# FGFR TYROSINE KINASE INHIBITORS FOR THE TREATMENT OF UROTHELIAL CARCINOMA

## TECHNICAL FIELD

Disclosed herein are methods of treating urothelial carcinoma with an approved drug product containing a fibroblast growth factor receptor (FGFR) inhibitor. Also disclosed are methods of selling or offering for sale an approved drug product containing a fibroblast growth factor receptor (FGFR) inhibitor.

## BACKGROUND

The identification of genetic abnormalities can be useful in selecting the appropriate therapeutic(s) for cancer patients. This is also useful for cancer patients failing the main therapeutic option (front-line therapy) for that cancer type, particularly if there is no accepted standard of care for second and subsequent-line therapy. Fibroblast growth factor receptors (FGFRs) are a family of receptor tyrosine kinases involved in regulating cell survival, proliferation, migration and differentiation. FGFR alterations including FGFR mutations and FGFR fusions or translocations have been observed in some cancers. To date, there are no approved therapies with an FGFR inhibitor that are efficacious in patients with FGFR alterations.

## SUMMARY

Described herein are methods of treating urothelial carcinoma comprising, consisting of, or consisting essentially of administering an approved drug product containing a fibroblast growth factor receptor (FGFR) inhibitor to a patient with a urothelial carcinoma in an amount that is described in a drug product label for said drug product.

In one aspect, disclosed herein is a use of erdafitinib in the manufacture of a medicament for the treatment of urothelial carcinoma in a patient, wherein the erdafitinib is to be administered once daily and is to be co-administered with a P-glycoprotein (P-gp) substrate with a narrow therapeutic index and administration of erdafitinib is to be separated by at least 6 hours before or after administration of the P-gp substrate.

In another aspect, disclosed herein is a use of an approved drug product comprising erdafitinib in the manufacture of a medicament for the treatment of urothelial carcinoma in

a patient, wherein said approved drug product further comprises a drug product label, wherein the drug product label includes instructions that erdafitinib is to be administered once daily and is to be co-administered with a P-glycoprotein (P-gp) substrate with a narrow therapeutic index, wherein the administration of erdafitinib is to be separated by at least 6 hours before or after administration of the P-gp substrate.

In certain examples, the urothelial carcinoma is locally advanced or metastatic. In further examples, administration of the FGFR inhibitor provides improved anti-tumor activity as measured by objective response rate or duration of response relative to a patient with urothelial carcinoma that is not receiving treatment with an FGFR inhibitor. In some examples, administration of the FGFR inhibitor results in no more than a grade 3 adverse event.

In further examples, the urothelial carcinoma is susceptible to an FGFR2 genetic alteration or an FGFR3 genetic alteration. In certain examples, the FGFR2 or FGFR3 genetic alteration is an FGFR3 gene mutation or an FGFR2 or FGFR3 gene fusion. In some examples, the FGFR3 gene mutation is R248C, S249C, G370C, Y373C, or any combination thereof. In further examples, the FGFR2 or FGFR3 gene fusion is

**What is claimed:**

1. A use of erdafitinib in the manufacture of a medicament for the treatment of urothelial carcinoma in a patient, wherein the erdafitinib is to be administered once daily and is to be co-administered with a P-glycoprotein (P-gp) substrate with a narrow therapeutic index and administration of erdafitinib is to be separated by at least 6 hours before or after administration of the P-gp substrate.

2. A use of an approved drug product comprising erdafitinib in the manufacture of a medicament for the treatment of urothelial carcinoma in a patient, wherein said approved drug product further comprises a drug product label, wherein the drug product label includes instructions that erdafitinib is to be administered once daily and is to be co-administered with a P-glycoprotein (P-gp) substrate with a narrow therapeutic index, wherein the administration of erdafitinib is to be separated by at least 6 hours before or after administration of the P-gp substrate.

3. The use of claim 1 or 2, wherein the urothelial carcinoma is locally advanced or metastatic.

4. The use of any one of claims 1 to 3, wherein the urothelial carcinoma is susceptible to an FGFR2 genetic alteration or an FGFR3 genetic alteration.

5. The use of claim 4, wherein the FGFR2 or FGFR3 genetic alteration is an FGFR3 gene mutation or an FGFR2 or FGFR3 gene fusion.

6. The use of claim 5, wherein the FGFR3 gene mutation is R248C, S249C, G370C, Y373C, or any combination thereof.

7. The use of claim 5, wherein the FGFR2 or FGFR3 gene fusion is FGFR3-TACC3, FGFR3-BAIAP2L1, FGFR2-BICC1, FGFR2-CASP7, or any combination thereof.

8. The use of any one of claims 1 to 7, wherein a biological sample from the patient is to be evaluated for the presence of one or more FGFR2 or FGFR3 genetic alterations prior to administration of erdafitinib.

9. The use of 8 9, wherein the biological sample is blood, lymph fluid, bone marrow, a solid tumor sample, or any combination thereof.

10. The use of any one of claims 1 to 9, wherein the patient is to receive at least one prior therapy for the treatment of urothelial carcinoma.

11. The use of claim 10, wherein the at least one prior therapy for the treatment of urothelial carcinoma is platinum-containing chemotherapy.

12. The use of claim 10, wherein the urothelial carcinoma progressed during or following at least one line of the platinum-containing chemotherapy.

13. The use of claim 11, wherein the platinum-containing chemotherapy is neoadjuvant platinum-containing chemotherapy or adjuvant platinum-containing chemotherapy.

14. The use of claim 13, wherein the urothelial carcinoma progressed during or within 12 months following at least one line of the neoadjuvant platinum-containing chemotherapy or adjuvant platinum-containing chemotherapy.

15. The use of any one of claims 1 to 14, wherein erdafitinib is to be administered orally.

16. The use of claim 15, wherein erdafitinib is to be administered orally on a continuous daily dosing schedule.

17. The use of claim 16, wherein erdafitinib is to be administered orally at a dose of about 8 mg once daily.

18. The use of claim 17, wherein the dose of erdafitinib is to be increased from 8 mg once daily to 9 mg once daily at 14 to 21 days after initiating treatment if:
(a) the patient exhibits a serum phosphate ($PO_4$) level that is less than about 5.5 mg/dL at 14-21 days after initiating treatment; and
(b) administration of erdafitinib at 8 mg once daily resulted in no ocular disorder; or
(c) administration of erdafitinib at 8 mg once daily resulted in no Grade 2 or greater adverse reaction.

19. The use of claim 17, wherein the dose of erdafitinib is to be increased from 8 mg once daily to 9 mg once daily at 14 to 21 days after initiating treatment if:
(a) the patient exhibits a serum phosphate ($PO_4$) level that is < 7 mg/dL or ranges from and includes 7 mg/dL to ≤9 mg/dL or is ≤9 mg/dL; and
(b) administration of erdafitinib at 8 mg once daily resulted in no ocular disorder; or
(a) (c) administration of erdafitinib at 8 mg once daily resulted in no Grade 2 or greater adverse reaction.

20. The use of any one of claims 1 to 19, wherein erdafitinib is present in a solid dosage form.

21. The use of claim 20, wherein the solid dosage form is a tablet.