

ANNEX I

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
Balversa 4 mg film-coated tablets
Balversa 5 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Balversa 3 mg film-coated tablets

Each film-coated tablet contains 3 mg of erdafitinib.

Balversa 4 mg film-coated tablets

Each film-coated tablet contains 4 mg of erdafitinib.

Balversa 5 mg film-coated tablets

Each film-coated tablet contains 5 mg of erdafitinib.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet (tablet).

3 mg tablets

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 mg tablets

Orange, round biconvex shaped film-coated tablet, 8.1 mm in diameter, debossed with “4” on one side; and “EF” on the other side.

5 mg tablets

Brown, round biconvex shaped film-coated tablet, 8.6 mm in diameter, debossed with “5” 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) assessed by a CE-marked *in vitro* diagnostic (IVD) medical device with the corresponding intended purpose. If a CE-marked IVD is not available, an alternative validated test should be used.

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, 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)	<p>Withhold Balversa treatment until serum phosphate level returns to <7.00 mg/dL (weekly testing recommended).</p> <p>Start phosphate binder with food until serum phosphate level returns to <7.00 mg/dL.</p> <p>Re-start treatment at the same dose level (see Table 1).</p> <p>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.</p>
>10.00 mg/dL (>3.20 mmol/L)	<p>Withhold Balversa treatment until serum phosphate level returns to <7.00 mg/dL (weekly testing recommended).</p> <p>Re-start treatment at the first reduced dose level (see Table 1).</p> <p>If serum phosphate level of ≥ 10.00 mg/dL is sustained for >2 weeks, Balversa should be discontinued permanently.</p> <p>Medical management of symptoms as clinically appropriate (see section 4.4).</p>
Significant alteration from baseline renal function or Grade 3 hypocalcaemia due to hyperphosphataemia.	<p>Balversa should be discontinued permanently.</p> <p>Medical management as clinically appropriate.</p>

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.	<p>Refer for an ophthalmologic examination (OE). If an OE cannot be performed within 7 days, withhold Balversa until an OE can be performed.</p> <p>If no evidence of eye toxicity on OE, continue Balversa at same dose level.</p> <p>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.</p> <p>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.</p>
Grade 2 Moderate; limiting age appropriate instrumental activities of daily living (ADL).	<p>Immediately withhold Balversa and refer for an OE.</p> <p>If there is no evidence of eye toxicity, resume erdafitinib therapy at the next lower dose level upon resolution.</p> <p>If resolved (complete resolution or stabilisation and asymptomatic) within 4 weeks on OE, resume Balversa at the next lower dose level.</p> <p>Upon restarting Balversa, monitor for recurrence every 1 to 2 weeks for a month and as clinically appropriate thereafter.</p>
Grade 3 Severe or medically	<p>Immediately withhold Balversa and refer for an OE.</p> <p>If resolved (complete resolution or stabilisation and asymptomatic)</p>

significant but not immediate sight-threatening; limiting self-care ADL.	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
<i>Nail disorder</i>	<i>Balversa dose management</i>
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.
<i>Dry skin and skin toxicity</i>	
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.
<i>Oral mucositis</i>	
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.
<i>Dry mouth</i>	
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.

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 erythrodysesthesia (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%), dry skin (28.0%), anaemia (28.2%), constipation (27.3%), dysgeusia (26.3%), palmar-plantar erythrodysesthesia syndrome (PPES) (25.5%), alopecia (23.2%), alanine aminotransferase increased (21.7%), onycholysis (21.7%), nausea (18.6%), weight decreased (21.7%), aspartate aminotransferase increased (18%), 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%) and nail disorder (10.2%).

Most common Grade 3 or higher ADRs were stomatitis (10.6%), hyponatraemia (8.8%), palmar-plantar erythrodysesthesia 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 erythrodysesthesia 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 ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1\,000$ to $< 1/100$); rare ($\geq 1/10\,000$ 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, 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 erythrodysesthesia syndrome, alopecia, dry skin
	common	onychalgia, onychoclasia, 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 erythrodysesthesia 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).

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 national reporting system listed in Appendix V.

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/m² once every 3 weeks or vinflunine 320 mg/m² 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

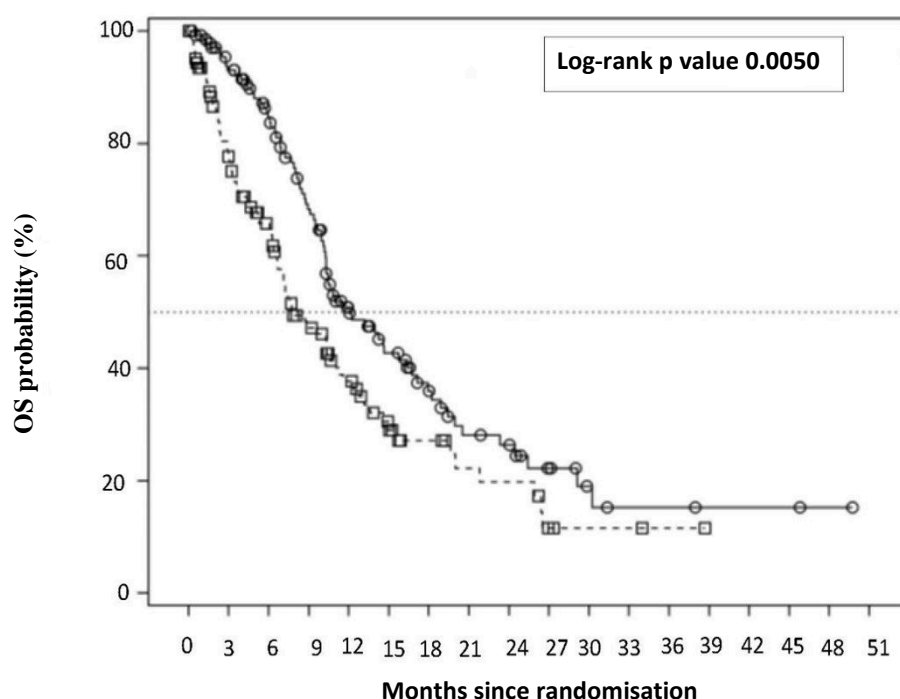
	Erdafitinib (N=136)	Chemotherapy (N=130)
Overall Survival (OS)		
Number of events (%)	77 (56.6%)	78 (60.0%)
Median, months (95% CI)	12.06 (10.28, 16.36)	7.79 (6.54, 11.07)
HR (95% CI)	0.64 (0.44, 0.93) ^a	
P-value	0.0050	
Progression-free survival (PFS)		
Number of events (%)	101 (74.3%)	90 (69.2%)
Median, 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)



Subjects at risk

Erdafitinib	136	117	97	74	46	35	25	17	15	9	5	3	3	2	2	2	1	0
Chemotherapy	130	87	66	43	30	18	13	9	8	3	2	2	1	0	0	0	0	0
	<div style="display: flex; justify-content: space-around; align-items: center;"> —○— Erdafitinib ---□--- Chemotherapy </div>																	

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 section 4.2 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 α_1 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, H₂-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 an irreversible 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

Balversa 3 mg film-coated tablets

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)

Balversa 4 mg film-coated tablets

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)
Iron oxide red (E172)

Balversa 5 mg film-coated tablets

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)
Iron oxide red (E172)
Iron oxide black (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Bottles

4 years

Blisters

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Bottle

HDPE (high-density polyethylene) bottle with a child-resistant PP (polypropylene) closure and induction seal liner. Each carton contains one bottle with 28, 56 or 84 film-coated tablets.

3 mg tablet:

- 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.

4 mg tablet:

- Each carton of 28 film-coated tablets contains one bottle of 28 tablets.
- Each carton of 56 film-coated tablets contains one bottle of 56 tablets.

5 mg tablet:

- Each carton of 28 film-coated tablets contains one bottle of 28 tablets.

Blister

PVC-PCTFE (polyvinyl chloride-polychlorotrifluoroethylene) blister with aluminium push-through foil. The blister(s) are supplied in a carton.

3 mg tablet:

- Each 28-day carton of 56 film-coated tablets contains two blister wallet packs of 28 tablets each.
- Each 28-day carton of 84 film-coated tablets contains two blister wallet packs of 42 tablets each.

4 mg tablet:

- Starter pack: 7-day carton which contains one blister wallet pack with a total 14 film-coated tablets of 4 mg for 1 week treatment. To be used for the starting dose before any dose up-titration or dose reduction.
- Each 28-day carton of 28 film-coated tablets contains one blister wallet pack of 28 tablets.
- Each 28-day carton of 56 film-coated tablets contains two blister wallet packs of 28 tablets each.

5 mg tablet:

- Each 28-day carton of 28 film-coated tablets contains one blister wallet pack of 28 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 International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1841/001
EU/1/24/1841/002
EU/1/24/1841/003
EU/1/24/1841/004
EU/1/24/1841/005
EU/1/24/1841/006
EU/1/24/1841/007
EU/1/24/1841/008
EU/1/24/1841/009
EU/1/24/1841/010
EU/1/24/1841/011

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency <https://www.ema.europa.eu>.

ANNEX II

- A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

Janssen Cilag SpA
Via C. Janssen
Borgo San Michele
Latina 04100, Italy

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING**CARTON 3 mg****1. NAME OF THE MEDICINAL PRODUCT**

Balversa 3 mg film-coated tablets
erdafitinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 3 mg of erdafitinib.

3. LIST OF EXCIPIENTS**4. PHARMACEUTICAL FORM AND CONTENTS**

56 film-coated tablets
84 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral Use. Swallow the tablet whole.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY**8. EXPIRY DATE**

EXP

9. SPECIAL STORAGE CONDITIONS**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

Dispose of unused medicines as per local requirements.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1841/001 56 film-coated tablets
EU/1/24/1841/002 84 film-coated tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

balversa 3 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING**OUTER WALLET 3 mg****1. NAME OF THE MEDICINAL PRODUCT**

Balversa 3 mg film-coated tablets
erdafitinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 3 mg of erdafitinib.

3. LIST OF EXCIPIENTS**4. PHARMACEUTICAL FORM AND CONTENTS**

28 film-coated tablets
42 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral Use. Swallow the tablet whole.

Press and hold
Pull out

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY**8. EXPIRY DATE**

EXP

9. SPECIAL STORAGE CONDITIONS**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

Dispose of unused medicines as per local requirements.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1841/001 28 film-coated tablets
EU/1/24/1841/002 42 film-coated tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

balversa 3 mg

17. UNIQUE IDENTIFIER – 2D BARCODE**18. UNIQUE IDENTIFIER - HUMAN READABLE DATA**

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

INNER WALLET 3 mg (56 film-coated tablets)

1. NAME OF THE MEDICINAL PRODUCT

Balversa 3 mg film-coated tablets
erdafitinib

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

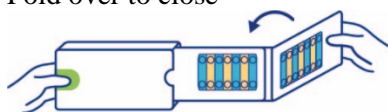
5. OTHER

START DATE

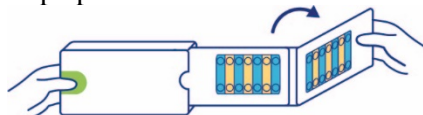


Day 1, Day 2, Day 3, Day 4, Day 5, Day 6, Day 7, Day 8, Day 9, Day 10, Day 11, Day 12, Day 13,
Day 14

Fold over to close



Flip open



Do not separate or cut



MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

INNER WALLET 3 mg (84 film-coated tablets)

1. NAME OF THE MEDICINAL PRODUCT

Balversa 3 mg film-coated tablets
erdafitinib

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

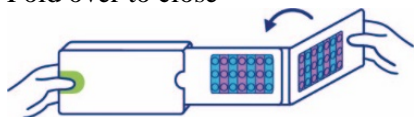
5. OTHER

START DATE

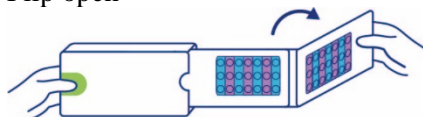


Day 1, Day 2, Day 3, Day 4, Day 5, Day 6, Day 7, Day 8, Day 9, Day 10, Day 11, Day 12, Day 13,
Day 14

Fold over to close



Flip open



Do not separate or cut



MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
--

BLISTER 3 mg

1. NAME OF THE MEDICINAL PRODUCT

Balversa 3 mg film-coated tablets
erdafitinib

2. NAME OF THE MARKETING AUTHORISATION HOLDER
--

Janssen-Cilag International NV

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING**CARTON 4 mg****1. NAME OF THE MEDICINAL PRODUCT**

Balversa 4 mg film-coated tablets
erdafitinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 4 mg of erdafitinib.

3. LIST OF EXCIPIENTS**4. PHARMACEUTICAL FORM AND CONTENTS**

14 film-coated tablets of 4 mg for 1 week treatment. Starter pack
28 film-coated tablets
56 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral Use. Swallow the tablet whole.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY**8. EXPIRY DATE**

EXP

9. SPECIAL STORAGE CONDITIONS**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

Dispose of unused medicines as per local requirements.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1841/005 14 film-coated tablets of 4 mg for 1 week treatment. Starter pack
EU/1/24/1841/006 28 film-coated tablets
EU/1/24/1841/007 56 film-coated tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

balversa 4 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

OUTER WALLET 4 mg

1. NAME OF THE MEDICINAL PRODUCT

Balversa 4 mg film-coated tablets
erdafitinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 4 mg of erdafitinib.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

14 film-coated tablets. Starter pack
28 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral Use. Swallow the tablet whole.

Press and hold
Pull out



6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

Dispose of unused medicines per local requirements.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1841/005 14 film-coated tablets. Starter pack
EU/1/24/1841/006 28 film-coated tablets
EU/1/24/1841/007 28 film-coated tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

balversa 4 mg

17. UNIQUE IDENTIFIER – 2D BARCODE**18. UNIQUE IDENTIFIER - HUMAN READABLE DATA**

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

INNER WALLET 4 mg. Starter pack.

1. NAME OF THE MEDICINAL PRODUCT

Balversa 4 mg film-coated tablets
erdafitinib

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

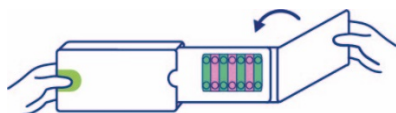
Starter pack

START DATE

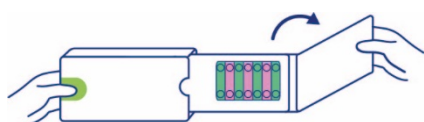


Day 1, Day 2, Day 3, Day 4, Day 5, Day 6, Day 7

Fold over to close



Flip open



Do not separate or cut



MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

INNER WALLET 4 mg (28 film-coated tablets)

1. NAME OF THE MEDICINAL PRODUCT

Balversa 4 mg film-coated tablets
erdafitinib

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

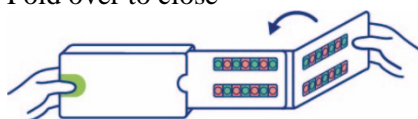
5. OTHER

START DATE

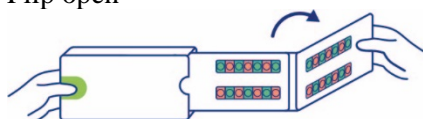


Day 1, Day 2, Day 3, Day 4, Day 5, Day 6, Day 7, Day 8, Day 9, Day 10, Day 11, Day 12, Day 13,
Day 14, Day 15, Day 16, Day 17, Day 18, Day 19, Day 20, Day 21, Day 22, Day 23, Day 24, Day 25,
Day 26, Day 27, Day 28

Fold over to close



Flip open



Do not separate or cut



MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

INNER WALLET 4 mg (56 film-coated tablets)

1. NAME OF THE MEDICINAL PRODUCT

Balversa 4 mg film-coated tablets
erdafitinib

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

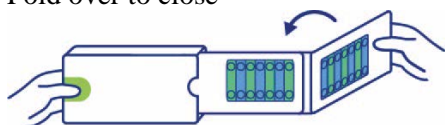
5. OTHER

START DATE

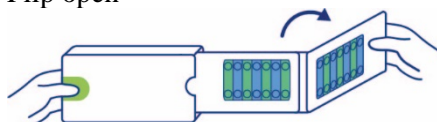


Day 1, Day 2, Day 3, Day 4, Day 5, Day 6, Day 7
Day 8, Day 9, Day 10, Day 11, Day 12, Day 13, Day 14

Fold over to close



Flip open



Do not separate or cut



MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
--

BLISTER 4 mg

1. NAME OF THE MEDICINAL PRODUCT

Balversa 4 mg film-coated tablets
erdafitinib

2. NAME OF THE MARKETING AUTHORISATION HOLDER
--

Janssen-Cilag International NV

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING**CARTON 5 mg****1. NAME OF THE MEDICINAL PRODUCT**

Balversa 5 mg film-coated tablets
erdafitinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 5 mg of erdafitinib.

3. LIST OF EXCIPIENTS**4. PHARMACEUTICAL FORM AND CONTENTS**

28 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral Use. Swallow the tablet whole.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY**8. EXPIRY DATE**

EXP

9. SPECIAL STORAGE CONDITIONS**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

Dispose of unused medicines as per local requirements.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1841/010

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

balversa 5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

OUTER WALLET 5 mg

1. NAME OF THE MEDICINAL PRODUCT

Balversa 5 mg film-coated tablets
erdafitinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 5 mg of erdafitinib.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

28 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral Use. Swallow the tablet whole.

Press and hold
Pull out



6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

Dispose of unused medicines as per local requirements.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1841/010

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

balversa 5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE**18. UNIQUE IDENTIFIER - HUMAN READABLE DATA**

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

INNER WALLET 5 mg

1. NAME OF THE MEDICINAL PRODUCT

Balversa 5 mg film-coated tablets
erdafitinib

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

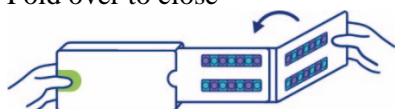
5. OTHER

START DATE

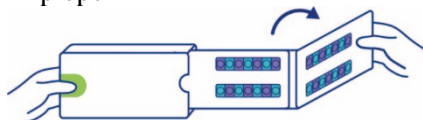


Day 1, Day 2, Day 3, Day 4, Day 5, Day 6, Day 7, Day 8, Day 9, Day 10, Day 11, Day 12, Day 13,
Day 14, Day 15, Day 16, Day 17, Day 18, Day 19, Day 20, Day 21, Day 22, Day 23, Day 24,
Day 25, Day 26, Day 27, Day 28

Fold over to close



Flip open



Do not separate or cut



MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER 5 mg

1. NAME OF THE MEDICINAL PRODUCT

Balversa 5 mg film-coated tablets
erdafitinib

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING**CARTON 3 mg (BOTTLE)****1. NAME OF THE MEDICINAL PRODUCT**

Balversa 3 mg film-coated tablets
erdafitinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 3 mg of erdafitinib.

3. LIST OF EXCIPIENTS**4. PHARMACEUTICAL FORM AND CONTENTS**

56 film-coated tablets
84 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral Use. Swallow the tablet whole.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY**8. EXPIRY DATE**

EXP

9. SPECIAL STORAGE CONDITIONS**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

Dispose of unused medicines as per local requirements.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1841/003 56 film-coated tablets
EU/1/24/1841/004 84 film-coated tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

balversa 3 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING**BOTTLE LABEL 3 mg****1. NAME OF THE MEDICINAL PRODUCT**

Balversa 3 mg film-coated tablets
erdafitinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 3 mg of erdafitinib.

3. LIST OF EXCIPIENTS**4. PHARMACEUTICAL FORM AND CONTENTS**

56 tablets
84 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral Use. Swallow the tablet whole.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY**8. EXPIRY DATE**

EXP

9. SPECIAL STORAGE CONDITIONS**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1841/003 56 tablets
EU/1/24/1841/004 84 tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE****17. UNIQUE IDENTIFIER – 2D BARCODE****18. UNIQUE IDENTIFIER - HUMAN READABLE DATA**

PARTICULARS TO APPEAR ON THE OUTER PACKAGING**CARTON 4 mg (BOTTLE)****1. NAME OF THE MEDICINAL PRODUCT**

Balversa 4 mg film-coated tablets
erdafitinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 4 mg of erdafitinib.

3. LIST OF EXCIPIENTS**4. PHARMACEUTICAL FORM AND CONTENTS**

28 film-coated tablets
56 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral Use. Swallow the tablet whole.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY**8. EXPIRY DATE**

EXP

9. SPECIAL STORAGE CONDITIONS**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

Dispose of unused medicines as per local requirements.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1841/008 28 film-coated tablets
EU/1/24/1841/009 56 film-coated tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

balversa 4 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING**BOTTLE LABEL 4 mg****1. NAME OF THE MEDICINAL PRODUCT**

Balversa 4 mg film-coated tablets
erdafitinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 4 mg of erdafitinib.

3. LIST OF EXCIPIENTS**4. PHARMACEUTICAL FORM AND CONTENTS**

28 tablets
56 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral Use. Swallow the tablet whole.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY**8. EXPIRY DATE**

EXP

9. SPECIAL STORAGE CONDITIONS**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1841/008 28 tablets
EU/1/24/1841/009 56 tablets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE****17. UNIQUE IDENTIFIER – 2D BARCODE****18. UNIQUE IDENTIFIER - HUMAN READABLE DATA**

PARTICULARS TO APPEAR ON THE OUTER PACKAGING**CARTON 5 mg (BOTTLE)****1. NAME OF THE MEDICINAL PRODUCT**

Balversa 5 mg film-coated tablets
erdafitinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 5 mg of erdafitinib.

3. LIST OF EXCIPIENTS**4. PHARMACEUTICAL FORM AND CONTENTS**

28 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral Use. Swallow the tablet whole.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY**8. EXPIRY DATE**

EXP

9. SPECIAL STORAGE CONDITIONS**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

Dispose of unused medicines as per local requirements.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1841/011

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

balversa 5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING**BOTTLE LABEL 5 mg****1. NAME OF THE MEDICINAL PRODUCT**

Balversa 5 mg film-coated tablets
erdafitinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 5 mg of erdafitinib.

3. LIST OF EXCIPIENTS**4. PHARMACEUTICAL FORM AND CONTENTS**

28 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral Use. Swallow the tablet whole.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY**8. EXPIRY DATE**

EXP

9. SPECIAL STORAGE CONDITIONS**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

12. MARKETING AUTHORISATION NUMBER(S)
--

EU/1/24/1841/011

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY
--

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA
--

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Balversa 3 mg film-coated tablets
Balversa 4 mg film-coated tablets
Balversa 5 mg film-coated tablets
erdafitinib

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Balversa is and what it is used for
2. What you need to know before you take Balversa
3. How to take Balversa
4. Possible side effects
5. How to store Balversa
6. Contents of the pack and other information

1. What Balversa is and what it is used for

Balversa is an a cancer medicine that contains the active substance erdafitinib. It belongs to a group of medicines called ‘tyrosine kinase inhibitors’.

Balversa is used in adults to treat urothelial carcinoma (bladder and urinary tract cancer) that is locally advanced (spread nearby) and is unresectable (meaning it cannot be removed by surgery) or metastatic (meaning it has spread to other parts of the body).

It is used when the cancer has:

- alterations in the fibroblast growth factor receptor 3 (*FGFR3*) gene, and
- worsened after treatment known as immunotherapy.

Balversa should only be used if the cancer cells have changes in the *FGFR3* gene. Before starting treatment, your doctor will test if you have such changes in the *FGFR3* gene to make sure this medicine is right for you.

The active substance in Balversa, erdafitinib, works by blocking proteins in the body called FGFR tyrosine kinases. This helps to slow down or stop the growth of cancer cells that have abnormal *FGFR3* receptors resulting from changes in the *FGFR3* gene.

2. What you need to know before you take Balversa

Do not take Balversa if

- you are allergic to erdafitinib or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor before using Balversa if you:

- have increased blood levels of phosphate
- have vision or eye problems
- are pregnant
- you are a woman who can become pregnant

Eye (sight) problems

Balversa increases your risk of central serous retinopathy (CSR; a condition where fluid builds up and separates the macula, the central part of the retina at the back of the eye, causing blurred and distorted vision). The risk of CSR is higher in people aged 65 years and older.

- Before starting treatment with Balversa, you will have an extensive eye exam, including tests to check your vision, retina and eye structure.
- Your doctor will monitor your eyes closely by performing monthly eye exams for the first 4 months of treatment, and every 3 months after that.
- If you experience any symptoms of abnormal vision, your doctor will perform an urgent eye examination.
- Tell your doctor immediately if you have any symptoms of CSR, including blurred vision or reduced peripheral (side vision), a dark spot in your central vision, distorted central vision, where lines appear crooked or bent, object appearing smaller or further away than they really are, colours appearing washed out, floaters or specks passing through your field of vision, flashes of light or feeling of looking through a curtain. Also see section 4 under 'Most important side effects'.
- If you experience CSR during treatment with Balversa, your doctor may need to stop your treatment temporarily. They will permanently stop your treatment if symptoms do not resolve within 4 weeks or are very severe.

During treatment with Balversa, you should use eye drops or gels regularly to prevent and treat dry eyes.

High phosphate levels in the blood (hyperphosphataemia)

Balversa can cause an increase in phosphate levels (hyperphosphataemia) in your blood. This is a known side effect with Balversa that usually occurs within the first few weeks of starting treatment. This can lead to a buildup of minerals such as calcium in your soft tissues, cutaneous calcinosis (a buildup of calcium in the skin, causing hard lumps or nodules) and non-uraemic calcinosis (a rare skin condition that causes painful skin ulcers due to a buildup of calcium in the blood vessels).

- Your doctor will monitor your blood phosphate levels during treatment. They may advise you to limit your intake of foods high in phosphate and avoid taking other medicines that could raise your phosphate levels.
- Vitamin D supplements are not recommended while taking Balversa, as this may also contribute to high phosphate and calcium levels.
- If your blood phosphate levels get too high, your doctor may suggest taking medicine to help control it.
- If you develop high blood levels of phosphate, your doctor may need to adjust your Balversa dose or stop your treatment altogether.
- Tell your healthcare provider right away if you develop the following symptoms, which may be signs of hyperphosphataemia:
 - painful skin lesions

- muscle cramps
- numbness, or
- tingling around your mouth.

Skin disorders

When taking Balversa, you may experience itching, dry skin or redness, swelling, peeling or tenderness, mainly on the hands or feet ('hand-foot syndrome'). You should monitor your skin and avoid unnecessary exposure to sunlight, excessive use of soap and bathing. You should use moisturisers regularly and avoid perfumed products.

Photosensitivity

When taking Balversa, you may become more sensitive to sunlight. This can cause skin damage. You should be careful and take precautions when spending time outside in the sun. Precautions can include wearing clothing that covers your skin and using sunscreen to protect yourself from harmful sun rays.

Nail disorders

When taking Balversa, you may experience nails separating from the bed, infected skin around the nail, or discoloured nails. You should monitor your nails for any signs of infection and practice preventative nail treatments such as good hygiene and using over-the-counter nail strengthener.

Mucosal disorders

When taking Balversa you may experience dry mouth and or mouth sores. You should practice good oral hygiene and avoid spicy or acidic foods while taking Balversa.

Children and adolescents

This medicine is not for use in children and adolescents. This is because there is no experience with using Balversa in this age group.

Other medicines and Balversa

Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. Taking Balversa with certain other medicines may affect how Balversa works and can cause side effects.

The following medicines may decrease the effectiveness of Balversa by decreasing the amount of Balversa in the blood:

- carbamazepine (used to treat epilepsy)
- rifampicin (used to treat tuberculosis)
- phenytoin (used to treat epilepsy)
- St. John's wort (used to treat depression)

The following medicines may increase the risk of side effects of Balversa by increasing the amount of Balversa in the blood:

- fluconazole (used to treat fungal infections)
- itraconazole (used to treat fungal infections)
- ketoconazole (used to treat fungal infections)
- posaconazole (used to treat fungal infections)
- voriconazole (used to treat fungal infections)
- miconazole (used to treat fungal infections)
- ceritinib (used to treat lung cancer)
- clarithromycin (used to treat infections)
- telithromycin (used to treat infections)
- elvitegravir (used to treat HIV)
- ritonavir (used to treat HIV)
- paritaprevir (used to treat hepatitis)
- saquinavir (used to treat HIV)
- nefazodone (used to treat depression)

- nelfinavir (used to treat HIV)
- tipranavir (used to treat HIV)
- lopinavir (used to treat HIV)
- amiodarone (used to treat arrhythmias)
- piperine (used as a supplement)

Balversa may increase the risk of side effects of some other medicines by increasing the amount of these medicines in the blood. These include:

- midazolam (used to treat seizures)
- hormonal contraceptives
- colchicine (used to treat gout)
- digoxin (used to treat certain arrhythmias or heart failure)
- dabigatran (used as a blood thinner)
- apixaban (used as a blood thinner)

Balversa with food

Do not take Balversa with grapefruit or Seville oranges (bitter oranges) – this includes eating them, drinking the juice or taking a supplement that might contain them. This is because it can increase the amount of Balversa in your blood.

Pregnancy, contraception and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice **before** taking this medicine.

Information for women

- Pregnancy
 - Balversa can harm your unborn baby.
 - You should not use Balversa during pregnancy unless you are told otherwise by your doctor.
 - You should not become pregnant during treatment with Balversa and for 1 month after the last dose of Balversa.
 - Tell your doctor immediately if you become pregnant.
- Pregnancy test
 - Your doctor will ask you to do a pregnancy test before you start treatment with Balversa.
- Contraception
 - Balversa may reduce the effectiveness of some birth control methods. Talk to your doctor about appropriate birth control while taking Balversa. Women who can become pregnant should use highly effective contraception during treatment and for at least 1 month after treatment with Balversa.
- Breast-feeding
 - Do not breast-feed during treatment with Balversa and for 1 month following the last dose of this medicine.

Information for men

Men must use effective contraception (condom) while being treated with Balversa and for 1 month after the last dose. Also, you must not donate or store semen during treatment and for 1 month after the last dose.

Driving and using machines

Eye problems have been reported in patients taking Balversa. If you have problems affecting your sight, do not drive or use any tools or machines until your sight returns to normal.

Balversa contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to take Balversa

Always take this medicine exactly as described in this leaflet or as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

How much to take

Your doctor will work out your dose and how often you should take this medicine.

- The recommended starting dose of Balversa is 8 mg once a day by mouth.
 - You may need to take one 5 mg tablet and one 3 mg tablet or two 4 mg tablets to get this dose.

After about 2 weeks of taking Balversa, your doctor will do a blood test. This is to check the phosphate level in your blood.

- Based on the results of this blood test and on whether or not you are experiencing side effects, your doctor may increase your dose to 9 mg a day.

The doctor may also decide to decrease the dose if you have certain side effects such as sores in the mouth, redness, swelling, peeling or tenderness, mainly on the hands or feet, nail separating from the nail bed, high level of phosphate in your blood.

Taking this medicine

- Swallow Balversa tablets whole.
- You can take this medicine with or without food.
- Try to take this medicine at the same time each day. This will help you remember to take it.
- If you vomit, do not take another tablet. Take your next dose at the regular time the next day.

If you take more Balversa than you should

If you take too much Balversa, call your doctor or go to the nearest hospital emergency room right away.

If you forget to take Balversa

- If you miss a dose, take it as soon as possible on the same day. Take your regular dose of Balversa the next day.
- Do not take a double dose to make up for a forgotten dose.

If you stop taking Balversa

Do not stop taking this medicine unless your doctor tells you.

If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Most important side effects

Tell your doctor immediately if you notice any of the serious side effects below:

Central serous retinopathy (**very common**: may affect more than 1 in 10 people)

The following symptoms may be signs of CSR:

- blurred vision or reduced peripheral (side) vision
- a dark spot in your central vision

- distorted central vision, where lines appear crooked or bent
- objects appearing smaller or further away than they really are
- colours appearing washed out
- floaters or specks passing through your field of vision, flashes of light or feeling of looking through a curtain.

Hyperphosphataemia (**very common**: may affect more than 1 in 10 people)

The following symptom may be a sign of hyperphosphataemia:

- high level of phosphate in the blood

Nail disorders (**very common**: may affect more than 1 in 10 people)

The following symptoms may be signs of nail disorders:

- nails separating from the bed (onycholysis)
- infected skin around the nail (paronychia)
- poor nail formation (nail disorder)
- discoloured nails (nail discolouration)

Skin disorders (**very common**: may affect more than 1 in 10 people)

The following symptoms may be signs of skin disorders:

- redness, swelling, peeling or tenderness, mainly on the hands or feet ('hand-foot syndrome')
- hair loss (alopecia)
- dry skin

Mucosal disorders (**very common**: may affect more than 1 in 10 people)

The following symptoms may be signs of mucosal disorders:

- sores in the mouth (stomatitis)
- dry mouth

Tell your doctor immediately if you notice any of the above signs of 'central serous retinopathy', 'hyperphosphataemia', 'nail disorders', 'skin disorders' or 'mucosal disorders'.

Your doctor may ask you to stop taking Balversa or send you to a specialist if you have eye or sight problems.

Other side effects may occur with the following frequencies:

Very common (may affect more than 1 in 10 people):

- diarrhoea
- decreased appetite
- change in sense of taste with food tasting metallic, sour, or bitter (dysgeusia)
- weight loss
- constipation
- feeling sick (nausea)
- vomiting
- stomach pain
- dry eyes
- feeling weak and very tired
- low level of sodium in blood (hyponatraemia)
- increased level of 'creatinine' in the blood (increased creatinine)
- increased level of the liver enzyme 'alanine aminotransferase' in the blood (ALT increased)
- increased level of the liver enzyme 'aspartate aminotransferase' in the blood (AST increased)
- low number of red blood cells (anaemia)
- nose bleeds (epistaxis)

Common (may affect up to 1 in 10 people):

- painful nails
- ridging or breaking of the nail or nails

- very dry skin
- cracked, thickened or flaky skin
- itching or itchy skin rash (eczema)
- abnormal growth or appearance on the skin
- rash
- dry or inflamed eyes (conjunctivitis)
- ulcers or inflamed front part of the eye ('cornea')
- red and swollen eyelids
- watery eyes
- high level of calcium in the blood
- low level of phosphate in the blood
- nasal dryness
- indigestion (dyspepsia)
- sudden decrease in kidney function
- high level of the hormone 'parathyroid' (PTH) (hyperparathyroidism)
- kidney failure (renal failure)
- problems with kidneys (renal impairment)
- liver damage (hepatic cytolysis)
- abnormal liver function
- high level of 'bilirubin' in the blood

Uncommon (may affect up to 1 in 100 people):

- bleeding under the nail
- nail discomfort or pain
- skin reaction
- thinning of the skin
- redness of the palms
- membrane dryness (including nose, mouth, eyes, vagina)

Talk to your doctor if you get any of the above side effects.

Reporting of side effects

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in [Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Balversa

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the blister, carton and bottle after "EXP". The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

Do not use this medicine if the packaging is damaged or shows signs of tampering.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Balversa contains

- The active substance is erdafitinib.
- Each film-coated tablet contains either 3 mg, or 4 mg or 5 mg of erdafitinib.
- The other ingredients are:
 - Tablet core: Croscarmellose sodium, Magnesium stearate (E572), Mannitol (E421), Meglumine, and 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), Iron oxide red (E172) (for the 4 mg and 5 mg tablets only), iron oxide black (E172) (for the 5 mg tablets only).

What Balversa looks like and contents of the pack

Balversa 3 mg film-coated tablets are yellow, round biconvex shaped tablet, debossed with “3” on one side; and “EF” on the other side.

Balversa 4 mg film-coated tablets are orange, round biconvex shaped tablet, debossed with “4” on one side; and “EF” on the other side.

Balversa 5 mg film-coated tablets are brown, round biconvex shaped tablet, debossed with “5” on one side; and “EF” on the other side.

Balversa film-coated tablets may be supplied either in a child-resistant blister pack or a child-resistant bottle.

Not all pack sizes may be marketed.

Bottle:

The tablets are supplied in a plastic bottle with a child-resistant closure. Each bottle contains either 28, 56, or 84 film-coated tablets. Each carton contains one bottle.

3 mg tablet:

- 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.

4 mg tablet:

- Each carton of 28 film-coated tablets contains one bottle of 28 tablets.
- Each carton of 56 film-coated tablets contains one bottle of 56 tablets.

5 mg tablet:

- Each carton of 28 film-coated tablets contains one bottle of 28 tablets.

Blister:

Balversa is supplied in a carton. Each carton contains either 14, 28, 56, or 84 film-coated tablets in one or two blister wallets.

3 mg tablet:

- Each 28-day carton of 56 film-coated tablets contains 2 blister wallet packs of 28 tablets each.
- Each 28-day carton of 84 film-coated tablets contains 2 blister wallet packs of 42 tablets each.

4 mg tablet:

- Starter pack: 7-day carton which contains 1 blister wallet pack with a total 14 film-coated tablets of 4 mg for 1 week treatment. To be used for the starting dose before your doctor increases your dose or decides to decrease it.

- Each 28-day carton of 28 film-coated tablets contains 1 blister wallet pack of 28 tablets.
- Each 28-day carton of 56 film-coated tablets contains 2 blister wallet packs of 28 tablets each.

5 mg tablet:

- Each 28-day carton of 28 film-coated tablets contains 1 blister wallet pack of 28 tablets.

Marketing Authorisation Holder

Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

Manufacturer

Janssen Cilag SpA
Via C. Janssen
Borgo San Michele
Latina 04100
Italy

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien

Janssen-Cilag NV
Tel/Tél: +32 14 64 94 11
janssen@jacbe.jnj.com

Lietuva

UAB "JOHNSON & JOHNSON"
Tel: +370 5 278 68 88
lt@its.jnj.com

България

„Джонсън & Джонсън България“ ЕООД
Тел.: +359 2 489 94 00
jjsafety@its.jnj.com

Luxembourg/Luxemburg

Janssen-Cilag NV
Tél/Tel: +32 14 64 94 11
janssen@jacbe.jnj.com

Česká republika

Janssen-Cilag s.r.o.
Tel: +420 227 012 227

Magyarország

Janssen-Cilag Kft.
Tel.: +36 1 884 2858
janssenhu@its.jnj.com

Danmark

Janssen-Cilag A/S
Tlf.: +45 4594 8282
jacdk@its.jnj.com

Malta

AM MANGION LTD
Tel: +356 2397 6000

Deutschland

Janssen-Cilag GmbH
Tel: 0800 086 9247 / +49 2137 955 6955
jancil@its.jnj.com

Nederland

Janssen-Cilag B.V.
Tel: +31 76 711 1111
janssen@jacnl.jnj.com

Eesti

UAB "JOHNSON & JOHNSON" Eesti filiaal
Tel: +372 617 7410
ee@its.jnj.com

Norge

Janssen-Cilag AS
Tlf: +47 24 12 65 00
jacno@its.jnj.com

Ελλάδα

Janssen-Cilag Φαρμακευτική Μονοπρόσωπη
Α.Ε.Β.Ε.
Τηλ: +30 210 80 90 000

Österreich

Janssen-Cilag Pharma GmbH
Tel: +43 1 610 300

España

Janssen-Cilag, S.A.
Tel: +34 91 722 81 00
contacto@its.jnj.com

France

Janssen-Cilag
Tél: 0 800 25 50 75 / +33 1 55 00 40 03
medisource@its.jnj.com

Hrvatska

Johnson & Johnson S.E. d.o.o.
Tel: +385 1 6610 700
jjsafety@JNJCR.JNJ.com

Ireland

Janssen Sciences Ireland UC
Tel: +1 800 709 122
medinfo@its.jnj.com

Ísland

Janssen-Cilag AB
c/o Vistor hf.
Sími: 354 535 7000
janssen@vistor.is

Italia

Janssen-Cilag SpA
Tel: 800.688.777 / +39 02 2510 1
janssenita@its.jnj.com

Κύπρος

Βαρνάβας Χατζηπαναγής Ατδ
Τηλ: +357 22 207 700

Latvija

UAB "JOHNSON & JOHNSON" filiāle Latvijā
Tel: +371 678 93561
lv@its.jnj.com

Polska

Janssen-Cilag Polska Sp. z o.o.
Tel.: +48 22 237 60 00

Portugal

Janssen-Cilag Farmacêutica, Lda.
Tel: +351 214 368 600

România

Johnson & Johnson România SRL
Tel: +40 21 207 1800

Slovenija

Johnson & Johnson d.o.o.
Tel: +386 1 401 18 00
Janssen_safety_slo@its.jnj.com

Slovenská republika

Johnson & Johnson, s.r.o.
Tel: +421 232 408 400

Suomi/Finland

Janssen-Cilag Oy
Puh/Tel: +358 207 531 300
jacfi@its.jnj.com

Sverige

Janssen-Cilag AB
Tfn: +46 8 626 50 00
jacse@its.jnj.com

United Kingdom (Northern Ireland)

Janssen Sciences Ireland UC
Tel: +44 1 494 567 444
medinfo@its.jnj.com

This leaflet was last revised in

Detailed information on this medicine is available on the European Medicines Agency web site:
<https://www.ema.europa.eu>.