These highlights do not include all the information needed to use BALVERSA safely and effectively. See full prescribing information for BALVERSA. BALVERSA® (erdafitinib) tablets, for oral use

Initial U.S. Approval: 2019

### RECENT MAJOR CHANGES

04/2022

### WARNING AND PRECAUTIONS

- Ocular disorders: BALVERSA can cause central serous retinopathy/retinal pigment epithelial detachment (CSR/RPED). Perform monthly ophthalmological examinations during the first four months of treatment, every 3 months afterwards, and at any time for visual symptoms. Withhold BALVERSA when CSR/RPED occurs and permanently discontinue if it does not resolve within 4 weeks or if Grade 4 in severity. (2.3, 5.1)
- Hyperphosphatemia: Increases in phosphate levels are a pharmacodynamic effect of BALVERSA. Monitor for hyperphosphatemia and manage with dose modifications when required. (2.3, 5.2)

### DOSAGE AND ADMINISTRATION

- Confirm the presence of FGFR genetic alterations in tumor specimens prior to initiation of treatment with BALVERSA. (2.1)
- Recommended initial dosage: 8 mg orally once daily with a dose increase to 9 mg daily if criteria are met. (2.2)
- Swallow whole with or without food. (2.2)

### DOSAGE FORMS AND STRENGTHS

Tablets: 3 mg, 4 mg, and 5 mg. (3)

### CONTRAINDICATIONS

None. (4)

### WARNINGS AND PRECAUTIONS

- Ocular disorders: BALVERSA can cause central serous retinopathy/retinal pigment epithelial detachment (CSR/RPED). Perform monthly ophthalmological examinations during the first four months of treatment, every 3 months afterwards, and at any time for visual symptoms. Withhold BALVERSA when CSR/RPED occurs and permanently discontinue if it does not resolve within 4 weeks or if Grade 4 in severity. (2.3, 5.1)
- Hyperphosphatemia: Increases in phosphate levels are a pharmacodynamic effect of BALVERSA. Monitor for hyperphosphatemia and manage with dose modifications when required. (2.3, 5.2)

### ADVERSE REACTIONS

The most common adverse reactions including laboratory abnormalities (≥20%) were phosphate increased, stomatitis, fatigue, creatinine increased, diarrhea, dry mouth, nail disorder, alanine aminotransferase increased, alkaline phosphatase increased, sodium decreased, decreased appetite, albumin decreased, dysgeusia, hemoglobin decreased, dry skin, aspartate aminotransferase increased, magnesium decreased, dry eye, alopecia, palmar-plantar erythrodysesthesia syndrome, constipation, phosphate decreased, abdominal pain, calcium increased, nausea, and musculoskeletal pain. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Janssen Products, LP. at 1-800-526-7736 (1-800-JANSSEN and www.BALVERSA.com) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

### DRUG INTERACTIONS

- Moderate CYP2C9 or strong CYP3A4 inhibitors: Avoid concomitant use with BALVERSA. (7.1)
- Moderate CYP2C9 or CYP3A4 inducers: Increase BALVERSA dose up to 9 mg. (7.1)
- Serum phosphate level-altering agents: Avoid concomitant use with agents that can alter serum phosphate levels before the initial dose modification period. (2.3, 7.1)
- CYP3A4 substrates: Avoid concomitant use with sensitive CYP3A4 substrates with narrow therapeutic indices. (7.2)
- OCT2 substrates: Consider alternative agents or consider reducing the dose of OCT2 substrates based on tolerability. (7.2)
- P-gp substrates: Separate BALVERSA administration by at least 6 hours before or after administration of P-gp substrates with narrow therapeutic indices. (7.2)

### USE IN SPECIFIC POPULATIONS

- Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 01/2023

### FULL PRESCRIBING INFORMATION: CONTENTS

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
   2.1 Patient Selection
   2.2 Recommended Dosage and Schedule
   2.3 Dose Modifications for Adverse Reactions
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
   5.1 Ocular Disorders
   5.2 Hyperphosphatemia and Soft Tissue Mineralization
   5.3 Embryo-Fetal Toxicity
6 ADVERSE REACTIONS
   6.1 Clinical Trials Experience
7 DRUG INTERACTIONS
   7.1 Effect of Other Drugs on BALVERSA
   7.2 Effect of BALVERSA on Other Drugs
8 USE IN SPECIFIC POPULATIONS
   8.1 Pregnancy
   8.2 Lactation
8.3 Females and Males of Reproductive Potential
8.4 Pediatric Use
8.5 Geriatric Use
8.6 Renal Impairment
8.7 Hepatic Impairment
8.8 CYP2C9 Poor Metabolizers
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
   12.1 Mechanism of Action
   12.2 Pharmacodynamics
   12.3 Pharmacokinetics
   12.5 Pharmacogenomics
13 NONCLINICAL TOXICOLOGY
   13.1 Carcinogenesis, Mutagenesis, and Impairment of Fertility
14 CLINICAL STUDIES
   14.1 Urothelial Carcinoma with Susceptible FGFR Genetic Alterations
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.
BALVERSA® (erdafitinib) tablets

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

BALVERSA® is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (mUC), that has:
• susceptible FGFR3 or FGFR2 genetic alterations, and
• progressed during or following at least one line of prior platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

Select patients for therapy based on an FDA-approved companion diagnostic for BALVERSA [see Dosage and Administration (2.1) and Clinical Studies (14.1)].

This indication is approved under accelerated approval based on tumor response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials [see Clinical Studies (14.1)].

2 DOSAGE AND ADMINISTRATION

2.1 Patient Selection

Select patients for the treatment of locally advanced or metastatic urothelial carcinoma with BALVERSA based on the presence of susceptible FGFR genetic alterations in tumor specimens as detected by an FDA-approved companion diagnostic [see Clinical Studies (14.1)].

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

2.2 Recommended Dosage and Schedule

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 serum phosphate (PO₄) levels and tolerability at 14 to 21 days [see Dosage and Administration (2.3)].

Swallow tablets whole with or without food. If vomiting occurs any time after taking BALVERSA, the next dose should be taken the next day. Treatment should continue until disease progression or unacceptable toxicity occurs.

If a dose of BALVERSA is missed, it can be taken as soon as possible on the same day.

2.3 Dose Modifications for Adverse Reactions

The recommended dose modifications for adverse reactions are listed in Table 1.

Table 1: BALVERSA Dose Reduction Schedule

<table>
<thead>
<tr>
<th>Dose</th>
<th>1st dose reduction</th>
<th>2nd dose reduction</th>
<th>3rd dose reduction</th>
<th>4th dose reduction</th>
<th>5th dose reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>9 mg (three 3 mg tablets)</td>
<td>8 mg (two 4 mg tablets)</td>
<td>6 mg (two 3 mg tablets)</td>
<td>5 mg (one 5 mg tablet)</td>
<td>4 mg (one 4 mg tablet)</td>
<td>Stop</td>
</tr>
<tr>
<td>8 mg (two 4 mg tablets)</td>
<td>6 mg (two 3 mg tablets)</td>
<td>5 mg (one 5 mg tablet)</td>
<td>4 mg (one 4 mg tablet)</td>
<td>Stop</td>
<td></td>
</tr>
</tbody>
</table>

Table 2 summarizes recommendations for dose interruption, reduction, or discontinuation of BALVERSA in the management of specific adverse reactions.

Table 2: Dose Modifications for Adverse Reactions

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>BALVERSA Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperphosphatemia</td>
<td></td>
</tr>
<tr>
<td>In all patients, restrict phosphate intake to 600-800 mg daily. If serum phosphate is above 7.0 mg/dL, consider adding an oral phosphate binder until serum phosphate level returns to &lt; 5.5 mg/dL.</td>
<td></td>
</tr>
<tr>
<td>5.6-6.9 mg/dL (1.8-2.3 mmol/L)</td>
<td>Continue BALVERSA at current dose.</td>
</tr>
<tr>
<td>7.0-9.0 mg/dL (2.3-2.9 mmol/L)</td>
<td>Withhold BALVERSA with weekly reassessments until level returns to &lt; 5.5 mg/dL (or baseline). Then restart BALVERSA at the same dose level. A dose reduction may be implemented for hyperphosphatemia lasting &gt; 1 week.</td>
</tr>
<tr>
<td>&gt; 9.0 mg/dL (&gt; 2.9 mmol/L)</td>
<td>Withhold BALVERSA with weekly reassessments until level returns to &lt; 5.5 mg/dL (or baseline). Then may restart BALVERSA at 1 dose level lower.</td>
</tr>
<tr>
<td>&gt; 10.0 mg/dL (&gt; 3.2 mmol/L) or significant alteration in baseline renal function or Grade 3 hypercalcemia</td>
<td>Withhold BALVERSA with weekly reassessments until level returns to &lt; 5.5 mg/dL (or baseline). Then may restart BALVERSA at 2 dose levels lower.</td>
</tr>
<tr>
<td>Central Serous Retinopathy/Retinal Pigment Epithelial Detachment (CSR/RPED)</td>
<td></td>
</tr>
<tr>
<td>Grade 1: Asymptomatic, clinical or diagnostic observations only</td>
<td>Withhold until resolution. If resolves within 4 weeks, resume at the next lower dose level. Then, if no recurrence for a month, consider re-escalation. If stable for 2 consecutive eye exams but not resolved, resume at the next lower dose level.</td>
</tr>
<tr>
<td>Grade 2: Visual acuity 20/40 or better or ≤ 3 lines of decreased vision from baseline</td>
<td>Withhold until resolution. If resolves within 4 weeks, may resume at the next lower dose level.</td>
</tr>
<tr>
<td>Grade 3: Visual acuity worse than 20/40 or &gt; 3 lines of decreased vision from baseline</td>
<td>Withhold until resolution. If resolves within 4 weeks, may resume two dose levels lower. If recurs, consider permanent discontinuation.</td>
</tr>
<tr>
<td>Grade 4: Visual acuity 20/200 or worse in affected eye</td>
<td>Permanently discontinue.</td>
</tr>
<tr>
<td>Other Adverse Reactions</td>
<td></td>
</tr>
<tr>
<td>Grade 3</td>
<td>Withhold BALVERSA until resolves to Grade 1 or baseline, then may resume dose level lower.</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Permanently discontinue.</td>
</tr>
</tbody>
</table>

* Dose adjustment graded using the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE v4.03).

3 DOSAGE FORMS AND STRENGTHS

Tablets:
• 3 mg: Yellow, round biconvex, film-coated, debossed with “3” on one side; and “EF” on the other side.
• 4 mg: Orange, round biconvex, film-coated, debossed with “4” on one side; and “EF” on the other side.
• 5 mg: Brown, round biconvex, film-coated, debossed with “5” on one side; and “EF” on the other side.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Ocular Disorders

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

CSR/RPED was reported in 25% of patients treated with BALVERSA, with a median time to first onset of 50 days. Grade 3 CSR/RPED, involving central field of vision, was reported in 3% of patients. CSR/RPED resolved in 13% of patients and was ongoing in 13% of patients at the study cutoff. CSR/RPED led to dose interruptions and reductions in 9% and 14% of patients, respectively and 3% of patients discontinued BALVERSA.
Dry eye symptoms occurred in 28% of patients during treatment with BALVERSA and were Grade 3 in 6% of patients. All patients should receive dry eye prophylaxis with ocular demulcents as needed.

Perform monthly ophthalmological examinations during the first 4 months of treatment, 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 BALVERSA when CRS occurs and permanently discontinue if it does not resolve within 4 weeks or if Grade 4 in severity. For ocular adverse reactions, follow the dose modification guidelines [see Dosage and Administration (2.3)].

5.2 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 [see Pharmacodynamics (12.2)]. Hyperphosphatemia was reported as adverse reaction in 76% of patients treated with BALVERSA. The median onset time for any grade event of hyperphosphatemia was 20 days (range: 8-116) after initiating BALVERSA. Thirty-two percent of patients received phosphate binders during treatment with BALVERSA. Cutaneous calcinosis, non-uremic calciphylaxis and vascular calcification have been observed in 0.3% of patients treated with BALVERSA.

Monitor for hyperphosphatemia throughout treatment. In all patients, restrict phosphate intake to 600-800 mg daily. If serum phosphate is above 7.0 mg/dL, consider adding an oral phosphate binder until serum phosphate level returns to ≤5.5 mg/dL. Withhold, dose reduce, or permanently discontinue BALVERSA based on duration and severity of hyperphosphatemia according to Table 2 [see Dosage and Administration (2.3)].

5.3 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 woman. In an embryo-fetal toxicity study, oral administration of erdafitinib to pregnant rats during the period of organogenesis caused malformations and embryo-fetal death at maternal exposures that were less than the human exposures at the maximum human recommended dose based on area under the curve (AUC). Advise pregnant women 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 [see Use in Specific Populations (8.1, 8.3) and Clinical Pharmacology (12.1)].

6 ADVERSE REACTIONS

The following serious adverse reactions are also described elsewhere in the labeling:

- Ocular Disorders [see Warning and Precautions (5.1)].
- Hyperphosphatemia [see Warning and Precautions (5.2)].

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of BALVERSA was evaluated in the BLC2001 study that included 87 patients with locally advanced or metastatic urothelial carcinoma which had susceptible FGFR3 or FGFR2 genetic alterations, and which progressed during or following at least one line of prior chemotherapy within 12 months of neoadjuvant or adjuvant chemotherapy [see Clinical Studies (14.1)]. Patients were treated with BALVERSA at 8 mg orally once daily; with a dose increase to 9 mg in patients with phosphate levels <5.5 mg/dL on Day 14 of Cycle 1. Median duration of treatment was 5.3 months (range: 0 to 17 months).

The most common adverse reactions (ARs) including laboratory abnormalities (≥20%) were phosphate increase, stomatitis, fatigue, creatinine increase, diarrhea, dry mouth, nail disorder, alanine aminotransferase increase, alkaline phosphatase increase, sodium decreased, decreased appetite, albumin decreased, dysgeusia, hemoglobin decreased, dry skin, aspartate aminotransferase increased, magnesium decreased, dry eye, alopecia, palmar-plantar erythrodysesthesia syndrome, constipation, phosphate decreased, abdominal pain, calcium increased, nausea, and musculoskeletal pain. The most common Grade 3 or greater ARs (≥1%) were stomatitis, nail dystrophy, palmar-plantar erythrodysesthesia syndrome, paronychia, nail disorder, keratitis, and hyperphosphatemia.

An adverse reaction with a fatal outcome in 1% of patients was acute myocardial infarction.

Serious adverse reactions occurred in 41% of patients including eye disorders (10%). Permanent discontinuation due to an adverse reaction occurred in 13% of patients. The most frequent reasons for permanent discontinuation included eye disorders (6%).

Dosage interruptions occurred in 68% of patients. The most frequent adverse reactions requiring dosage interruption included hyperphosphatemia (24%), stomatitis (17%), eye disorders (17%), and palmar-plantar erythrodysesthesia syndrome (8%).

Dose reductions occurred in 53% of patients. The most frequent adverse reactions for dose reductions included eye disorders (23%), stomatitis (15%), hyperphosphatemia (7%), palmar-plantar erythrodysesthesia syndrome (7%), paronychia (7%), and nail dystrophy (6%).

Table 3 presents ARs reported in ≥10% of patients treated with BALVERSA at 8 mg once daily.

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>BALVERSA 8 mg (N=87)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Grades (%)</strong></td>
<td><strong>Grade 3-4 (%)</strong></td>
</tr>
<tr>
<td><strong>Any</strong></td>
<td>100</td>
</tr>
<tr>
<td><strong>Gastrointestinal disorders</strong></td>
<td>92</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>56</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>47</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>45</td>
</tr>
<tr>
<td>Constipation</td>
<td>28</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>23</td>
</tr>
<tr>
<td>Nausea</td>
<td>21</td>
</tr>
<tr>
<td>Vomiting</td>
<td>13</td>
</tr>
<tr>
<td><strong>Metabolism and nutrition disorders</strong></td>
<td>90</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>38</td>
</tr>
<tr>
<td><strong>General disorders and admin. site conditions</strong></td>
<td>69</td>
</tr>
<tr>
<td>Fatigue</td>
<td>54</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>14</td>
</tr>
<tr>
<td><strong>Skin and subcutaneous disorders</strong></td>
<td>75</td>
</tr>
<tr>
<td>Nail disorder</td>
<td>45</td>
</tr>
<tr>
<td>Dry skin</td>
<td>34</td>
</tr>
<tr>
<td>Palmar-plantar erythrodysesthesia</td>
<td>26</td>
</tr>
<tr>
<td>Alopecia</td>
<td>26</td>
</tr>
<tr>
<td>Nail discoloration</td>
<td>11</td>
</tr>
<tr>
<td><strong>Eye disorders</strong></td>
<td>62</td>
</tr>
<tr>
<td>Dry eye</td>
<td>28</td>
</tr>
<tr>
<td>Vision blurred</td>
<td>17</td>
</tr>
<tr>
<td>Lacrimation increased</td>
<td>10</td>
</tr>
<tr>
<td><strong>Nervous system disorders</strong></td>
<td>57</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>37</td>
</tr>
<tr>
<td><strong>Infections and infestations</strong></td>
<td>56</td>
</tr>
<tr>
<td>Paronychia</td>
<td>17</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>17</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>11</td>
</tr>
<tr>
<td><strong>Respiratory, thoracic and mediastinal disorders</strong></td>
<td>40</td>
</tr>
<tr>
<td>Oropharyngeal pain</td>
<td>11</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>10</td>
</tr>
<tr>
<td><strong>Renal and urinary tract disorders</strong></td>
<td>38</td>
</tr>
<tr>
<td>Hematuria</td>
<td>11</td>
</tr>
<tr>
<td><strong>Musculoskeletal and connective tissue disorders</strong></td>
<td>31</td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>20</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>11</td>
</tr>
<tr>
<td><strong>Investigations</strong></td>
<td>44</td>
</tr>
<tr>
<td>Weight decreased</td>
<td>16</td>
</tr>
</tbody>
</table>

- Includes abdominal pain, abdominal discomfort, abdominal pain upper, and abdominal pain lower
- Includes asthenia, fatigue, lethargy, and malaise
- Includes onycholysis, onychoclastic, nail disorder, nail dystrophy, nail ridging, and onychomadesis
- Includes dry skin and xeroderma
- Includes dry eye, xerophthalmia, keratitis, foreign body sensation, and corneal erosion
- Includes dyspnea and dyspnea exertional
- Includes back pain, musculoskeletal discomfort, musculoskeletal pain, musculoskeletal chest pain, neck pain, pain in extremity
- Includes weight decreased and cachexia
7 DRUG INTERACTIONS

7.1 Effect of Other Drugs on BALVERSA
Table 5 summarizes drug interactions that affect the exposure of BALVERSA or serum phosphate level and their clinical management.

Table 5: Drug Interactions that Affect BALVERSA

<table>
<thead>
<tr>
<th>Clinical Impact</th>
<th>Moderate CYP2C9 or Strong CYP3A4 Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Co-administration of BALVERSA with moderate CYP2C9 or strong CYP3A4 inhibitors increased erdafitinib plasma concentrations [see Clinical Pharmacology (12.3)].</td>
</tr>
<tr>
<td></td>
<td>Increased erdafitinib plasma concentrations may lead to increased drug-related toxicity [see Warnings and Precautions (5)].</td>
</tr>
<tr>
<td></td>
<td>Consider alternative therapies that are not moderate CYP2C9 or strong CYP3A4 inhibitors during treatment with BALVERSA.</td>
</tr>
<tr>
<td></td>
<td>If co-administration of a moderate CYP2C9 or strong CYP3A4 inhibitor is unavoidable, monitor closely for adverse reactions and consider dose modifications accordingly [see Dosage and Administration (2.3)]. If the moderate CYP2C9 or strong CYP3A4 inhibitor is discontinued, the BALVERSA dose may be increased in the absence of drug-related toxicity.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Impact</th>
<th>Strong CYP2C9 or CYP3A4 Inducers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Co-administration of BALVERSA with strong inducers of CYP2C9 or CYP3A4 may decrease erdafitinib plasma concentrations significantly [see Clinical Pharmacology (12.3)].</td>
</tr>
<tr>
<td></td>
<td>Decreased erdafitinib plasma concentrations may lead to decreased activity.</td>
</tr>
<tr>
<td></td>
<td>Avoid co-administration of strong inducers of CYP2C9 or CYP3A4 with BALVERSA.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Impact</th>
<th>Moderate CYP2C9 or CYP3A4 Inducers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Co-administration of BALVERSA with moderate inducers of CYP2C9 or CYP3A4 may decrease erdafitinib plasma concentrations [see Clinical Pharmacology (12.3)].</td>
</tr>
<tr>
<td></td>
<td>Decreased erdafitinib plasma concentrations may lead to decreased activity.</td>
</tr>
<tr>
<td></td>
<td>If a moderate CYP2C9 or CYP3A4 inducer must be co-administered at the start of BALVERSA treatment, administer BALVERSA dose as recommended (8 mg once daily with potential to increase to 9 mg once daily based on serum phosphate levels on Days 14 to 21 and tolerability).</td>
</tr>
<tr>
<td></td>
<td>If a moderate CYP2C9 or CYP3A4 inducer must be co-administered after the initial dose increase period based on serum phosphate levels and tolerability, increase BALVERSA dose up to 9 mg.</td>
</tr>
<tr>
<td></td>
<td>When a moderate inducer of CYP2C9 or CYP3A4 is discontinued, continue BALVERSA at the same dose, in the absence of drug-related toxicity.</td>
</tr>
</tbody>
</table>

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Risk Summary
Based on the mechanism of action and findings in animal reproduction studies, BALVERSA can cause fetal harm when administered to a pregnant woman [see Clinical Pharmacology (12.1)]. There are no available data on BALVERSA use in pregnant women to inform a drug-associated risk. Oral administration of erdafitinib to pregnant rats during organogenesis caused malformations and embryo-fetal death at maternal exposures that were less than the human exposures at the maximum recommended human dose based on AUC [see Data]. Advise pregnant women and females of reproductive potential of the potential risk to the fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.
8.2 Lactation

Risk Summary

There are no data on the presence of erdafitinib in human milk, or the effects of erdafitinib on the breastfed child, or on milk production. Because of the potential for serious adverse reactions from erdafitinib in a breastfed child, advise lactating women not to breastfeed during treatment with BALVERSA and for one month following the last dose.

8.3 Females and Males of Reproductive Potential

8.3.1 Pregnancy Testing

Pregnancy testing is recommended for females of reproductive potential prior to initiating treatment with BALVERSA.

Contraception

Females

BALVERSA can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with BALVERSA and for one month after the last dose [see Use in Specific Populations (8.1)].

Males

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 [see Use in Specific Populations (8.1)].

Infertility

Based on findings from animal studies, BALVERSA may impair fertility in females of reproductive potential [see Nonclinical Toxicology (13.1)].

8.4 Pediatric Use

Safety and effectiveness of BALVERSA in pediatric patients have not been established.

In 4 and 13-week repeat-dose toxicology studies in rats and dogs, toxicities in bone and teeth were observed at an exposure less than the human exposure (AUC) at the maximum recommended human dose. Chondroid dysplasia/metaplasia were reported in multiple bones in both species, and tooth abnormalities included abnormal/irregular denting in rats and dogs and discoloration and degeneration of odontoblasts in rats.

8.5 Geriatric Use

Of the 416 patients treated with BALVERSA in clinical studies, 45% were 65 years of age or older, and 12% were 75 years of age or older. No overall differences in safety or effectiveness were observed between these patients and younger patients [see Clinical Studies (14.1)].

8.6 Renal Impairment

No dose adjustment is recommended for patients with mild to moderate renal impairment [estimated glomerular filtration rate (eGFR) 30 to 89 mL/min/1.73 m²]. No data are available in patients with severe renal impairment [see Clinical Pharmacology (12.3)].

8.7 Hepatic Impairment

No dose adjustment is recommended for patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment. Limited data are available in patients with severe (Child-Pugh C) hepatic impairment. [see Clinical Pharmacology (12.3)].

8.8 CYP2C9 Poor Metabolizers

CYP2C9*3/*3 Genotype: Erdafitinib plasma concentrations were predicted to be higher in patients with the CYP2C9*3/*3 genotype. Monitor for increased adverse reactions in patients who are known or suspected to have CYP2C9*3/*3 genotype [see Pharmacogenomics (12.5)].

11 DESCRIPTION

Erdafitinib, the active ingredient in BALVERSA, is a kinase inhibitor. The chemical name is N-[3,5-dimethoxyphenyl]-N’-[1-methylhexyl]-N-[2-[1-methyl-1H-pyrazol-4-yl]quinazolin-6-yl]ethane-1,2-diamine. Erdafitinib is a yellow powder. It is practically insoluble, or insoluble to freely soluble in organic solvents, and slightly soluble to practically insoluble, or insoluble in aqueous media over a wide range of pH values. The molecular formula is C₃₀H₂₈N₄O₂ and molecular weight is 446.56.
14.1 Urothelial Carcinoma with Susceptible FGFR Genetic Alterations

Study BLC2001 (NCT02365597) was a multicenter, open-label, single-arm study to evaluate the efficacy and safety of BALVERSA in patients with locally advanced or metastatic urothelial carcinoma (mUC). Fibroblast growth factor receptor (FGFR) genetic alterations were selected for screening and enrollment of patients. Patients were determined by a clinical trial assay (CTA). The efficacy population consists of a cohort of eighty-seven patients who were enrolled in this study with disease that had progressed on or after at least one prior chemotherapy and that had at least 1 of the following genetic alterations: FGFR3 gene mutations (R248C, S249C, G370C, Y373C) or FGFR3 gene fusions (FGFR3-TACC3, FGFR3-BAIAP2L1, FGFR2-BICC1, FGFR2-CASP7), as determined by the CTA performed at a central laboratory. Tumor samples from 69 patients were tested retrospectively by the OIAGEN therascreen® FGFR RGD.RT-PCR Kit, which is the FDA-approved test for selection of patients with mUC for BALVERSA.

Patients received a starting dose of BALVERSA at 8 mg once daily with a dose increase to 9 mg once daily in patients whose serum phosphate levels were below the target of 5.5 mg/dL between days 14 and 17; a dose increase occurred in 41% of patients. BALVERSA was administered until disease progression or unacceptable toxicity. The major efficacy outcome measures were objective response rate (ORR) and duration of response (DoR), as determined by blinded independent review committee (BIRC) according to RECIST v1.1.

The median age was 67 years (range: 36 to 87 years), 79% were male, and 74% were Caucasian. Most patients (92%) had a baseline Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Sixty-six percent of patients had visceral metastases. Eighty-four (97%) patients received at least one dose of cisplatin or carboplatin previously. Fifty-six percent of patients only received prior cisplatin-based regimens, 29% received only prior carboplatin-based regimens, and 15% received both cisplatin and carboplatin-based regimens. Thirty (3%) patients had disease progression following prior platinum-containing neoadjuvant or adjuvant therapy only.

Efficacy results are summarized in Table 7 and Table 8. Overall response rate was 32.2%. Responders included patients who had previously not responded to anti PD-L1/PD-1 therapy.

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>BIRC® Assessment</th>
<th>N=87</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR (95% CI)</td>
<td>32.2% (22.4, 42.0)</td>
<td></td>
</tr>
<tr>
<td>Complete response (CR)</td>
<td>2.3%</td>
<td></td>
</tr>
<tr>
<td>Partial response (PR)</td>
<td>29.9%</td>
<td></td>
</tr>
<tr>
<td>Median DoR in months (95% CI)</td>
<td>5.4 (4.2, 6.9)</td>
<td></td>
</tr>
</tbody>
</table>

* BIRC: Blinded Independent Review Committee

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>BIRC® Assessment</th>
<th>N=84</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR (95% CI)</td>
<td>40.6% (28.6, 52.7)</td>
<td></td>
</tr>
<tr>
<td>FGFR3 Fusion b,c</td>
<td>N=18</td>
<td></td>
</tr>
<tr>
<td>ORR (95% CI)</td>
<td>11.1% (0, 25.6)</td>
<td></td>
</tr>
<tr>
<td>FGFR2 Fusion c</td>
<td>N=6</td>
<td></td>
</tr>
<tr>
<td>ORR</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

* BIRC: Blinded Independent Review Committee
b Both responders had FGFR3-TACC3_V1 fusion
c One patient with a FGFR2-CASP7/FGFR3-TACC3_V3 fusion is reported in both FGFR2 fusion and FGFR3 fusion above

16 HOW SUPPLIED/STORAGE AND HANDLING

BALVERSA® (erdafitinib) tablets are available in the strengths and packages listed below:

- 3 mg tablets: Yellow, round biconvex, film-coated, debossed with “3” on one side and “EF” on the other side.
  - Bottle of 56-tablets with child resistant closure (NDC 59676-030-56).
  - Bottle of 84-tablets with child resistant closure (NDC 59676-030-84).
BALVERSA® (erdafitinib) tablets

- 4 mg tablets: Orange, round biconvex, film-coated, debossed with “4” on one side and “EF” on the other side.
  - Bottle of 28-tablets with child resistant closure (NDC 59676-040-28).
  - Bottle of 56-tablets with child resistant closure (NDC 59676-040-56).
- 5 mg tablets: Brown, round biconvex, film-coated, debossed with “5” on one side and “EF” on the other side.
  - Bottle of 28-tablets with child resistant closure (NDC 59676-050-28).

Store at 20°C-25°C (68°F-77°F); excursions permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

FGFR Genetic Alterations

Advise patients that evidence of a susceptible FGFR3 or FGFR2 mutation or gene fusion within the tumor specimen is necessary to identify patients for whom treatment is indicated [see Dosage and Administration (2.1)].

Ocular Disorders

Advise patients to contact their healthcare provider if they experience any visual changes [see Warnings and Precautions (5.1)]. In order to prevent or treat dry eyes, advise patients to use artificial tear substitutes, hydrating or lubricating eye gels or ointments frequently, at least every 2 hours during waking hours [see Dosage and Administration (2.3)].

Skin, Mucous or Nail Disorders

Advise patients to contact their healthcare provider if they experience progressive or intolerable skin, mucous or nail disorders [see Adverse Reactions (6.1)].

Hyperphosphatemia and Soft Tissue Mineralization

Inform patients that BALVERSA may cause hyperphosphatemia and soft tissue mineralization. Advise patients to immediately inform their healthcare provider of painful skin lesions or any symptoms related to acute change in phosphate levels such as muscle cramps, numbness, or tingling around the mouth [see Warnings and Precautions (5.2)].

Advise patients that their healthcare provider will assess their serum phosphate level between 14 and 21 days of initiating treatment and will adjust the dose if needed [see Warnings and Precautions (5.2)]. Advise patients to restrict phosphate intake to 800-1000 mg daily. During this initial phosphate-assessment period, advise patients to avoid concomitant use with agents that can alter serum phosphate levels. Advise patients that, after the initial phosphate assessment period, monthly phosphate level monitoring for hyperphosphatemia should be performed during treatment with BALVERSA [see Drug Interactions (7.1)].

Drug Interactions

Advise patients to inform their healthcare providers of all concomitant medications, including prescription medicines, over-the-counter drugs, and herbal products [see Drug Interactions (7.1, 7.2)].

Dosing Instructions

Instruct patients to swallow the tablets whole once daily with or without food. If vomiting occurs any time after taking BALVERSA, advise patients to take the next dose the next day. [see Dosage and Administration (2.1)].

Missed Dose

If a dose is missed, advise patients to take the missed dose as soon as possible. Resume the regular daily dose schedule for BALVERSA the next day. Extra tablets should not be taken to make up for the missed dose [see Dosage and Administration (2.3)].

Embryo-Fetal Toxicity

Advise pregnant women and females of reproductive potential of the potential risk to the fetus. Advise females to inform their healthcare providers of a known or suspected pregnancy [see Warning and Precautions (5.3) and Use in Specific Population (8.1)].

Advise female patients of reproductive potential to use effective contraception during treatment and for one month after the last dose of BALVERSA. Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for one month after the last dose of BALVERSA [see Use in Specific Populations (8.3)].

Lactation

Advise females not to breastfeed during treatment with BALVERSA and for one month after the last dose [see Use in Specific Populations (8.2)].

Product of Switzerland

Manufactured for:
Janssen Products, LP
Horsham, PA 19044

Under license from Astex Therapeutics Limited.

©2019 Janssen Pharmaceutical Companies
What is BALVERSA?
BALVERSA is a prescription medicine used to treat adults with bladder cancer (urothelial cancer) that has spread or cannot be removed by surgery:
• which has a certain type of abnormal “FGFR” gene, and
• who have tried at least one other chemotherapy medicine that contains platinum, and it did not work or is no longer working.
Your healthcare provider will test your cancer for certain types of abnormal FGFR genes and make sure that BALVERSA is right for you. It is not known if BALVERSA is safe and effective in children.

Before taking BALVERSA tell your healthcare provider about all of your medical conditions, including if you:
• have vision or eye problems.
• are pregnant or plan to become pregnant. BALVERSA can harm your unborn baby. You should not become pregnant during treatment with BALVERSA.
  Females who can become pregnant:
  ° Your healthcare provider may do a pregnancy test before you start treatment with BALVERSA.
  ° You should use effective birth control during treatment and for 1 month after the last dose of BALVERSA. Talk to your healthcare provider about birth control methods that may be right for you.
  ° Tell your healthcare provider right away if you become pregnant or think you may be pregnant.
  Males with female partners who can become pregnant:
  ° You should use effective birth control when sexually active during treatment with BALVERSA and for 1 month after the last dose.
• are breastfeeding or plan to breastfeed. Do not breastfeed during treatment and for 1 month after the last dose of BALVERSA.
  Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How should I take BALVERSA?
• Take BALVERSA exactly as your healthcare provider tells you.
• Take BALVERSA 1 time each day.
• Swallow BALVERSA tablets whole with or without food.
• Your healthcare provider may change your dose of BALVERSA, temporarily stop or completely stop treatment if you get certain side effects.
• If you miss a dose of BALVERSA, take the missed dose as soon as possible on the same day. Take your regular dose of BALVERSA the next day. Do not take more BALVERSA than prescribed to make up for the missed dose.
• If you vomit after taking BALVERSA, do not take another BALVERSA tablet. Take your regular dose of BALVERSA the next day.
What are the possible side effects of BALVERSA?
BALVERSA may cause serious side effects, including:

- **Eye problems.** Eye problems are common with BALVERSA but can also be serious. Eye problems include dry or inflamed eyes, inflamed cornea (front part of the eye) and disorders of the retina, an internal part of the eye. Tell your healthcare provider right away if you develop blurred vision, loss of vision or other visual changes. You should use artificial tear substitutes, hydrating or lubricating eye gels or ointments at least every 2 hours during waking hours to help prevent dry eyes. During treatment with BALVERSA, your healthcare provider will send you to see an eye specialist.

- **High phosphate levels in the blood (hyperphosphatemia).** Hyperphosphatemia is common with BALVERSA but can also be serious. High levels of phosphate in your blood may lead to build-up of minerals such as calcium in different tissues in your body. Your healthcare provider will check your blood phosphate level between 14 and 21 days after starting treatment with BALVERSA, and then monthly.
  - Your healthcare provider may prescribe changes in your diet or phosphate lowering therapy, or change or stop treatment with BALVERSA if needed.
  - Tell your healthcare provider right away if you develop painful skin lesions, any muscle cramps, or numbness or tingling around your mouth.

The most common side effects of BALVERSA include:

- mouth sores
- feeling tired
- change in kidney function
- diarrhea
- dry mouth
- nails separate from the bed or poor formation of the nail
- change in liver function
- low salt (sodium) levels
- decreased appetite
- change in sense of taste
- low red blood cells (anemia)
- dry skin
- dry eyes
- hair loss
- redness, swelling, peeling or tenderness, mainly on the hands or feet (‘hand-foot syndrome’)
- constipation
- stomach (abdominal) pain
- nausea
- muscle pain

Tell your healthcare provider right away if you develop any nail or skin problems including nails separating from the nail bed, nail pain, nail bleeding, breaking of the nails, color or texture changes in your nails, infected skin around the nail, an itchy skin rash, dry skin, or cracks in the skin.

BALVERSA may affect fertility in females who are able to become pregnant. Talk to your healthcare provider if this is a concern for you.

These are not all possible side effects of BALVERSA. For more information, ask your healthcare provider or pharmacist.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store BALVERSA?
- Store BALVERSA tablets at room temperature between 68°F to 77°F (20°C to 25°C).

Keep BALVERSA and all medicines out of the reach of children.

General information about the safe and effective use of BALVERSA.
Medicines are sometimes prescribed for purposes other than those listed in Patient Information leaflets. Do not use BALVERSA for a condition for which it was not prescribed. Do not give BALVERSA to other people, even if they have the same symptoms that you have. It may harm them. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider for information about BALVERSA that is written for healthcare professionals.

What are the ingredients in BALVERSA?
**Active ingredient:** erdafitinib

**Inactive ingredients:**
Tablet Core: Croscarmellose sodium, Magnesium stearate (from vegetable source), Mannitol, Meglumine, and Microcrystalline Cellulose.
Film Coating (Opadry amb II): Glycerol monocaprylocaprate Type I, Polyvinyl alcohol-partially hydrolyzed, Sodium lauryl sulfate, Talc, Titanium dioxide, Iron oxide yellow, Iron oxide red (for the orange and brown tablets only), Ferrosoferric oxide/iron oxide black (for the brown tablets only).

Manufactured by: Janssen-Cilag SpA, Latina, Italy
Manufactured for: Janssen Products, LP, Horsham, PA 19044
© 2019 Janssen Pharmaceutical Companies
For more information call Janssen Products, LP at 1-800-526-7736 (1-800-JANSSEN) or go to www.BALVERSA.com.

This Patient Information has been approved by the U.S. Food and Drug Administration.

Revised: 01/2023

9 cp-69603v9