to 6mg OD, second dose reduction to 5mg OD, third dose reduction to 4mg OD. ○ If a dose of 4mg OD cannot be tolerated erdafitinib should be discontinued. ○ Dose modification is required due to drug interactions when erdafitinib is co-administered with moderate CYP2C9 and strong CYP3A4 inhibitors and moderate CYP3A4 inducers, see **Common Drug interactions** below. Co-administration with strong CYP3A4 inducers is not recommended. • **Hyperphosphatemia:** ○ Monitor for hyperphosphatemia throughout treatment. Dietary phosphate intake (600-800 mg daily) should be restricted and concomitant use of agents that may increase serum phosphate levels should be avoided for serum phosphate levels >/=5.5 mg/dL (>/=1.75mmol/L). Supplementation with vitamin D in patients receiving erdafitinib is not recommended due to potential contribution to increased serum phosphate and calcium levels. ○ If serum phosphate levels >7 mg/dL (>2.25mmol/L), consider initiating phosphate lowering therapy and dose reduce, withhold, or permanently discontinue erdafitinib based on duration and severity of hyperphosphatemia (see table 1). For persistently elevated phosphate concentrations, adding a non-calcium containing phosphate binder as per trust formulary (e.g. sevelamer carbonate) should be considered as needed. ○ If the serum phosphate level falls below normal, phosphate-lowering therapy and dietary phosphate restrictions (if applicable) should be discontinued. • **Ocular disorders:** Erdafitinib can cause ocular disorders, including central serous retinopathy (CSR) (a grouped term including retinal pigment epithelial detachment (RPED)) resulting in visual field defect. Monitoring is required throughout treatment (see note above,) closer clinical monitoring is recommended in patients aged >/= 65 years and patients that have clinically significant medical eye disorders. If abnormality is observed follow table 2 below for management guidelines. Patients who are restarted on erdafitinib following an ocular event should be closely monitored. • **Nail and skin disorders:** Patients should be monitored for signs and symptoms of nail disorders (including onycholysis, nail discolouration and paronychia), patients should be advised on preventative treatment such as good hygiene and nail strengthener products, see table 3 for management of nail toxicity. Skin disorders (including dry skin, palmar-plantar erythrodysaesthesia (PPES) syndrome, alopecia and pruritus) have been reported in patients whilst taking erdafitinib. Patients should be advised to limit excessive use of soap and bathing, use moisturisers and sunscreen regularly, avoid perfumed products and avoid unnecessary exposure to sunlight, see table 3 for management of skin toxicity. • **Mucosal disorders:** Stomatitis and dry mouth can occur very commonly with, patients should be counselled to seek medical attention should symptoms worsen. Patients should be monitored and provided supportive care as such as good oral hygiene, baking soda mouthwashes 3 or 4 times per day as needed and avoidance of spicy and/or acidic foods. Treatment with erdafitinib should be discontinued or modified based on toxicity as described in table 3. • **Common drug and food interactions (for comprehensive list refer to BNF/SPC):** ○ Administer with caution to patients who have a history of or predisposition for QTc prolongation. Caution is advised when administering erdafitinib with medicinal products known to prolong the QT interval or medicinal products with a potential to induce torsades de pointes, such as class IA (e.g., quinidine, disopyramide) or class III (e.g., amiodarone, sotalol, ibutilide) antiarrhythmic medicinal products, macrolide antibiotics, SSRIs (e.g., citalopram, escitalopram), methadone, moxifloxacin, and antipsychotics (e.g., haloperidol and thioridazine). ○ Medicinal products that can alter serum phosphate levels should be avoided until assessment of serum phosphate level between 14 and 21 days after initiating treatment due to potential impact on up-titration decision. ○ Avoid co-administration with strong CYP3A4 inducers (such as apalutamide, enzalutamide, rifampicin, carbamazepine, phenytoin, and St. John's wort).

	○ If co-administered with a moderate CYP3A4 inducer (such as dabrafenib, lorlatinib, modafinil, phenobarbital, primidone), erdafitinib dose should be cautiously increased by 1 to 2 mg and adjusted gradually every two to three weeks based on clinical monitoring for adverse reactions, not to exceed 9 mg. If the moderate CYP3A4 inducer is discontinued, the erdafitinib dose may be adjusted as tolerated. ○ Co-administration with a moderate CYP2C9 or strong CYP3A4 inhibitor (itraconazole, ketoconazole, posaconazole, voriconazole, fluconazole, miconazole, ceritinib, clarithromycin) increased erdafitinib exposure and may lead to increased drug-related toxicity, consider alternative agents with no or minimal enzyme inhibition potential. If co-administration cannot be avoided erdafitinib should be reduced to the next lower dose. If the moderate CYP2C9 or strong CYP3A4 inhibitor is discontinued, the erdafitinib dose may be adjusted as tolerated. ○ Erdafitinib may increase exposure of drugs that are substrates of P-gp, oral narrow therapeutic index P gp substrates (such as colchicine, digoxin, dabigatran, and apixaban) should be taken at least 6 hours before or after erdafitinib to minimise the potential for interactions ○ Erdafitinib may reduce the efficacy of hormonal contraceptives, patients using hormonal contraceptives should be advised to use an alternative contraceptive not affected by enzyme inducers (e.g., non-hormonal intrauterine device) or an additional nonhormonal contraception (e.g., condom) during treatment with and until 1 month after the last dose. ○ Avoid Grapefruit or Seville oranges. • **Missed dose:** If a dose is missed it should be taken as soon as possible, treatment should then resume with the next scheduled dose, additional tablets should not be taken to make up for a missed dose or if the patient vomits. • **Driving and machinery:** If patients experience treatment related symptoms affecting their vision, it is recommended that they do not drive or use machines.
References	SPC accessed online 22.04.2025 BlueTeq form accessed online 16.04.20245 CDF list V1.359 accessed online 16.04.2025

NB For funding information, refer to CDF and NICE Drugs Funding List

Table 1: Recommended dose modifications based on serum phosphate concentrations with the use of erdafitinib after up-titration and (if applicable) on day 14-21 of cycle 1.

Serum phosphate concentration	**Recommended dose modification of erdafitinib**
For phosphate concentrations ≥5.5 mg/dL (1.75 mmol/L), restrict phosphate intake to 600-800 mg/day.	
<6.99 mg/dL (<2.24 mmol/L)	Continue at current dose.
7.00-8.99 mg/dL (2.25-2.90 mmol/L)	Continue treatment. Start phosphate binder with food until phosphate level is <7.00 mg/dL. A dose reduction should be implemented for a sustained serum phosphate level of ≥7.00 mg/dL for a period of 2 months or in the presence of additional adverse events or additional electrolyte disturbances linked to prolonged hyperphosphataemia.
9.00-10.00 mg/dL (2.91-3.20 mmol/L)	Withhold treatment until serum phosphate level returns to <7.00 mg/dL (weekly testing recommended). Start phosphate binder with food until serum phosphate level returns to <7.00 mg/dL. Re-start treatment at the same dose level (see Table 1). A dose reduction should be implemented for sustained serum phosphate level of ≥9.00 mg/dL for a period of 1 month or in the presence of additional adverse events or additional electrolyte disturbances linked to prolonged hyperphosphataemia.
>10.00 mg/dL (>3.20 mmol/L)	Withhold treatment until serum phosphate level returns to <7.00 mg/dL (weekly testing recommended). Re-start treatment at the first reduced dose level (see Table 1). If serum phosphate level of ≥10.00 mg/dL is sustained for >2 weeks, discontinue permanently. Medical management of symptoms as clinically appropriate.
Significant alteration from baseline renal function or Grade 3 hypocalcaemia due to hyperphosphataemia.	Discontinue permanently. Medical management as clinically appropriate.

Table 2 Guideline for management of eye disorders.

Severity grading	Dose management
Grade 1 Asymptomatic or mild symptoms; clinical or diagnostic observations only, or abnormal Amsler grid test.	Refer for an ophthalmologic examination (OE). If an OE cannot be performed within 7 days, withhold until an OE can be performed. If no evidence of eye toxicity on OE, continue at same dose level. If diagnosis from OE is keratitis or retinal abnormality (e.g., CSR[a]), withhold until resolution. If reversible in 4 weeks on OE, resume at next lower dose. Upon restarting, monitor for recurrence every 1-2 weeks for a month and as clinically appropriate thereafter. Consider dose re-escalation if no recurrence.
Grade 2 Moderate; limiting age appropriate instrumental activities of daily living (ADL).	Immediately withhold and refer for an OE. If there is no evidence of eye toxicity, resume erdafitinib therapy at the next lower dose level upon resolution. If resolved (complete resolution or stabilisation and asymptomatic) within 4 weeks on OE, resume at the next lower dose level. Upon restarting, monitor for recurrence every 1 to 2 weeks for a month and as clinically appropriate thereafter.
Grade 3 Severe or medically significant but not immediate sight-threatening; limiting self-care ADL.	Immediately withhold and refer for an OE. If resolved (complete resolution or stabilisation and asymptomatic) within 4 weeks, then may be resumed at 2 dose levels lower. Upon restarting, monitor for recurrence every 1 to 2 weeks for a month and as clinically appropriate thereafter. Consider permanent discontinuation for recurrence.
Grade 4 Sight-threatening consequences; blindness (20/200 or worse).	Permanently discontinue. Monitor until complete resolution or stabilisation.
[a] CSR-central serous retinopathy, when CSR occurs treatment should be withheld and permanently discontinued if it does not resolve with-in 4 weeks or if Grade 4 in severity.	

Table 3: Recommended dose modifications for nail, skin and mucosal adverse reactions

Severity of adverse reaction	**Erdafitinib**
Nail disorder	***Erdafitinib dose management***
Grade 1	Continue at current dose.
Grade 2	Withhold with reassessment in 1-2 weeks. If first occurrence and it resolves to ≤Grade 1 or baseline within 2 weeks, restart at same dose. If recurrent event or takes >2 weeks to resolve to ≤Grade 1 or baseline, then restart at next lower dose.
Grade 3	Withhold, with reassessment in 1-2 weeks. When resolves to ≤Grade 1 or baseline, restart at next lower dose.
Grade 4	Discontinue.
Dry skin and skin toxicity	
Grade 1	Continue at current dose.
Grade 2	Continue at current dose.
Grade 3	Withhold (for up to 28 days), with weekly reassessments of clinical condition. When resolves to ≤Grade 1 or baseline, restart at next lower dose.
Grade 4	Discontinue.
Oral mucositis	
Grade 1	Continue at current dose.
Grade 2	Withhold if the subject has other concomitant erdafitinib related Grade 2 adverse reactions. Withhold if the subject was already on symptom management for more than a week. If erdafitinib is withheld, reassess in 1-2 weeks. If this is the first occurrence of toxicity and resolves to ≤Grade 1 or baseline within 2 weeks, restart at same dose. If recurrent event or takes >2 weeks to resolve to ≤Grade 1 or baseline, then restart at next lower dose.
Grade 3	Withhold, with reassessments of clinical condition in 1-2 weeks. When resolves to ≤Grade 1 or baseline, restart at next lower dose.
Grade 4	Discontinue.
Dry mouth	
Grade 1	Continue at current dose.
Grade 2	Continue at current dose.
Grade 3	Withhold (for up to 28 days), with weekly reassessments of clinical condition. When resolved to ≤Grade 1 or baseline, restart at next lower dose.

Table 4: Recommended dose modifications for other adverse reactions.

Other adverse reactions[a]	
Grade 3	Withhold until toxicity resolves to Grade 1 or baseline, then may resume at the next lower dose.
Grade 4	Permanently discontinue.
[a] Dose adjustment graded using NCI CTCAE v5.0	

Repeat every 28 days

TTO	Drug	Dose	Route	Directions
Day 1	**ERDAFITINIB**	**Starting dose of 8mg** **Increasing to 9mg once daily based on tolerability, at day 14 to 21 days i.e. if the serum phosphate level is <9.0 mg/dL (<2.91 mmol/L), and there is no drug-related toxicity.** **See notes above**	PO	OD. Swallow whole, do not chew crush or dissolve tablets. Available as 3mg, 4mg and 5 mg tablets
	Hypromellose	0.3%	topical	One drop into each eye every 2 hours during waking hours.
	Metoclopramide	10mg	PO	10mg up to three times a day PRN. Do not take for more than 5 days continuously. Dispense on Cycle 1 only, then only if required
	Loperamide	2mg-4mg	PO	Take two capsules (4mg) after first loose stool, then one capsule (2mg) after each loose stool when required. (Maximum 16mg per day). Dispense on Cycle 1 only, then only if required.