DOSING AND ADMINISTRATION GUIDE

Balversa®
(erdafitinib)
3, 4, 5 mg tablets

Once-Daily Oral Dosing

BALVERSA® (erdafitinib) is a kinase inhibitor indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (mUC) with susceptible *FGFR3* genetic alterations whose disease has progressed on or after at least one line of prior systemic therapy.

Select patients for therapy based on an FDA-approved companion diagnostic for BALVERSA®.

Limitations of Use

BALVERSA® is not recommended for the treatment of patients who are eligible for and have not received prior PD-1 or PD-L1 inhibitor therapy.

Information on FDA-approved tests for the detection of *FGFR3* genetic alterations in urothelial cancer is available at: **https://www.fda.gov/CompanionDiagnostics**.

Important Safety Information

Warnings and Precautions

The safety population described in the Warnings and Precautions reflect a pooled safety population of 479 patients with advanced urothelial cancer and *FGFR* alterations who received BALVERSA®.

Ocular Disorders – BALVERSA® can cause ocular disorders, including central serous retinopathy/retinal pigment epithelial detachment (CSR/RPED) resulting in visual field defect.

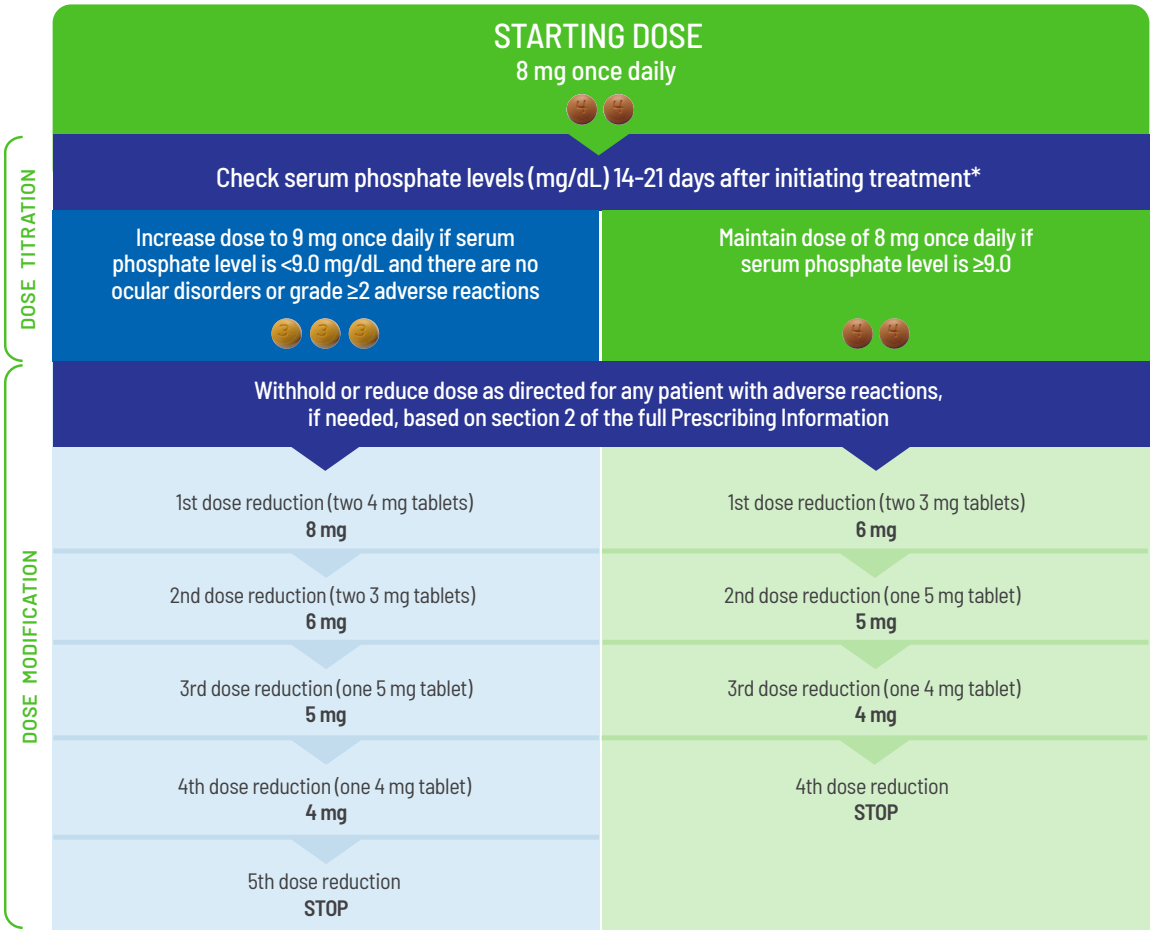
CSR/RPED occurred in 22% of patients treated with BALVERSA®, with a median time to first onset of 46 days. In 104 patients with CSR, 40% required dose interruptions and 56% required dose reductions; 2.9% of BALVERSA®-treated patients required permanent discontinuation for CSR. Of the 24 patients who restarted BALVERSA® after dose interruption with or without dose reduction, 67% had recurrence and/or worsening of CSR after restarting. CSR was ongoing in 41% of the 104 patients at the time of last evaluation.

Dry eye symptoms occurred in 26% of BALVERSA®-treated patients. All patients should receive dry eye prophylaxis with ocular demulcents as needed.

Perform monthly ophthalmological examinations during the first 4 months of treatment and every 3 months afterwards, and urgently at any time for visual symptoms. Ophthalmological examination should include assessment of visual acuity, slit lamp examination, fundoscopy, and optical coherence tomography. Withhold or permanently discontinue BALVERSA® based on severity and/or ophthalmology exam findings.

Please see full Important Safety Information on page 4 and click here to see full BALVERSA® Prescribing Information.

DOSING AND DOSE ADJUSTMENTS OVERVIEW



*The recommended starting dose of BALVERSA® is 8 mg (two 4 mg tablets) orally once daily, with a dose increase to 9 mg (three 3 mg tablets) once daily based on tolerability, including hyperphosphatemia, at day 14 to 21 days. Treatment should continue until disease progression or unacceptable toxicity occurs.

Drug interactions

Effects of other drugs on BALVERSA®

For coadministration with moderate CYP2C9 or strong CYP3A4 inhibitors, consider alternative agents or monitor closely for adverse reactions.

Avoid concomitant use of strong CYP3A4 inducers with BALVERSA®.

For coadministration with moderate CYP3A4 inducers, administer BALVERSA® at a dose of 9 mg.

Serum phosphate level-altering agents: Avoid concomitant use with agents that can alter serum phosphate levels before the initial dose modification period.

Effect of BALVERSA® on other drugs

P-gp substrates: Separate BALVERSA® administration by at least 6 hours before or after administration of P-gp substrates with narrow therapeutic indices.

Important Safety Information (continued)

Hyperphosphatemia and Soft Tissue Mineralization - BALVERSA® can cause hyperphosphatemia leading to soft tissue mineralization, cutaneous calcinosis, non-uremic calciphylaxis and vascular calcification. Increases in phosphate levels are a pharmacodynamic effect of BALVERSA®. Increased phosphate occurred in 73% of BALVERSA®-treated patients. The median onset time of increased phosphate was 16 days (range: 8–421) after initiating BALVERSA®. Twenty-four percent of patients received phosphate binders during treatment with BALVERSA®. Vascular calcification was observed in 0.2% of patients treated with BALVERSA®.

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MONITORING AND ADMINISTRATION

Managing hyperphosphatemia

- Increases in serum phosphate levels are a pharmacodynamic effect of BALVERSA®
- In all patients, restrict phosphate intake to 600-800 mg daily
- If serum phosphate is above 7 mg/dL, consider adding an oral phosphate binder until serum phosphate level returns to <7 mg/dL. If hyperphosphatemia (≥10 mg/dL) for >2 weeks, discontinue BALVERSA® permanently
- Monitor phosphate levels monthly for hyperphosphatemia and withhold, dose reduce, or permanently discontinue BALVERSA® based on duration and severity of hyperphosphatemia
  - See Table 2, Dose Modifications for Adverse Reactions, DOSAGE AND ADMINISTRATION (2.3) in the full Prescribing Information for BALVERSA®

Managing eye disorders

- Perform monthly ophthalmological examinations during the first 4 months of treatment and every 3 months afterwards, and urgently at any time for visual symptoms
  - Ophthalmological examination should include assessment of visual acuity, slit lamp examination, fundoscopy, and optical coherence tomography
  - For ocular adverse reactions, follow dose modification guidelines

To treat and prevent dry eyes, instruct patients to use the following at least every 2 hours during waking hours:

artificial tear substitutes	
OR	
hydrating or lubricating eye gels	
OR	
hydrating or lubricating ointments	

- Please see full **Prescribing Information** for additional recommendations on managing potential eye disorders with BALVERSA®

Dose modifications for adverse reactions

Follow dose modification guidelines regarding any patient with adverse reactions, if needed (on previous page), and in **Table 2 of the full Prescribing Information**.

Administration

No fasting restrictions. Tablets can be taken with or without food

Tablets should be swallowed whole

Missed doses should be taken as soon as possible on the same day and the regular daily dose taken on the next day; extra tablets should not be taken to make up for the missed dose

Visit balversahcp.com for more detailed information about dosage and administration for BALVERSA®

Important Safety Information (continued)

Hyperphosphatemia and Soft Tissue Mineralization (continued) - Monitor for hyperphosphatemia throughout treatment. In all patients, restrict phosphate intake to 600-800 mg daily and avoid concomitant use of agents that may increase serum phosphate 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. Withhold, dose reduce, or permanently discontinue BALVERSA® based on duration and severity of hyperphosphatemia.

Balversa® (erdafitinib) 3, 4, 5 mg tablets

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Indication

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Monitor for hyperphosphatemia throughout treatment. In all patients, restrict phosphate intake to 600-800 mg daily and avoid concomitant use of agents that may increase serum phosphate 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. Withhold, dose reduce, or permanently discontinue BALVERSA® based on duration and severity of hyperphosphatemia.

Embryo-Fetal Toxicity – Based on the mechanism of action and findings in animal reproduction studies, BALVERSA® can cause fetal harm when administered to a pregnant female. In a rat embryo-fetal toxicity study, erdafitinib caused malformations and embryo-fetal death at maternal exposures that were less than the human exposures at the maximum human recommended dose based on AUC. Advise pregnant patients of the potential risk to the fetus. Advise female patients of reproductive potential to use effective contraception during treatment with BALVERSA® and for one month after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with BALVERSA® and for one month after the last dose.

Adverse Reactions

In the pooled safety population described in Warnings and Precautions, the median duration of treatment was 4.8 months (range: 0.1 to 43 months). The most common (>20%) adverse reactions, including laboratory abnormalities, were increased phosphate, nail disorders, stomatitis, diarrhea, increased creatinine, increased alkaline phosphatase, increased alanine aminotransferase, decreased hemoglobin, decreased sodium, increased aspartate aminotransferase, fatigue, dry mouth, dry skin, decreased phosphate, decreased appetite, dysgeusia, constipation, increased calcium, dry eye, palmar-plantar erythrodysesthesia syndrome, increased potassium, alopecia, and central serous retinopathy.

In Cohort 1 of the BLC3001 (NCT03390504, THOR) study:

- Serious adverse reactions occurred in 41% of patients who received BALVERSA®. Serious reactions in >2% of patients included urinary tract infection (4.4%), hematuria (3.7%), hyponatremia (2.2%), and acute kidney injury (2.2%). Fatal adverse reactions occurred in 4.4% of patients who received BALVERSA®, including sudden death (1.5%), pneumonia (1.5%), renal failure (0.7%), and cardiorespiratory arrest (0.7%).
- Permanent discontinuation of BALVERSA® due to an adverse reaction occurred in 14% of patients. Adverse reactions which resulted in permanent discontinuation of BALVERSA® in >2% of patients included nail disorders (3%) and eye disorders (2.2%).
- Dosage interruptions of BALVERSA® due to an adverse reaction occurred in 72% of patients. Adverse reactions which required dosage interruption in >4% of patients included nail disorders (22%), stomatitis (19%), eye disorders (16%), palmar-plantar erythrodysesthesia syndrome (15%), diarrhea (10%), hyperphosphatemia (7%), increased aspartate aminotransferase (6%), and increased alanine aminotransferase (5%).
- Dose reductions of BALVERSA® due to an adverse reaction occurred in 69% of patients. Adverse reactions which required dose reductions in >4% of patients included nail disorders (27%), stomatitis (19%), eye disorders (17%), palmar-plantar erythrodysesthesia syndrome (12%), diarrhea (7%), dry mouth (4.4%), and hyperphosphatemia (4.4%).
- Clinically relevant adverse reactions in <15% of patients who received BALVERSA® included nausea (15%), pyrexia (15%), epistaxis (13%), vomiting (10%), and arthralgia (10%).

Drug Interactions

Effects of Other Drugs on BALVERSA®

- Moderate CYP2C9 or Strong CYP3A4 Inhibitors: Consider alternative agents; however, if co-administration is unavoidable, monitor closely for adverse reactions.
- Strong CYP3A4 inducers: Avoid co-administration with BALVERSA®.
- Moderate CYP3A4 inducers: If co-administration is required at the start of BALVERSA® treatment, administer BALVERSA® at a dose of 9 mg daily.
- Serum phosphate level-altering agents: Avoid co-administration with agents that can alter serum phosphate levels before the initial dose increase period based on serum phosphate levels.

Effect of BALVERSA® on Other Drugs

- P-gp substrates: If co-administration is unavoidable, separate BALVERSA® administration by at least 6 hours before or after administration of P-gp substrates with narrow therapeutic indices.

Please click here to see full BALVERSA® Prescribing Information.

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Reference: BALVERSA® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

Johnson&Johnson

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