Chemotherapy Protocol

UROTHELIAL CANCER

ERDAFITINIB

Regimen

- Urothelial - Erdafitinib

Indication

- Monotherapy treatment of unresectable or metastatic urothelial cancer 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.

All indications require a Blueteq application, see individual form (ERD1) for specific eligibility criteria. Ensure patient meets Blueteq criteria before consenting for treatment.

Toxicity

Drug	Adverse Effect
Erdafitinib	**Metabolism disorders** – hyperphosphataemia, hyponatraemia, decreased appetite **Nervous system disorders** – dysgeusia **Eye disorders** – Central serous retinopathy (CSR)[a], dry eye **Respiratory/thoracic disorders** – epistaxis **Gastrointestinal disorders** – diarrhoea, stomatitis, dry mouth, constipation, vomiting, abdominal pain **Skin and subcutaneous disorders** – paronychia, onycholysis, onychomadesis, nail changes, palmar plantar erythrodysesthesia, alopecia, dry skin **General** – asthenia, fatigue **Blood disorders** – anaemia **Investigations** – weight loss, increased creatinine, increased ALT and or AST
[a] Central serous retinopathy includes retinal detachment, vitreous detachment, retinal oedema, retinopathy, chorioretinopathy, detachment of retinal pigment epithelium, detachment of macular retinal pigment epithelium, macular detachment, serous retinal detachment, subretinal fluid, retinal thickening, chorioretinitis, serous retinopathy, maculopathy, choroidal effusion, vision blurred, visual impairment, visual acuity reduced.	

The adverse effects listed are not exhaustive. Please refer to the relevant summary of product characteristics for further details.

Monitoring

Regimen

At baseline – prior to cycle one

- FBC, U&Es, LFTs (including AST)
- Magnesium & Phosphate
- Formal ophthalmology assessment at baseline to include Amsler grid test, fundoscopy, visual acuity and if available optical coherence tomography. (This can be undertaken once the patient is known to have a relevant FGFR3 alteration and at any time prior to starting treatment)
- Height and weight
- ECG

During cycle one

- Phosphate between 14-21 days after starting erdafitinib

Prior to each subsequent cycle

- FBC, U&Es, LFTs, phosphate
- Ophthalmology assessment by oncologist utilising Amsler Grid test. Urgent referral back to ophthalmology specialist if any visual changes noted for full ophthalmology assessment.
- For Amsler Grid test instructions/printable chart see https://www.aop.org.uk/advice-and-support/for-patients/sight-tests/amsler-chart

Dose Modifications

The dose modifications listed are for hepatic function, renal function and drug specific toxicities only.

Dose adjustments may be necessary for other toxicities as well. In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Recommended dose reduction schedule

Dose	**1st dose reduction**	**2nd dose reduction**	**3rd dose reduction**	**4th dose reduction**	**5th dose reduction**
9mg (3 x 3mg tablets	8mg	6mg	5mg	4mg	stop
8mg (2 x 4mg tablets)	6mg	5mg	4mg	Stop	

Hepatic Impairment

No dose adjustment is required for patients with mild or moderate hepatic impairment. Limited data are available on the use of erdafitinib in patients with severe hepatic impairment.

Alternative treatment should be considered in patients with severe hepatic impairment.

Renal Impairment

No dose adjustment is required for patients with mild or moderate renal impairment. There are no data on the use of erdafitinib in patients with severe renal impairment.

Alternative treatment should be considered in patients with severe renal impairment.

Non-haematological toxicities

Hyperphosphataemia

Hyperphosphataemia is an expected, transient pharmacodynamic effect of FGFR inhibitors. Phosphate concentrations should be assessed prior to the first dose and then monitored monthly.

For elevated phosphate concentrations in patients treated with erdafitinib follow the dose modification guidelines in the table below. For persistently elevated phosphate concentrations, adding a non-calcium containing phosphate binder (e.g., sevelamer carbonate) should be considered as needed.

For phosphate concentrations >1.75mmol/L (5.5mg/dL), restrict phosphate intake to 600-800mg/day.

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

Eye disorders

Severity grading	Erdafitinib 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 erdafitinib until an OE can be performed. If no evidence of eye toxicity on OE, continue erdafitinib at same dose level. If diagnosis from OE is keratitis or retinal abnormality (e.g., central serous retinopathy), withhold erdafitinib until resolution. If reversible in 4 weeks on OE, resume at next lower dose. Upon restarting erdafitinib, 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 erdafitinib 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 erdafitinib at the next lower dose level. Upon restarting erdafitinib, 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 erdafitinib and refer for an OE. If resolved (complete resolution or stabilisation and asymptomatic) within 4 weeks, then erdafitinib may be resumed at 2 dose levels lower. Upon restarting erdafitinib, monitor for recurrence every 1 to 2 weeks for a month and as clinically appropriate thereafter. Consider permanent discontinuation of erdafitinib for recurrence.
Grade 4 Sight-threatening consequences; blindness (20/200 or worse).	Permanently discontinue erdafitinib Monitor until complete resolution or stabilisation
Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events Version 5.0 (NCI-CTCAE v5.0) where Grade 1 is mild, Grade 2 is moderate, Grade 3 is severe, and Grade 4 is life-threatening.	

Nail, skin and mucosal changes

Severity of adverse reaction	Erdafitinib dose management
Nail disorder	
Grade 1	Continue erdafitinib at current dose
Grade 2	Withold erdafitinib 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 level.
Grade 3	Withhold erdafitinib, with reassessment in 1-2 weeks. When resolves to ≤Grade 1 or baseline, restart at next lower dose.
Grade 4	Discontinue erdafitinib
Dry skin and skin toxicity	

Grade 1	Continue erdafitinb at current dose
Grade 2	Continue erdafitinib at current dose.
Grade 3	Withhold erdafitinib (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 erdafitinib
Oral mucositis	
Grade 1	Continue erdafitinib at current dose.
Grade 2	Withhold erdafitinib if the subject has other concomitant erdafitinib related Grade 2 adverse reactions. Withhold erdafitinib 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 erdafitinib, with reassessments of clinical condition in 1-2 weeks. When resolves to ≤Grade 1 or baseline, restart at next lower dose.
Grade 4	Discontinue erdafitinib
Dry mouth	
Grade 1	Continue erdafitinib at current dose
Grade 2	Continue erdafitinib at current dose
Grade 3	Withhold erdafitinib (for up to 28 days), with weekly reassessments of clinical condition. When resolved to ≤Grade 1 or baseline, restart at next lower dose.
Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events Version 5.0 (NCI-CTCAE v5.0) where Grade 1 is mild, Grade 2 is moderate, Grade 3 is severe, and Grade 4 is life-threatening.	

Other adverse effects

Grade 3	Withold erdafitinib until toxicity resolves to grade 1 or baseline, then may resume erdafitinib at the next lowest dose level
Grade 4	Permanently discontinue
Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events Version 5.0 (NCI-CTCAE v5.0) where Grade 1 is mild, Grade 2 is moderate, Grade 3 is severe, and Grade 4 is life-threatening.	

Regimen

28-day cycle until disease progression or intolerance (12 cycles will be set in ARIA)

Drug	Dose	Days	Administration
Erdafitinib	8mg	1-28 inclusive	Oral

Treatment will be continued until loss of clinical benefit or excessive toxicity or patient choice to discontinue, whichever is sooner.

Dose Information

- The recommended starting dose of erdafitinib is 8mg orally once daily.
- 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 once daily if the serum phosphate level is <2.91 mmol/L (<9.0 mg/dL), and there is no drug-related toxicity. If the phosphate level is 2.91mmol/L (9.0 mg/dL) or higher follow the relevant dose modifications in the hyperphosphataemia table above.
- After day 21 the serum phosphate level should not be used to guide decisions regarding further dose increase.
- Erdafitinib is available as 3mg, 4mg and 5mg film-coated tablets to allow for dose modifications.

Administration Information

- Erdafitinib tablets should be swallowed whole with or without food at about the same time each day.
- If vomiting occurs any time after taking erdafitinib, the next dose should be taken the next day.
- If a dose is missed, it can be taken as soon as possible. The regular daily dose schedule should be resumed the next day.
- Grapefruit or Seville oranges should be avoided while taking erdafitinib due to strong CYP3A4 inhibition.
- 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 non-hormonal contraception (e.g., condom) during treatment with and until 1 month after the last dose of erdafitinib.

Additional Therapy

- Low emetogenic risk, consider metoclopramide 10mg three times a day if required.
- For persistently elevated phosphate concentrations, adding a non-calcium containing phosphate binder (e.g sevelamer carbonate) should be considered.

Interactions with other medicines

This list is not exhaustive, please check the summary of product characteristics /BNF or an oncology pharmacist for further information

Erdafitinib is primarily metabolised by CYP2C9 and CYP3A4 and is a substrate for P-gp

Moderate CYP2C9 and strong CYP3A4 inhibitors (such as itraconazole, ketoconazole, posaconazole,	Increase exposure to erdafitinib Consider alternative agent with no or minimal

voriconazole, fluconazole, miconazole, ceritinib, clarithromycin, telithromycin, elvitegravir, ritonavir, paritaprevir, saquinavir, nefazodone, nelfinavir, tipranavir, lopinavir, amiodarone, piperine)	enzyme inhibition potential. If co-administration is unavoidable, reduce erdafitinib dose to the next lower dose based on tolerability. If the **moderate CYP2C9 or strong CYP3A4 inhibitor** is discontinued, the erdafitinib dose may be adjusted as tolerated.
Strong CYP3A4 inducers (e.g., apalutamide, enzalutamide, lumacaftor, ivosidenib, mitotane, rifapentine, rifampicin, carbamazepine, phenytoin, and St. John's wort)	Avoid co-administration of erdafitinib
Moderate CYP3A4 inducer (such as dabrafenib, bosentan, cenobamate, elagolix, efavirenz, etravirine, lorlatinib, mitapivat, modafinil, pexidartinib, phenobarbital, primidone, repotrectinib, rifabutin, sotorasib, telotristat ethyl)	If co-administration is unavoidable the 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
Grapefruit or Seville orange	Avoid while taking erdafitinib due to strong CYP3A4 inhibition
P-gp inhibitors	P-gp inhibitors are not expected to affect exposure to erdafitinib in a clinically relevant manner.
P-gp substrates with a narrow therapeutic index (such as colchicine, digoxin, dabigatran, and apixaban)	Should be taken at least 6 hours before or after erdafitinib to minimise the potential for interactions.

Additional Information

- The National Patient Safety Agency alert NPSA/2008/RRR001 must be followed when prescribing, dispensing or administering oral chemotherapy.
- It must be made clear to all staff, including those in the community, that this is a course of oral chemotherapy that must be prescribed by specialist oncology professionals.
- Patients should be assessed for suitability for oral SACT prior to starting treatment.

References

1. Janssen-Cilag Ltd. Balversa 3mg film-coated tablets Summary of Product Characteristics [Internet]. High Wycombe. Janssen-Cilag Ltd; 2025 (Accessed 21/11/2025). Available at: https://www.medicines.org.uk/emc/product/100244/smpc
2. National Institute for Health and Care Excellence (NICE) (2025). Erdafitinib for treating unresectable or metastatic urothelial cancer with FGFR3 alterations after a PD-1 or PD-L1 inhibitor. TA1062. Available at https://www.nice.org.uk/guidance/ta1062 (Accessed: 12 May 2025)
3. Thames Valley Cancer Alliance (2025) Erdafitinib Protocol. Available at https://thamesvalleycanceralliance.nhs.uk/wp-content/uploads/2025/07/Erdafitinib.pdf (Accessed 21/11/2025)
4. The Clatterbridge Cancer Centre NHS Foundation Trust. (2025) Erdafitinib Protocol. Available at: https://www.clatterbridgecc.nhs.uk/application/files/7817/5499/3137/Erdafitinib_Urothelial_Cancer.pdf (Accessed 21/11/2025)

5. Common Toxicity Criteria for Adverse Events v 5. (2017) Available at https://www.ctc.ucl.ac.uk/TrialDocuments/Uploaded/Common%20Terminology%20Criteria%20for%20Adverse%20Events%20(CTCAE)%20v5.0_14092023_0.pdf (Accessed 21/11/2025)

REGIMEN SUMMARY

Erdafitinib (Balversa)

Day One

Take home medicines

1. Erdafitinib 8mg once a day for 28 days oral
   Administration Instructions

   Oral systemic anticancer therapy (SACT).

   Erdafitinib tablets should be swallowed whole and not crushed either with or without food.
   If vomiting occurs any time after taking erdafitinib, the next dose should be taken the next day
   Avoid grapefruit or Seville oranges while taking erdafitinib

   Available as 3mg, 4mg and 5mg tablets, please ensure dose modifications occur in multiples of these strengths.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.0	March 2026	New Protocol	Eleanor Taylor Oncology Pharmacist	Prof Simon Crabb Consultant Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts: -

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines.