# ERDAFITINIB (Balversa)

## INDICATION (ICD10) C67

*Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/)* (ERD1)

1. Erdafitinib monotherapy for unresectable locally advanced or metastatic urothelial carcinoma which has a susceptible fibroblast growth factor receptor 3 (FGFR3) genetic alteration in patients previously treated with at least one line of therapy containing a PD-1 or PD-L1 inhibitor administered in the unresectable locally advanced or metastatic treatment setting but no previous FGR3-targeted therapy. Has no known brain metastases or if the patient has brain metastases, the patient is symptomatically stable prior to starting treatment with erdafitinib. PS 0, 1 or 2.

## REGIMEN

Days 1 to 28 ERDAFITINIB starting dose 8mg tablet oral 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 9mg once daily if the serum phosphate level is <9.0mg/dL (<2.91mmol/L), and there is no drug-related toxicity.
If the phosphate level is 9.0mg/dL or higher follow the relevant dose modifications.
After day 21 the serum phosphate level should not be used to guide up-titration decision.

## CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days whilst deriving benefit or until unacceptable toxicity

## ADMINISTRATION

Available as 3mg, 4mg and 5mg tablets
Swallow whole with or without food.
Grapefruit and seville oranges should be avoided while on erdafitinib.

## ANTI-EMETICS

Low risk days 1 to 28

## CONCURRENT MEDICATION REQUIRED

For persistently elevated phosphate concentrations, adding a non-calcium containing phosphate binder (e.g., sevelamer carbonate) should be considered as needed.

## EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

## INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs monthly
Seum phosphate baseline, between days 14 and 21, then monthly
Neutrophils x $10^9$/L ≥1.0 Consultant's discretion if neutrophils low
Platelets x $10^9$/L ≥100 Consultant's discretion if platelets low
Opthalmological formal examinations prior to initiation (including an Amsler grid test, fundoscopy, visual acuity and if available optical coherence tomography), monthly for the first 4 months of treatment, 3-monthly from then on and otherwise urgently as required (including at least an Amsler grid test).
Baseline weight and every cycle

## MAIN TOXICITES AND ADVERSE REACTIONS

| | |
|---|---|
| Erdafitinib | Ocular toxicity (central serous retinopathy (CSR))<br>Gastrointestinal disorders<br>Hyperphosphataemia and tissue mineralisation<br>Hypophosphataemia<br>Nail, skin or mucosal disorders |

## INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS (not exhaustive list check SPC/BNF/Stockleys)

| | |
|---|---|
| | Moderate CYP2C9 and strong CYP3A4 inhibitors increase erdafitinib exposure. Consider alternative agents with no or minimal enzyme inhibition potential. If erdafitinib is co-administered with a moderate CYP2C9 or strong CYP3A4 inhibitor (such as itraconazole, ketoconazole, posaconazole, voriconazole, fluconazole, miconazole, ceritinib, clarithromycin, telithromycin, elvitegravir, ritonavir, paritaprevir, saquinavir, nefazodone, nelfinavir, tipranavir, lopinavir, amiodarone, piperine), reduce the erdafitinib dose to the next lower dose based on tolerability.<br><br>Strong or moderate CYP3A4 inducers. Avoid co-administration of erdafitinib with strong CYP3A4 inducers (such as apalutamide, enzalutamide, lumacaftor, ivosidenib, mitotane, rifapentine, rifampicin, carbamazepine, phenytoin, and St. John's wort). If erdafitinib is co-administered with a moderate CYP3A4 inducer (such as dabrafenib, bosentan, cenobamate, elagolix, efavirenz, etravirine, lorlatinib, mitapivat, modafinil, pexidartinib, phenobarbital, primidone, repotrectinib, rifabutin, sotorasib, telotristat ethyl), the dose should be cautiously increased by 1 to 2mg and adjusted gradually every two to three weeks based on clinical monitoring for adverse reactions, not to exceed 9mg.<br>Grapefruit or Seville oranges. |

## DOSE MODIFICATIONS

Erdafitinib

Recommended starting dose 8mg once daily

| Dose | 1st dose reduction | 2nd dose reduction | 3rd dose reduction | 4th dose reduction | 5th dose reduction |
|---|---|---|---|---|---|
| 9mg | 8mg | 6mg | 5mg | 4mg | Stop |
| 8mg | 6mg | 5mg | 4mg | Stop | |

**Non-haematological**

Erdafitinib

Eye disorders

| | |
|---|---|
| Grade 1<br>Asymptomatic or mild symptoms; clinical or diagnostic observations only, or abnormal Amsler grid test. | Refer for an ophthalmologic examination (OE).<br>If an OE cannot be performed within 7 days, withhold erdafitinib until an OE can be performed.<br>If no evidence of eye toxicity on OE, continue erdafitinib at same dose level.<br>If diagnosis from OE is keratitis or retinal abnormality (eg CSR), withhold erdafitinib until resolution. If reversible in 4 weeks on OE, resume at next lower dose.<br>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<br>Moderate; limiting age appropriate instrumental activities of daily living (ADL). | Immediately withhold erdafitinib and refer for an OE.<br>If there is no evidence of eye toxicity, resume erdafitinib therapy at the next lower dose level upon resolution.<br>If resolved (complete resolution or stabilisation and asymptomatic) within 4 weeks on OE, resume erdafitinib at the next lower dose level.<br>Upon restarting erdafitinib monitor for recurrence every 1 to 2 weeks for a month and as clinically appropriate thereafter. |
| Grade 3<br>Severe or medically significant but not immediate sight-threatening; limiting self-care ADL. | Immediately withhold erdafitinib and refer for an OE.<br>If resolved (complete resolution or stabilisation and asymptomatic) within 4 weeks, then erdafitinib may be resumed at 2 dose levels lower.<br>Upon restarting erdafitinib, monitor for recurrence every 1 to 2 weeks for a month and as clinically appropriate thereafter.<br>Consider permanent discontinuation of erdafitinib for recurrence. |
| Grade 4<br>Sight-threatening consequences; blindness (20/200 or worse). | Permanently discontinue erdafitinib.<br>Monitor until complete resolution or stabilisation. |

Hyperphosphataemia

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

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

Nail, skin and mucosal changes

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

Other adverse effects

| | |
|---|---|
| Grade 3 | Withhold erdafitinib until toxicity resolves to grade 1 or baseline, then may resume erdafitinib at the next lower dose. |
| Grade 4 | Permanently discontinue. |

**Hepatic impairment**
Erdafitinib
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**
Erdafitinib
Based on population pharmacokinetic (PK) analyses, 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.

**REFERENCES**
1. SPC April 2025
2. CDF list