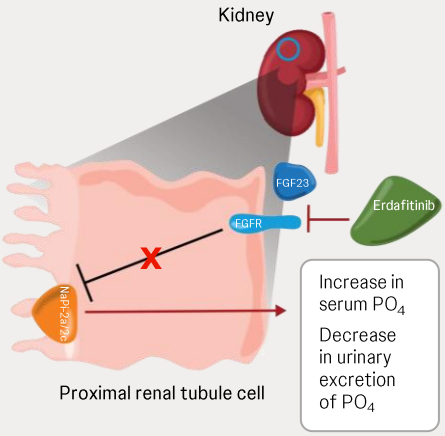
Hyperphosphatemia associated with erdafitinib treatment

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.[1]



Erdafitinib inhibits FGFR signaling and affects renal phosphate homeostasis[2-8]

- Renal reabsorption from the proximal tubules is one of the key steps in maintaining phosphate (PO_4) homeostasis
- FGF23 binding to FGFR inhibits renal PO_4 reabsorption in the proximal tubules

- **FGFR inhibition with erdafitinib increases the reabsorption of PO_4 from the proximal tubules which leads to elevated serum phosphate levels**
- **Increases in phosphate levels are a pharmacodynamic effect of BALVERSA®[1]**

Management of hyperphosphatemia while on erdafitinib[1,7]

Erdafitinib 8 mg daily with uptitration to 9 mg based on serum PO_4 levels (N = 135)[1,7]

Incidence[7]	**Onset**[1]*	**Dosing Modifications**[1]	**Treatment Discontinuation**[1,7]
Any grade, n (%): 108 (80) **Grade ≥3, n (%):** 7 (5.2)	**Median (range) onset:** 16 (8-421) days	**Dose reduction:** 4.4% **Dose interruption:** 7%	**Discontinuation:** NR

Monitoring	Comprehensive metabolic panel[7]	Serum PO_4 levels between 14-21 days† then monthly[1]

Please refer to full prescribing information for monitoring and dose modification guidelines for hyperphosphatemia.

Guidelines for Management of Elevated Phosphate Levels in the THOR (BLC3001) Study:

Serum PO_4 Level[7]	Erdafitinib dose modification[7]	Symptom management[7]
<5.5 mg/dL (<1.8 mmol/L)	• Continue treatment	• None
5.5-6.9 mg/dL (1.8-2.2mmol/L)	• Continue treatment	• Restrict PO_4 intake to 600-800 mg daily
7.0 – 9.0 mg/dL (2.3-2.9 mmol/L)	• Continue treatment • A dose reduction may be implemented for persistent‡ hyperphosphatemia (≥7 mg/dL) if clinically necessary	• Restrict PO_4 intake to 600-800 mg daily • Sevelamer§ 800-1600 mg TID with food until PO_4 level is <7.0 mg/dL
>9.0 – 10.0 mg/dL (>2.9-3.2 mmol/L)	• Withholdǁ treatment until serum PO_4 returns to <7.0 mg/dL (weekly testing recommended) • Then restart at the same dose level • A dose reduction may be implemented if needed or clinically indicated for persistent‡ hyperphosphatemia (≥9 mg/dL) at every cycle	• Restrict PO_4 intake to 600-800 mg daily • Sevelamer§ up to 1600 mg TID with food until PO_4 level is <7.0 mg/dL
>10.0 mg/dL (>3.2 mmol/L)	• Withholdǁ treatment until serum PO_4 returns to <7.0 mg/dL (weekly testing recommended). • Then restart at the first reduced dose level • Discontinue treatment permanently if serum PO_4 is ≥10 mg/dL for >2 weeks	• Medical management as clinically appropriate
Significant alteration in baseline renal function or Grade 3 hypocalcemia	• Discontinue treatment permanently¶	• Medical management as clinically appropriate

Concomitant medications and food considerations[7,9]

Some medications that may increase serum PO_4:

- Potassium phosphate supplements
- Vitamin D supplements
- Antacids
- Phosphate-containing enemas or laxatives

Select examples of high-phosphorus foods:

- **Dairy products**
- **Protein-rich foods**
- **Phosphorus food additives**
- **Beverages** (dark colas, beer, cocoa/chocolate drinks, etc.)

Scan the QR code for additional information on dietary phosphorus

*Based on the pooled safety population reflecting exposure to erdafitinib as a single agent in 479 patients with advanced urothelial cancer and FGFR alterations. †After initiating erdafitinib treatment. ‡Considered to be more than 1 sequential phosphate value above the cut-off. §If sevelamer hydrochloride (Renagel®) was not available, investigators in the THOR study were advised to use other phosphate binders (non-calcium containing) based on the local standard, including sevelamer carbonate (Renvela) or lanthanum carbonate (Fosrenol®). ǁStudy drug interruptions for hyperphosphatemia suggested to be 7 days duration. ¶In situations where the subject is having clinical benefit and the investigator and the sponsor's medical monitor agree that continuation of treatment is in the best interest of the subject, the drug may be restarted at 2 dose levels lower if appropriate. Follow other recommendations described above. FGFR, fibroblast growth factor receptor; FGF23, fibroblast growth factor 23; NaPi-2a/2c, sodium-phosphate cotransporters NaPi-2a and NaPi-2c; NR, not reported; PO_4, phosphate; TID, three times daily.

1. BALVERSA® (erdafitinib) [prescribing information]. Horsham, PA: Janssen Biotech, Inc. 2. Takeshita A, et al. *Sci Rep.* 2018;8(1):6917. 3. Erben RG. *Toxicol Pathol.* 2017;45(7):904-910. 4. Roubal K, et al. *Am J Health Syst Pharm.* 2020;77(5):346-351. 5. D'Angelo A, et al. *Expert Rev Clin Pharmacol.* 2020;13(10):1139-1146. 6. Kommalapati A, et al. *Cancers.* 2021;13(12): 2968. 7. Loriot Y, et al. *N Engl J Med.* 2023;389:1961-71. 8. Siefker-Radtke AO, et al. *Lancet Oncol.* 2022;23(2)248-258. 9. National Kidney Foundation. Phosphorus and Your Diet. Accessed March 7, 2024. https://www.kidney.org/atoz/content/phosphorus.

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