SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1 NAME OF THE MEDICINAL PRODUCT

Balversa 3 mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 3 mg of erdafitinib.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet (tablet).

Yellow, round biconvex shaped film-coated tablet, 7.6 mm in diameter, debossed with “3” on one side; and “EF” on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Balversa as monotherapy is indicated for the treatment of adult patients with unresectable or metastatic urothelial carcinoma (UC), harbouring susceptible FGFR3 genetic alterations who have previously received at least one line of therapy containing a PD-1 or PD-L1 inhibitor in the unresectable or metastatic treatment setting (see section 5.1).

4.2 Posology and method of administration

Treatment with Balversa should be initiated and supervised by a physician experienced in the use of anticancer therapies.

Before taking Balversa, the physician must have confirmation of (a) susceptible FGFR3 gene alteration(s) (see section 5.1) as determined by a validated test method.

Posology

The recommended starting dose of Balversa is 8 mg 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 <9.0 mg/dL (<2.91 mmol/L), and there is no drug-related toxicity. If the phosphate level is 9.0 mg/dL or higher follow the relevant dose modifications in Table 2. After day 21 the serum phosphate level should not be used to guide up-titration decision.

If vomiting occurs any time after taking Balversa, the next dose should be taken the next day.

Duration of treatment

Treatment should continue until disease progression or unacceptable toxicity occurs.

Missed dose

If a dose of Balversa is missed, it can be taken as soon as possible. The regular daily dose schedule for Balversa should be resumed the next day. Extra tablets should not be taken to make up for the missed dose.

Dose reduction and management of adverse reactions

For recommended dose reduction schedule, see Tables 1 to 5.

Table 1: Balversa dose reduction schedule

Dose	**1st dose reduction**	**2nd dose reduction**	**3rd dose reduction**	**4th dose reduction**	**5th dose reduction**
9 mg → (e.g., three 3 mg tablets)	8 mg (e.g., two 4 mg tablets)	6 mg (two 3 mg tablets)	5 mg (one 5 mg tablet)	4 mg (one 4 mg tablet)	Stop
8 mg → (e.g., two 4 mg tablets)	6 mg (two 3 mg tablets)	5 mg (one 5 mg tablet)	4 mg (one 4 mg tablet)	Stop	

Hyperphosphataemia management

Hyperphosphataemia is an expected, transient pharmacodynamic effect of FGFR inhibitors (see sections 4.4, 4.8 and 5.1). Phosphate concentrations should be assessed prior to the first dose and then monitored monthly. For elevated phosphate concentrations in patients treated with Balversa dose modification guidelines in Table 2 should be followed. For persistently elevated phosphate concentrations, adding a non-calcium containing phosphate binder (e.g., sevelamer carbonate) should be considered as needed (see Table 2).

Table 2: Recommended dose modifications based on serum phosphate concentrations with the use of Balversa after up-titration

Serum phosphate concentration	**Balversa management**
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 Balversa at current dose.
7.00-8.99 mg/dL (2.25-2.90 mmol/L)	Continue Balversa 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 Balversa 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 Balversa 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, Balversa should be discontinued permanently. Medical management of symptoms as clinically appropriate (see section 4.4).
Significant alteration from baseline renal function or Grade 3 hypocalcaemia due to hyperphosphataemia.	Balversa should be discontinued permanently. Medical management as clinically appropriate.

Eye disorder management

Treatment with Balversa should be discontinued or modified based on erdafitinib-related toxicity as described in Table 3.

Table 3: Guideline for management of eye disorders with use of Balversa

Severity grading	Balversa 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 Balversa until an OE can be performed. If no evidence of eye toxicity on OE, continue Balversa at same dose level. If diagnosis from OE is keratitis or retinal abnormality (e.g., CSR[a]), withhold Balversa until resolution. If reversible in 4 weeks on OE, resume at next lower dose. Upon restarting Balversa, 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 Balversa 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 Balversa at the next lower dose level. Upon restarting Balversa, 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 Balversa and refer for an OE. If resolved (complete resolution or stabilisation and asymptomatic) within 4 weeks, then Balversa may be resumed at 2 dose levels lower. Upon restarting Balversa, monitor for recurrence every 1 to 2 weeks for a month and as clinically appropriate thereafter. Consider permanent discontinuation of Balversa for recurrence.
Grade 4 Sight-threatening consequences; blindness (20/200 or worse).	Permanently discontinue Balversa. Monitor until complete resolution or stabilisation.

[a] CSR-central serous retinopathy, see section 4.4

Nail, skin, and mucosal changes

Nail, skin, and mucosal changes have been observed with Balversa. Treatment with Balversa should be discontinued or modified based on erdafitinib-related toxicity as described in Table 4.

Table 4: Recommended dose modifications for nail, skin and mucosal adverse reactions with use of Balversa

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

Table 5: Recommended dose modifications for other adverse reactions with use of Balversa

Other adverse reactions[a]	
Grade 3	Withhold Balversa until toxicity resolves to Grade 1 or baseline, then may resume Balversa at the next lower dose.

Grade 4	Permanently discontinue.

[a] Dose adjustment graded using the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAEv5.0).

Special populations

Renal impairment

Based on population pharmacokinetic (PK) analyses, no dose adjustment is required for patients with mild or moderate renal impairment (see section 5.2). There are no data on the use of Balversa in patients with severe renal impairment. Alternative treatment should be considered in patients with severe renal impairment (see section 5.2).

Hepatic impairment

No dose adjustment is required for patients with mild or moderate hepatic impairment (see section 5.2). Limited data are available on the use of Balversa in patients with severe hepatic impairment. Alternative treatment should be considered in patients with severe hepatic impairment (see section 5.2).

Elderly

No specific dose adjustments are considered necessary for elderly patients (see section 5.2).

Limited data are available in patients older than 85 years old.

Paediatric population

There is no relevant use of erdafitinib in the paediatric population for the treatment of urothelial carcinoma. The safety and efficacy of erdafitinib in paediatric patients (< 18 years of age) have not been established. Currently available safety data are described in section 4.8.

Method of administration

Balversa is for oral use. The tablets should be swallowed whole with or without food at about the same time each day.

Grapefruit or Seville oranges should be avoided while taking Balversa due to strong CYP3A4 inhibition (see section 4.5).

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Ocular disorders

Prior to initiating Balversa, a baseline ophthalmological exam including an Amsler grid test, fundoscopy, visual acuity and, if available, an optical coherence tomography (OCT) should be performed.

Balversa can cause ocular disorders, including central serous retinopathy (CSR) (a grouped term including retinal pigment epithelial detachment (RPED)) resulting in visual field defect (see sections 4.7 and 4.8). The overall incidence of central serous retinopathy was higher in patients ≥65 years of age (33.3%) compared with patients <65 years of age (28.8%). Events of RPED were reported more frequently in patients ≥65 years of age (6.3%) compared with patients <65 years of age (2.1%). Close clinical monitoring is recommended in patients aged 65 years and older as well as with patients that have clinically significant medical eye disorders, such as retinal disorders, including but not limited to, central serous retinopathy, macular/retinal degeneration, diabetic retinopathy, and previous retinal detachment (see section 4.8).

Dry eye symptoms occurred in 16.7% of patients during treatment with Balversa and were Grade 3 or 4 in 0.3% of patients (see section 4.8). All patients should receive dry eye prophylaxis or treatment with ocular demulcents (for example artificial tear substitutes, hydrating or lubricating eye gels or ointment) at least every 2 hours during waking hours. Severe treatment-related dry eye should be evaluated by an ophthalmologist.

Perform monthly ophthalmological examinations including an Amsler grid test during the first 4 months of treatment and every 3 months afterwards, and urgently at any time for visual symptoms (see section 4.2). If any abnormality is observed, follow the management guidelines in Table 3. Ophthalmological examination should include assessment of visual acuity, slit lamp examination, fundoscopy, and optical coherence tomography. Close monitoring including clinical ophthalmological examinations should be performed in patients who have restarted Balversa after an ocular adverse event.

When CSR occurs Balversa should be withheld and permanently discontinued if it does not resolve within 4 weeks or if Grade 4 in severity. For ocular adverse reactions, follow the dose modification guidelines (see section 4.2, Eye disorder management).

Hyperphosphataemia

Balversa can cause hyperphosphataemia. Prolonged hyperphosphataemia can lead to soft tissue mineralisation, cutaneous calcinosis, non-uraemic calciphylaxis, hypocalcaemia, anaemia, secondary hyperparathyroidism, muscle cramps, seizure activity, QT interval prolongation and arrhythmias. Hyperphosphataemia was reported early during Balversa treatment, with most events occurring within the first 3-4 months and Grade 3 events occurring within the first month.

Monitor for hyperphosphataemia 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 (see section 4.2). 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 is above 7.0 mg/dL, consider adding an oral phosphate binder until serum phosphate level returns to <7.0 mg/dL. Consider withholding, reducing the dose, or permanently discontinuing Balversa based on duration and severity of hyperphosphataemia, according to Table 2 (see section 4.2).

Use with products known to prolong QT interval

Caution is advised when administering Balversa 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).

Hypophosphataemia

Hypophosphataemia can occur during treatment with Balversa. Serum phosphate level should be monitored during erdafitinib treatment and erdafitinib treatment breaks. If the serum phosphate level falls below normal, phosphate-lowering therapy and dietary phosphate restrictions (if applicable) should be discontinued. Severe hypophosphataemia may present with confusion, seizures, focal neurologic findings, heart failure, respiratory failure, muscle weakness, rhabdomyolysis, and haemolytic anaemia. For dose modifications see section 4.2. Hypophosphataemia reactions were Grade 3-4 in 1.0% of patients.

Nail disorders

Nail disorders including onycholysis, nail discolouration and paronychia can occur very commonly with Balversa treatment (see section 4.8).

Patients should be monitored for signs and symptoms of nail toxicities. Patients should be advised on preventative treatment such as good hygiene practices, over-the-counter nail strengthener as needed and monitor for signs of infection. Treatment with Balversa should be discontinued or modified based on erdafitinib-related toxicity as described in Table 4.

Skin disorders

Skin disorders including dry skin, palmar-plantar erythrodysaesthesia (PPES) syndrome, alopecia and pruritus can occur very commonly with Balversa treatment (see section 4.8). Patients should be monitored and provided supportive care such as avoiding unnecessary exposure to sunlight and excessive use of soap and bathing. Patients should use moisturisers regularly and avoid perfumed products. Treatment with Balversa should be discontinued or modified based on erdafitinib-related toxicity as described in Table 4.

Photosensitivity reactions

Care should be taken with sun exposure by wearing protective clothing and/or sunscreen due to the potential risk of phototoxicity reactions associated with Balversa treatment.

Mucosal disorders

Stomatitis and dry mouth can occur very commonly with Balversa treatment (see section 4.8). 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 Balversa should be discontinued or modified based on erdafitinib-related toxicity as described in Table 4.

Laboratory tests

Creatinine elevations, hyponatraemia, transaminase elevations, and anaemia have been reported in patients receiving Balversa (see section 4.8). Complete blood counts and serum chemistries should be performed regularly during treatment with Balversa to monitor for these changes.

Reproductive and developmental toxicity

Based on the mechanism of action and findings in animal reproduction studies, erdafitinib is embryotoxic and teratogenic (see section 5.3). Pregnant women should be advised of the potential risk to the foetus. Female patients of reproductive potential should be advised to use highly effective contraception prior to and during treatment, and for 1 month after the last dose (see section 4.6). Male patients should be counselled to use effective contraception (e.g., condom) and not donate or store semen during treatment with and for 1 month after the last dose of Balversa (see section 4.6).

Pregnancy testing with a highly sensitive assay is recommended for females of reproductive potential prior to initiating Balversa.

Combination with strong or moderate CYP2C9 or CYP3A4 inhibitors

Concomitant use of Balversa with moderate CYP2C9 or strong CYP3A4 inhibitors requires dose adjustment (see section 4.5).

Combination with strong or moderate CYP3A4 inducers
Concomitant use of Balversa with strong CYP3A4 inducers is not recommended. Concomitant use of Balversa with moderate CYP3A4 inducers requires dose adjustment (see section 4.5).

Combination with hormonal contraceptives
Concomitant administration of Balversa 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 of Balversa (see sections 4.5 and 4.6).

Excipients with known effect
Each film-coated tablet contains less than 1 mmol sodium (23 mg), that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Effect of other medicinal products on Balversa

Moderate CYP2C9 or strong CYP3A4 inhibitors

Co-administration with a moderate CYP2C9 or strong CYP3A4 inhibitor increased erdafitinib exposure and may lead to increased drug-related toxicity. Erdafitinib mean ratios (90% CI) for C_{max} and AUC_{∞} were 121% (99.9, 147) and 148% (120, 182), respectively, when co-administered with fluconazole, a moderate CYP2C9 and CYP3A4 inhibitor, relative to erdafitinib alone. C_{max} of erdafitinib was 105% (90% CI: 86.7, 127) and AUC_{∞} was 134% (90% CI: 109, 164) when co-administered with itraconazole, a strong CYP3A4 inhibitor and P-gp inhibitor, relative to erdafitinib alone. Consider alternative agents with no or minimal enzyme inhibition potential. If Balversa 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 Balversa dose to the next lower dose based on tolerability (see section 4.2). If the moderate CYP2C9 or strong CYP3A4 inhibitor is discontinued, the Balversa dose may be adjusted as tolerated (see section 4.4).

Grapefruit or Seville oranges should be avoided while taking Balversa due to strong CYP3A4 inhibition (see section 4.2).

Strong or moderate CYP3A4 inducers

Co-administration with carbamazepine, a strong CYP3A4 and weak CYP2C9 inducer leads to decreased erdafitinib exposure. Mean ratios of C_{max} and AUC_{∞} for erdafitinib was 65.4% (90% CI: 60.8, 70.5) and 37.7% (90% CI: 35.4, 40.2), respectively, when co-administered with carbamazepine relative to erdafitinib alone. Avoid co-administration of Balversa with strong CYP3A4 inducers (such as apalutamide,

enzalutamide, lumacaftor, ivosidenib, mitotane, rifapentine, rifampicin, carbamazepine, phenytoin, and St. John's wort). If Balversa 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 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 Balversa dose may be adjusted as tolerated (see sections 4.2 and 4.4).

Effect of Balversa on other medicinal products

Major CYP isoform substrates (including hormonal contraceptives)

Mean ratios of C_{max} and AUC_{∞} for midazolam (a sensitive CYP3A4 substrate) were 86.3% (90% CI: 73.5, 101) and 82.1% (90% CI: 70.8, 95.2), respectively, when co-administered with erdafitinib relative to midazolam alone. Erdafitinib does not have a clinically meaningful effect on midazolam PK. However, it cannot be excluded that CYP3A4 induction after administration of Balversa alone or concomitant administration of other CYP3A4 inducers together with Balversa 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 of Balversa (see section 4.4).

P-Glycoprotein (P-gp) substrates

Erdafitinib is an inhibitor of P-gp. Concomitant administration of Balversa with P-gp substrates may increase their systemic exposure. 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.

Organic cation transporter 2 (OCT2) substrates

Mean ratios of C_{max} and AUC_{∞} for metformin (a sensitive OCT2 substrate) were 109% (90% CI: 90.3, 131) and 114% (90% CI: 93.2, 139), respectively, when co-administered with erdafitinib relative to metformin alone. Erdafitinib does not have a clinically meaningful effect on metformin PK.

Medicinal products that can alter serum phosphate levels

In patients receiving Balversa, 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.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/Contraception in males and females

Based on the mechanism of action and findings in animal reproduction studies, erdafitinib can cause foetal harm when administered to pregnant women. Female patients of child-bearing potential should be advised to use highly effective contraception prior to and during treatment, and for 1 month after the last dose of Balversa. Male patients should be advised to use effective contraception (e.g., condom) and not donate or store semen during treatment with and for 1 month after the last dose of Balversa.

Concomitant administration of Balversa 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 for 1 month after the last dose of Balversa (see section 4.5).

Pregnancy testing

Pregnancy testing with a highly sensitive assay is recommended for females of reproductive potential prior to initiating Balversa.

Pregnancy

There are no data from the use of erdafitinib in pregnant women. Animal studies have shown reproductive toxicity (see section 5.3). Based on the mechanism of action of erdafitinib and the findings in animal reproduction studies, Balversa should not be used during pregnancy unless the clinical condition of the women requires treatment with erdafitinib.

If Balversa is used during pregnancy, or if the patient becomes pregnant while taking Balversa, advise the patient of the potential hazard to the foetus and counsel the patient about her clinical and therapeutic options. Patients should be advised to contact their healthcare professional if they become pregnant or pregnancy is suspected while being treated with Balversa and up to 1 month afterwards.

Breast-feeding

There are no data on the presence of erdafitinib in human milk, or the effects of erdafitinib on the breast-fed infant, or on milk production.
A risk to the suckling child cannot be excluded. Breast-feeding should be discontinued during treatment and for 1 month following the last dose of Balversa.

Fertility

There are no human data on the impact of erdafitinib on fertility. Dedicated animal fertility studies have not been conducted with erdafitinib (see section 5.3). Based on preliminary fertility assessment in general animal studies (see section 5.3) and on the pharmacology of erdafitinib, impairment of male and female fertility cannot be excluded.

4.7 Effects on ability to drive and use machines

Balversa has moderate influence on the ability to drive and use machines. Eye disorders such as central serous retinopathy or keratitis have been noted with FGFR inhibitors and with Balversa treatment. If patients experience treatment related symptoms affecting their vision, it is recommended that they do not drive or use machines until the effect subsides (see section 4.4).

4.8 Undesirable effects

Summary of the safety profile

The most common adverse reactions were hyperphosphataemia (78.5%), diarrhoea (55.5%), stomatitis (52.8%), dry mouth (39.9%), decreased appetite (31.7%), anaemia (28.2%), dry skin (28.0%), central serous retinopathy (28.0%), constipation (27.3%), dysgeusia (26.3%), palmar-plantar erythrodysaesthesia syndrome (PPES) (25.5%), alopecia (23.2%), asthenia (23.0%), alanine aminotransferase increased (21.7%), onycholysis (21.7%), fatigue (20.3%), nausea (18.6%), weight decreased (18.4%), aspartate aminotransferase increased (18.0%), dry eye (16.7%), nail discolouration (15.9%), vomiting (13.8%), blood creatinine increased (13.8%), hyponatraemia (13.4%), paronychia (12.5%), nail dystrophy (11.9%), onychomadesis (11.5%), epistaxis (10.6%), nail disorder (10.2%) and abdominal pain (10.0%).
Most common Grade 3 or higher ADRs were stomatitis (10.6%), hyponatraemia (8.8%), palmar-plantar erythrodysaesthesia syndrome (7.9%), onycholysis (4.8%), diarrhoea (4.0%), hyperphosphataemia (2.9%), decreased appetite (2.5%), and nail dystrophy (2.5%). Grade 3 or 4 related TEAEs (47.6% vs 43.5%) and related serious adverse events (14.6% vs 10.5%) were reported more frequently for patients 65 years and older versus patients <65 years.

Adverse reactions leading to dose reduction occurred in 59.7% of patients. Stomatitis (15.4%), palmar-plantar erythrodysaesthesia syndrome (9.6%), onycholysis (7.3%) and hyperphosphataemia (5.2%) were the most common adverse events leading to dose reduction.

Adverse reactions leading to treatment discontinuation occurred in 19.4% of patients. Detachment of retinal pigment epithelium (1.7%) and stomatitis (1.5%) were the most common adverse events leading to treatment discontinuations.

Tabulated list of adverse reactions

The safety profile is based on pooled data from 479 locally advanced unresectable or metastatic urothelial carcinoma patients who were treated with Balversa in clinical studies. Patients were treated with Balversa at 8/9 mg starting dose orally once daily. Median duration of treatment was 4.8 months (range 0.1 to 43.4 months).

Adverse reactions observed during clinical studies are listed below in Table 6 by frequency category. Frequency categories are defined as follows: 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).

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Table 6: Adverse reactions identified in clinical studies

System organ class	Frequency	Adverse reaction
Endocrine disorders	common	hyperparathyroidism
Metabolism and nutrition disorders	very common	hyperphosphataemia, hyponatraemia, decreased appetite
	common	hypercalcaemia, hypophosphataemia
Nervous system disorders	very common	dysgeusia
Eye disorders	very common	central serous retinopathy[a], dry eye
	common	ulcerative keratitis, keratitis, conjunctivitis, xerophthalmia, cataract, blepharitis, lacrimation increased
Vascular disorders	uncommon	vascular calcification
Respiratory, thoracic and mediastinal disorders	very common	epistaxis
	common	nasal dryness
Gastrointestinal disorders	very common	diarrhoea, stomatitis[b], dry mouth, constipation, nausea, vomiting, abdominal pain
	common	dyspepsia
Skin and subcutaneous tissue disorders	very common	paronychia, onycholysis, onychomadesis, nail dystrophy, nail disorder, nail discolouration, palmar-plantar erythrodysaesthesia syndrome, alopecia, dry skin
	common	onychalgia, onychoclasis, nail ridging, skin fissures, pruritus, skin exfoliation, xeroderma, hyperkeratosis, skin lesion, eczema, rash
	uncommon	nail bed bleeding, nail discomfort, skin atrophy, palmar erythema, skin toxicity
Renal and urinary disorders	common	acute kidney injury, renal impairment, renal failure
Hepatobiliary disorders	common	hepatic cytolysis, hepatic function abnormal, hyperbilirubinaemia
General disorders and administration site conditions	very common	asthenia, fatigue
	uncommon	mucosal dryness
Blood and lymphatic system disorders	very common	anaemia
Investigations	very common	weight decreased, blood creatinine increased, alanine aminotransferase increased, aspartate aminotransferase increased

[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.

[b] Stomatitis includes mouth ulceration.

Description of selected adverse reactions

Central serous retinopathy (CSR)

Adverse reactions of CSR were reported in 31.5% of patients with a median time to first onset, for an event of any grade, of 51 days (see section 4.4). The most commonly reported events were vision blurred, chorioretinopathy, detachment of RPE, visual acuity reduced, visual impairment, retinal detachment, retinopathy, and subretinal fluid. Grade 3 or 4 CSR was reported in 2.7% of patients. The majority of central serous retinopathy events occurred within the first 90 days of treatment. At the time of data cutoff, CSR had resolved for 43.0% of patients. In patients with CSR, 11.3% had dose interruptions and 14.6% had dose reductions. There were 3.3% of patients who discontinued Balversa due to: detachment of RPE (1.7%), chorioretinopathy (0.6%), visual acuity reduced (0.6%), maculopathy (0.4%), vision blurred (0.2%), visual impairment (0.2%), retinal detachment (0.2%), and subretinal fluid (0.2%).

Other eye disorders

Eye disorders (other than central serous retinopathy) were reported in 36.3% of patients. The most commonly reported events were dry eye (16.7%), conjunctivitis (9.8%) and lacrimation increased (9.2%). Of patients with events, 4.8% had dose reductions and 6.7% had dose interruptions. There were 1.3% who discontinued erdafitinib due to eye disorders. The median time to first onset for eye disorders was 53 days (see section 4.4).

Nail disorders

Nail disorders were reported in 62.6% of patients. The most commonly reported events included onycholysis (21.7%), nail discolouration (15.9%), paronychia (12.5%), nail dystrophy (11.9%) and onychomadesis (11.5%). The incidence of nail disorders increased after the first month of exposure. The median time to onset for any grade nail disorder was 63 days.

Skin disorders

Skin disorders were reported in 54.5% of patients. The most commonly reported events were dry skin (28%), and palmar-plantar erythrodysaesthesia syndrome (25.5%). The median time to onset for any grade skin disorder was 47 days.

Gastrointestinal disorders

Gastrointestinal disorders were reported in 83.9% of patients. The most commonly reported events were diarrhoea (55.5%), stomatitis (52.8%), and dry mouth (39.9%). The median time to onset for any grade gastrointestinal disorder was 15 days.

Hyperphosphataemia and soft tissue mineralisation

Erdafitinib can cause hyperphosphataemia. Increases in phosphate concentrations are an expected and transient pharmacodynamic effect (see section 5.1). Hyperphosphataemia was reported as an adverse event in 78.5% of patients treated with Balversa. Hyperphosphataemia was reported early during erdafitinib treatment, with Grade 1-2 events generally occurring within the first 3 or 4 months and Grade 3 events occurring within the first month. The median onset time for any grade event of

hyperphosphataemia was 16 days. Vascular calcification has been observed in 0.2% of patients treated with Balversa
(see section 4.2). Hypercalcaemia and hyperparathyroidism have been observed in 6.1% and 2.9%, respectively, in patients treated with Balversa (see Table 2 in section 4.2).

Hypophosphataemia
Erdafitinib can cause hypophosphataemia. Hypophosphataemia occurred in 5.6% of patients. Hypophosphataemia reactions were Grade 3-4 in 1.0% of patients. The median time to onset for Grade 3 was 140 days. None of the events were serious, led to discontinuation or to dose reduction. Dose interruption occurred in 0.2% of patients.

Abnormal laboratory findings
Abnormal laboratory findings (other than hyperphosphataemia, which is described separately), occurred in 53.4% of patients. The most commonly reported laboratory abnormalities were anaemia (28.2% (135 patients); median time to onset 44 days, 38.5% (52/135) resolved), alanine aminotransferase increased (21.7% (104 patients); median time to onset 41 days; 75% (78/104 resolved), aspartate aminotransferase increased (18% (86 patients); median time to onset 37 days; 73.3% (63/86) resolved), blood creatinine increased (14.2% (68 patients); median time to onset 57 days; 44.1% (30/68) resolved), and hyponatraemia (13.4% (64 patients); median time to onset 55 days; 51.6% (33/64) resolved).

Paediatric population
Growth acceleration and epiphysiolysis of the femoral head have been reported in paediatric patients (< 18 years of age) receiving erdafitinib in clinical trials outside of the authorised indication and off label in the post-marketing setting.

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 the Yellow Card Scheme Website: www.yellowcard.mhra.gov.uk or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

There is no known specific antidote for Balversa overdose. In the event of an overdose, stop Balversa, undertake general supportive measures until clinical toxicity has diminished or resolved.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antineoplastic agents, protein kinase inhibitors. ATC code: L01EN01

Mechanism of action

Erdafitinib is a pan-fibroblast growth factor receptor (FGFR) tyrosine kinase inhibitor.

Pharmacodynamic effects

Serum phosphate

Erdafitinib increases serum phosphate concentration, a secondary effect of FGFR inhibition (see sections 4.2 and 4.8).

Clinical efficacy

The efficacy of Balversa was evaluated in BLC3001 Study Cohort 1, a Phase 3, randomised, open-label, multicentre study to evaluate the overall survival (OS) of erdafitinib versus chemotherapy (docetaxel or vinflunine) in patients with advanced (unresectable or metastatic) urothelial cancer harbouring selected FGFR alterations, who have progressed after 1 or 2 prior treatments, at least 1 of which includes a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor (anti-PD-(L)1) used in the locally advanced unresectable or metastatic treatment setting.

Patients who received neoadjuvant or adjuvant chemotherapy or immunotherapy and showed disease progression within 12 months of the last dose are considered to have received systemic therapy in the metastatic setting. Patients with uncontrolled cardiovascular disease within the preceding 3 months or with grade 2 or higher (≥481 ms) QTc prolongation and impaired wound healing were excluded from the study, as well as patients with central serous retinopathy or retinal pigment epithelial detachment of any grade.

Main efficacy data are based on 266 patients who received prior anti-PD-(L)1 treatment and were randomised to erdafitinib (8 mg with individualised up-titration to 9 mg if the serum phosphate level is <9.0 mg/dL, and there was no drug-related toxicity) versus chemotherapy (docetaxel 75 mg/m^2 once every 3 weeks or vinflunine 320 mg/m^2 once every 3 weeks).

In the study, eligible patients were required to have at least 1 of the following FGFR fusions: FGFR2-BICC1, FGFR2-CASP7, FGFR3-TACC3, FGFR3-BAIAP2L1; or 1 of the following FGFR3 gene mutations: R248C, S249C, G370C, Y373C. Molecular eligibility was determined using central (74.6%) or local (25.4%) FGFR results. Tumour samples were tested for FGFR genetic alterations with the Qiagen Therascreen® FGFR RGQ RT-PCR Kit at the central laboratory. Local historical test on tumour or blood samples were based on local next generation sequencing (NGS) tests. Among the limited number of patients enrolled by local tests who had tumour samples available for confirmation testing, a 75.6% agreement was observed when tested using the central test.

In the study cohort, 99.2% of patients had FGFR genetic alterations (2 patients did not have FGFR alterations: 80.8% of patients had FGFR3 mutations, 16.5% of patients had FGFR3 fusions, and 1.9% of patients had both FGFR3 mutations and fusions). No patients were observed with FGFR2 alterations in this study cohort. A tumour harbouring susceptible FGFR3 genetic alterations is a tumour with at least 1 of the

following FGFR fusions: FGFR3-TACC3, FGFR3-BAIAP2L1; or 1 of the following FGFR3 gene mutations: R248C, S249C, G370C, Y373C. All patients in the study cohort with FGFR alterations had at least 1 FGFR3 alteration. FGFR3-S249C was the most prevalent alteration (46.6%) followed by FGFR3-Y373C (16.9%), and FGFR3-TACC3 fusion (9.8%).

The demographic characteristics were balanced across the erdafitinib and chemotherapy treatment groups. The median age at full-study screening was 67 years (range: 32 to 86 years). The majority of patients were 65 years or older: 19.9% 65 to 69 years; 19.9% 70 to 74 years; 21.1% 75 years or older. The majority of patients were male (71.4%), white (54.1%), and from Europe (60.9%).

All patients had transitional cell carcinoma, with a small percentage (5.3%) of patients having minor components (<50% overall) of variant histology. The primary tumour location was the upper tract for 33.5% of patients and lower tract for 66.5%. Patients had baseline ECOG scores of 0 (42.9%), 1 (47.7%), or 2 (9.4%).

All patients received at least 1 prior line of anti-cancer therapy and must have included an anti-PD-(L)-1. The most frequently received anti-PD-(L)1 therapies, included pembrolizumab (35.3%), avelumab (22.2%) and atezolizumab (19.5%). Prior treatment with chemotherapy was not required, however, the majority of patients (89.1%) received at least one line of prior chemotherapy. Almost all patients received platinum-based chemotherapy (89.7% in erdafitinib group, 85.4% in chemotherapy group): most frequently cisplatin (55.9% in erdafitinib group, 45.4% in chemotherapy group) followed by carboplatin (27.2% in erdafitinib group, 31.5% in chemotherapy group).

The primary efficacy endpoint was Overall Survival. Assessment of radiographic response was performed by investigators according to RECIST (Response Evaluation Criteria in Solid Tumours Version 1.1) until disease progression, intolerable toxicity, withdrawal of consent, or decision by the investigator to discontinue treatment, or the end of the study, whichever occurred first. Progression-Free Survival (PFS), Objective Response Rate (ORR) and Duration of Response were included as secondary efficacy endpoints.

Treatment with erdafitinib showed a statistically significant improvement in OS for patients treated with erdafitinib, with erdafitinib prolonging OS compared to treatment with chemotherapy (median OS of 12.1 vs 7.8 months) (see Table 7).

Efficacy results are summarised in Table 7.

Table 7: Overview of efficacy results for Study BLC3001 Cohort 1

	Erdafitinib (N=136)	**Chemotherapy (N=130)**
Overall Survival (OS)		
Number of events (%)	77 (56.6%)	78 (60.0%)
Median, months (95% CI)	12.06 (10.28, 16.36)	7.79 (6.54, 11.07)
HR (95% CI)	0.64 (0.44, 0.93)[a]	
P-value	0.0050	

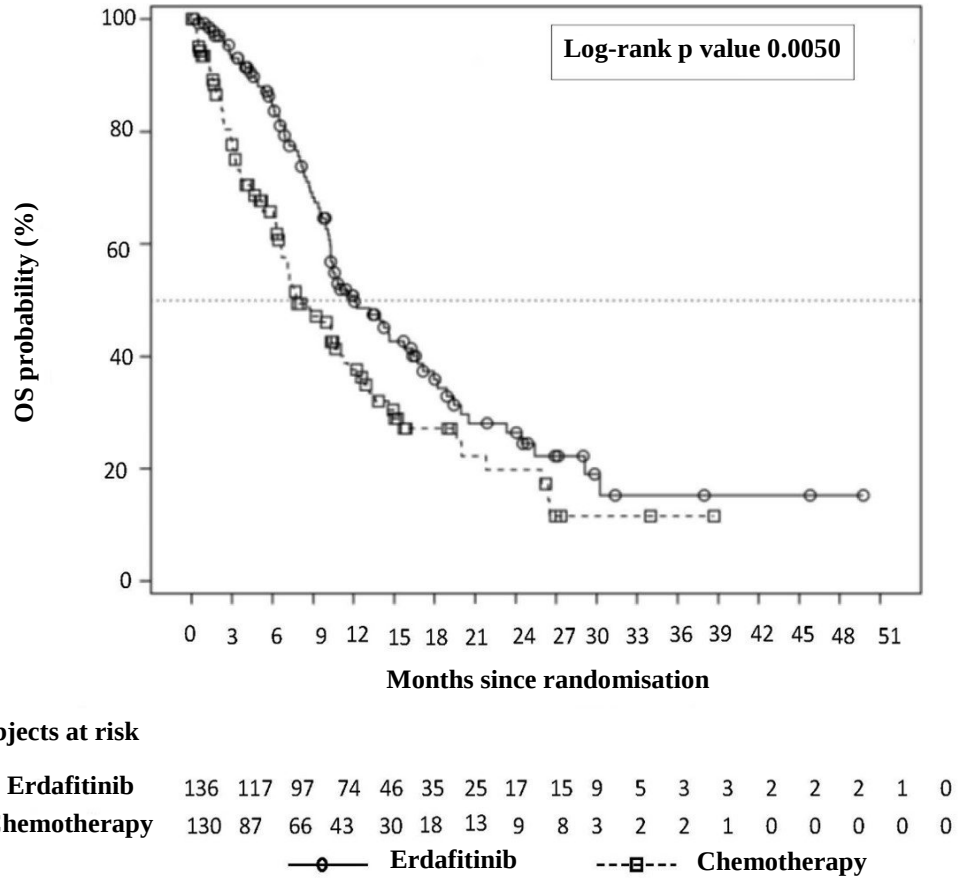
Progression-free survival (PFS)		
Number of events (%)	101 (74.3%)	90 (69.2%)
Median, months (95% CI)	5.55 (4.40, 5.65)	2.73 (1.81, 3.68)
HR (95% CI)	0.58 (0.41, 0.82)[a]	
P-value	0.0002	
Objective response rate (ORR), confirmed		
ORR (CR + PR)	48 (35.3%)	11 (8.5%)
Duration of response (DoR), investigator assessed, confirmed		
Median, months (95% CI)	5.55 (4.17, 8.31)	5.75 (4.86, 7.16)

All p-values reported are 2-sided.

[a] Repeated confidence intervals are provided.

The Kaplan-Meier OS curve for the two treatment arms is presented in Figure 1.

Figure 1. Kaplan-Meier Plot of Overall Survival – Unstratified Analysis (BLC3001 Study Cohort 1)



Elderly patients
In the clinical study of Balversa, 60.9% of patients were 65 years and older (39.8% were 65<75 years old and 21.1% of patients were 75 years and older). No overall difference in efficacy was observed between elderly and younger adult patients.

Paediatric population
The European Medicines Agency has waived the obligation to submit the results of studies with erdafitinib in all subsets of the paediatric population in urothelial carcinoma (see sections 4.2 and 4.8 for information on paediatric use).

5.2 Pharmacokinetic properties

Following single and repeat once daily dosing, erdafitinib exposure (maximum observed plasma concentration [C_{max}] and area under the plasma concentration time curve [AUC]) increased in a dose-proportional manner across the dose range of 0.5 to 12 mg. Steady state was achieved after 2 weeks with once daily dosing and the mean accumulation ratio was 4-fold in patients with cancer. Following administration of 8 mg once daily, the proposed starting dose, mean (coefficient of variation [CV%]) erdafitinib steady-state C_{max}, AUC_{τ}, and minimum observed plasma concentration (C_{min}) were 1399 ng/mL (50.8%), 29268 ng.h/mL (59.9%), and 936 ng/mL (64.9%) in patients with cancer. Daily fluctuations in erdafitinib plasma concentrations were low, with a mean (CV%) peak-to-trough ratio of 1.47 (23%) at steady state upon daily dosing.

Absorption
After single dose oral administration, median time to achieve peak plasma concentration (t_{max}) was 2.5 hours (range: 2 to 6 hours) in healthy volunteers and oral absorption is near complete.

Effect of food
Administration of erdafitinib to healthy volunteers under fasting conditions and with a high-fat meal did not result in clinically relevant changes in C_{max} and AUC. The mean AUC_{∞} and C_{max} decreased by 6% and 14%, respectively, when erdafitinib is co-administered with a high-fat meal. Median time to reach t_{max} was delayed about 1.5 hours with food (see section 4.2).

Distribution
The mean apparent volume of distribution of erdafitinib in patients with cancer was 0.411 L/kg. Erdafitinib was 99.7% bound to human plasma proteins, preferentially to α1 acid glycoprotein.

Biotransformation
Metabolism is the main route of elimination for erdafitinib. Erdafitinib is primarily metabolised in human by CYP2C9 and CYP3A4 to form the O demethylated major metabolite. The contribution of CYP2C9 and CYP3A4 in the total clearance of erdafitinib is estimated to be 39% and 20%, respectively.

Unchanged erdafitinib was the major drug-related moiety in plasma, there were no circulating metabolites.

Elimination

Mean total apparent clearance (CL/F) of erdafitinib was 0.362 L/h in patients with cancer.

The mean effective half-life of erdafitinib in patients with cancer was 58.9 hours.

Up to 16 days following a single oral administration of radiolabelled [^{14}C]-erdafitinib, 69% of the dose was recovered in faeces (14-21% as unchanged erdafitinib) and 19% in urine (13% as unchanged erdafitinib) in healthy volunteers.

Special populations

No clinically meaningful differences in the pharmacokinetics of erdafitinib were observed based on age (21-92 years), sex, race (White, Hispanic or Asian), body weight (36-166 kg), mild or moderate renal impairment and mild or moderate hepatic impairment.

Paediatric population

Pharmacokinetics of erdafitinib has not been studied in paediatric patients.

Renal impairment

No clinically meaningful differences in the pharmacokinetics of erdafitinib were observed between subjects with normal renal function (absolute GFR-MDRD [absolute glomerular filtration rate modification of diet in renal disease] ≥90 mL/min), and subjects with mild (absolute GFR MDRD 60 to 89 mL/min) and moderate renal impairment (absolute GFR MDRD 30 to 59 mL/min) based on population PK analysis. No information is available for subjects with severe renal impairment (absolute GFR MDRD less than 30 mL/min) or renal impairment requiring dialysis due to scarcity of PK data (n=7, 0.8%).

Hepatic impairment

The pharmacokinetics of erdafitinib was examined in participants with preexisting mild n=8) or moderate n=8) hepatic impairment (Child-Pugh Class A and B, respectively) and in healthy control participants with normal hepatic function (n=8). The total AUC_{∞} were 82% and 61% in participants with mild and moderate hepatic impairment compared with participants with normal hepatic function, respectively. The total C_{max} were 83% and 74% in participants with mild and moderate hepatic impairment compared with participants with normal hepatic function, respectively. The free AUC_{∞} were 95% and 88% in participants with mild and moderate hepatic impairment compared with participants with normal hepatic function, respectively. The free C_{max} were 96% and 105% in participants with mild and moderate hepatic impairment compared with participants with normal hepatic function, respectively. No clinically meaningful differences in the pharmacokinetics of erdafitinib were observed in subjects with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment and subjects with normal hepatic function.

The pharmacokinetics of erdafitinib in subjects with severe hepatic impairment is unknown due to limited data.

Drug interactions

Effect of P-gp inhibitors on erdafitinib
Erdafitinib is a substrate for P-gp. P-gp inhibitors are not expected to affect the PK of erdafitinib in a clinically relevant manner.

Effect of acid lowering agents on erdafitinib
Erdafitinib has adequate solubility across the pH range of 1 to 7.4. Acid lowering agents (e.g., antacids, H_2-antagonists, or proton pump inhibitors) are not expected to affect the bioavailability of erdafitinib.

Effect of Sevelamer on erdafitinib
No clinically meaningful differences in the pharmacokinetics of erdafitinib were observed in patients taking sevelamer.

5.3 Preclinical safety data

Repeat-dose toxicity
The main toxicological findings following repeat-dose administration of erdafitinib in both rats and dogs were related to the pharmacological activity of erdafitinib as a reversible inhibitor of FGFR, including increased inorganic phosphorus and calcium in plasma, ectopic mineralisation in various organs and tissues, lesions in bone/cartilage at erdafitinib exposures lower than the human exposure at the recommended clinical dose. Corneal atrophy (thinning of the corneal epithelium) was seen in rats and lacrimal gland atrophy, changes to haircoat and nails as well as dental changes after 3 months of treatment was seen in rats and dogs. Disturbance of phosphate homeostasis was observed in rats and dogs at exposures less than the human exposures at all doses studied.

Soft tissue mineralisations (except for the aorta mineralisation in dogs) and chondroid dysplasia in rats and dogs and mammary gland atrophy in rats were partially to fully recovered at the end of a 4-week drug-free recovery period.

Erdafitinib is an intrinsic human ether-à-go-go-related gene (hERG) blocker with a proarrhythmic liability which translated into a prolonged repolarisation (corrected QT interval) after intravenous dosing in the anaesthetised dog and guinea pig, and after oral dosing in the conscious dog. The no effect level represents a safety margin of 2.4 relative to the clinical steady-state free maximum plasma concentration (C_{max}, u) for a 9 mg once daily dose.

Carcinogenicity and mutagenicity
Long-term animal studies have not been conducted to evaluate the carcinogenic potential of erdafitinib. Erdafitinib was considered not genotoxic in the standard panel of good laboratory practice (GLP) genotoxicity assays.

Reproductive toxicology
Erdafitinib was teratogenic and embryotoxic in rats at exposures less than the human exposures. Foetal toxicity was characterised by hand/foot defects and malformations of some major blood vessels, such as the aorta (see sections 4.4 and 4.6).

Fertility
Dedicated animal fertility studies have not been conducted with erdafitinib. However, in the 3-month general toxicity study, erdafitinib showed effects on female reproductive organs (necrosis of the corpora lutea) in rats at an exposure approximating the AUC in patients at maximum recommended dose of 9 mg, QD.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core
Croscarmellose sodium
Magnesium stearate (E572)
Mannitol (E421)
Meglumine
Microcrystalline cellulose (E460)

Film-coating (Opadry amb II)
Glycerol monocaprylocaprate Type I
Polyvinyl alcohol-partially hydrolysed
Sodium lauryl sulfate
Talc
Titanium dioxide (E171)
Iron oxide yellow (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

HDPE (high-density polyethylene) bottle with a child-resistant PP (polypropylene) closure and induction seal liner.

- Each carton of 56 film-coated tablets contains one bottle of 56 tablets.
- Each carton of 84 film-coated tablets contains one bottle of 84 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

Janssen-Cilag Ltd

50-100 Holmers Farm Way

High Wycombe

Buckinghamshire

HP12 4EG

UK

8 MARKETING AUTHORISATION NUMBER(S)

PLGB 00242/0768

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17/10/2024

10 DATE OF REVISION OF THE TEXT

20/05/2026