PHARMACY COVERAGE GUIDELINE

BALVERSA™ (erdafitinib)
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Balversa (erdafitinib) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Locally advanced or metastatic urothelial carcinoma (mUC), that has susceptible fibroblast growth factor receptor (FGFR) 3 genetic alterations and has progressed during or following at least one line of prior systemic therapy

b. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

4. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
   a. Fibroblast growth factor receptor (FGFR) genetic alteration testing of FGFR 3
   b. Ophthalmologic examination
   c. Negative pregnancy test in a woman of childbearing potential
   d. Eastern Co-operative Oncology Group (ECOG) performance status of 0-2

5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual is not eligible for and has not received prior PD-1 or PD-L1 inhibitor therapy

7. Individual is not currently taking any other drugs which cause severe adverse reactions or any drug interactions requiring discontinuation such as use with strong CYP3A inducers such (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, others)

8. Individual does not have moderate to severe hepatic impairment (Child-Pugh Class C)

9. Individual does not have severe renal impairment or renal impairment requiring dialysis

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Balversa (erdafitinib) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

2. Individual's condition has responded while on therapy with response defined as there is no evidence of disease progression or unacceptable toxicity

3. Individual has been adherent with the medication

4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any significant adverse drug effects that may exclude continued use such as:
   a. Ophthalmologic toxicity such as central serious retinopathy/retinal pigment epithelia detachment (CRS/RPED)

b. Hyperphosphatemia that cannot be controlled with phosphate binders and has led to soft tissue mineralization, cutaneous calcinosis, non-uremic calciphylaxis and vascular calcification
c. Hyperphosphatemia (greater than or equal to 10mg/dL) for greater than 2 weeks
d. Any serum phosphate with life-threatening consequences or urgent intervention indicated

6. Individual does not have moderate to severe hepatic impairment (Child-Pugh Class C)

7. Individual does not have severe renal impairment or renal impairment requiring dialysis

8. Individual is not currently taking any other drugs which cause severe adverse reactions or any drug interactions requiring discontinuation such as use with strong CYP3A inducers such (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, others)

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Balversa (erdafitinib) is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma that has susceptible fibroblast growth factor receptor (FGFR) 3 genetic alterations and has progressed during or following at least one line of prior systemic therapy. The indication is approved under an 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. Select patients for therapy based on an FDA-approved companion diagnostic test for Balversa (erdafitinib). The QIAGEN therascreen® FGFR RGQ RT-PCR Kit, is the FDA-approved test for selection of patients with mUC for Balversa (erdafitinib).

Erdafitinib is a kinase inhibitor that binds to and inhibits the enzymatic activity of FGFR1, FGFR2, FGFR3 and FGFR4 based on *in vitro* data. Erdafitinib also binds to RET, CSF1R, PDGFRA, PDGFRB, FLT4, KIT, and VEGFR2. Erdafitinib inhibited FGFR phosphorylation and signaling and decreased cell viability in cell lines expressing FGFR genetic alterations, including point mutations, amplifications, and fusions. Erdafitinib demonstrated antitumor activity in FGFR-expressing cell lines and xenograft models derived from tumor types, including bladder cancer

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Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

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Neo-adjuvant therapy:

Drugs, radiation, or other forms of supplemental treatment given prior to cancer surgery intended to reduce tumor burden in reparation for surgery

Adjuvant therapy:

Drugs, radiation, or other forms of supplemental treatment following cancer surgery intended to decrease the risk of disease recurrence or to treat residual disease, whether gross or microscopic, following cytoreduction

Examples of platinum-containing chemotherapy include: cisplatin and carboplatin

Examples of other chemotherapy include: gemcitabine, paclitaxel, and doxorubicin

Examples of checkpoint inhibitors include intravenous infusions: Keytruda (pembrolizumab), Opdivo (nivolumab), Tecentriq (atezolizumab), Imfinzi (durvalumab), and Bavencio (avelumab)

ECOG Performance status:

Eastern Co-operative Oncology Group (ECOG) Performance Status	
Grade	ECOG description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982	

NCCN recommendation definitions:

Category 1:
Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A:
Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B:
Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3:
Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0:

Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*

Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL**
Grade 4	Life-threatening consequences; urgent intervention indicated
Grade 5	Death related to AE
U.S. department of Health and Human Services, National Institutes of Health, and National Cancer Institute	

The Child-Pugh classification system:
The Child-Pugh classification is a scoring system used to determine the prognosis of individuals with cirrhosis. Scoring is based upon several factors: albumin, ascites, total bilirubin, prothrombin time, and encephalopathy, as follows:

	Score: 1 point	Score: 2 points	Score: 3 points
Serum Albumin (g/dL)	> 3.5	3.0 - 3.5	< 3.0
Serum Bilirubin (mg/dL)	< 2.0	2.0 - 3.0	> 3.0
Prothrombin time (seconds)	1 - 4	4 - 6	> 6
Ascites	none	moderate	severe
Encephalopathy	none	mild	severe

The three classes and their scores are:
- **Class A** is score 5 – 6: Well compensated
- **Class B** is score 7 – 9: Significant functional compromise
- **Class C** is score > 9: Decompensated disease

Activities of daily living (ADL):
Instrumental ADL:
Prepare meals, shop for groceries or clothes, use the telephone, manage money, etc.

Self-care ADL:
Bathe, dress and undress, feed self, use the toilet, take medications, not bedridden

Resources:

Balversa (erdafitinib) product information, revised by Janssen Products L.P 10-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 21, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Bladder Cancer Version 1.2025 – Updated March 25, 2025. Available at https://www.nccn.org. Accessed April 01, 2025.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.