Avmapki™ Fakzynja™ Co-Pack (avutometinib; defactinib) – New orphan drug approval

- On May 8, 2025, the FDA announced the approval of Verastem's Avmapki Fakzynja Co-Pack (avutometinib; defactinib), for the **treatment of adult patients with KRAS-mutated recurrent low-grade serous ovarian cancer (LGSOC) who have received prior systemic therapy**.
    - This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- Approximately 6,000 to 8,000 women in the U.S. are living with LGSOC. The disease affects younger women with peaks of diagnosis at ages between 20 to 30 and 50 to 60 and has a median survival of approximately ten years. Approximately 70% of LGSOC shows RAS pathway-associated mutations, and 30% of people with LGSOC have a KRAS mutation.
- The two components of Avmapki Fakzynja are kinase inhibitors.
- The efficacy of Avmapki and Fakzynja was established in RAMP-201, an open-label study that included 57 adult patients with measurable KRAS-mutated recurrent LGSOC. Patients were required to have received at least one prior systemic therapy, including a platinum-based regimen. Patients received Avmapki and Fakzynja until disease progression or unacceptable toxicity. The major outcome measure was overall response rate (ORR). An additional efficacy outcome measure was duration of response (DOR).
    - **The ORR was 44%** (95% CI: 31,58).
    - The DOR range was 3.3 months to 31.1 months.
- Warnings and precautions for Avmapki Fakzynja Co-Pack include ocular toxicities, serious skin toxicities, hepatotoxicity, rhabdomyolysis, and embryo-fetal toxicity.
- The most common adverse reactions (≥ 25%) with Avmapki Fakzynja Co-Pack use were increased creatine phosphokinase, nausea, fatigue, increased aspartate aminotransferase, rash, diarrhea, musculoskeletal pain, edema, decreased hemoglobin, increased alanine aminotransferase, vomiting, increased blood bilirubin, increased triglycerides, decreased lymphocyte count, abdominal pain, dyspepsia, dermatitis acneiform, vitreoretinal disorders, increased alkaline phosphatase, stomatitis, pruritus, visual impairment, decreased platelet count, constipation, dry skin, dyspnea, cough, urinary tract infection, and decreased neutrophil count.
- The recommended dosage of **Avmapki capsules is 3.2 mg (four 0.8 mg capsules) taken orally twice weekly** (day 1 and day 4) for the first 3 weeks of each 4-week cycle until disease progression or unacceptable toxicity.
- The recommended dosage of **Fakzynja tablets is 200 mg (one tablet) taken orally twice daily** for the first 3 weeks of each 4-week cycle until disease progression or unacceptable toxicity.
- Patients should be selected for the treatment of recurrent LGSOC with Avmapki Fakzynja Co-Pack based on the presence of a KRAS mutation in tumor specimens.
    - An FDA-approved test for the detection of a KRAS mutation in LGSOC for selecting patients for treatment with Avmapki Fakzynja Co-Pack is not available.

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- Verastem plans to launch Avmapki Fakzynja Co-Pack in a week. Avmapki Fakzynja Co-Pack is Avmapki 0.8 mg capsules co-packaged with Fakzynja 200 mg tablets.