SKIN TOXICITY

SEE IT. GRADE IT. ACT.



A proactive approach to help prepare for, identify, and address skin toxicities

AVMAPKI® FAKZYNJA® CO-PACK
(avutometinib capsules; defactinib tablets)
0.8 mg; 200 mg

INDICATION

Avmapki Fakzynja Co-Pack is indicated 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.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- **Ocular Toxicities:** Ocular toxicities, including visual impairment and vitreoretinal disorders, occurred. Perform comprehensive ophthalmic evaluation at baseline, prior to cycle 2, every three cycles thereafter, and as clinically indicated. Withhold Avmapki Fakzynja Co-Pack for ocular toxicities until improvement at the same or reduced dose. Permanently discontinue Avmapki Fakzynja Co-Pack for any grade 4 toxicity.
- **Serious Skin Toxicities:** Skin toxicities, including photosensitivity and severe cutaneous adverse reactions (SCARs), occurred. Adhere to concomitant medications. Monitor for skin toxicities and interrupt, reduce or permanently discontinue Avmapki Fakzynja Co-Pack based on severity, tolerability and duration.

Please see additional Important Safety Information throughout and click here for full Prescribing Information.

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94% of patients with recurrent LGSOC treated with Avmapki Fakzynja Co-Pack experienced skin toxicities[1]

- Avmapki Fakzynja Co-Pack can cause serious skin toxicities, including severe cutaneous adverse reactions (SCARs). Cases of acute generalized exanthematous pustulosis, erythema multiforme, and drug reaction with eosinophilia and systemic symptoms have been reported in clinical trials of avutometinib (a drug in Avmapki Fakzynja Co-Pack)

Most common skin toxicities (≥10%) were mild to moderate	• rash (67%) • dermatitis acneiform (43%) • dry skin (43%) • pruritus (32%) • photosensitivity (13%) • bacterial skin infections (10%)
Grade 3 skin adverse events (12%)	• dermatitis acneiform (7%) • rash (7%) • pruritus (1.5%)
No treatment-emergent Grade 4 skin adverse events occurred.	

- 66% of patients had ongoing skin toxicity at last follow-up

Skin toxicity led to dose interruption in 10% of patients, dose reduction in 7%, and permanent discontinuation in 0.7%.[1]

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At treatment initiation

Proactive skin management begins at baseline

To help mitigate skin toxicities

- **Assess** patient history of severe skin disorders[1]*
- **Initiate** prophylactic medications for skin-related adverse events[1]
- **Inform** patient on limiting unnecessary exposure to sunlight and applying daily sunscreen SPF ≥30

Topical corticosteroids

Apply medication to the most commonly affected areas, such as the face, scalp, neck, upper chest, and upper back[1,2]

Systemic oral antibiotics

Administer as recommended

Prophylactic medication schedule[1]

Treatment initiation — **Early cycles†** (cycles 1–2) — **As clinically needed**

Continue prophylactic medications through early cycles. Administer with initiation and during at least the first 2 cycles of Avmapki Fakzynja Co-Pack.



*Patients who had an active skin disorder requiring systemic therapy within the past year were excluded from the RAMP 201 trial.

†A cycle consists of 4 weeks: 3 weeks of treatment followed by 1 week off.

SPF, sun protection factor.

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After treatment initiation

Monitoring and management of skin toxicities

To help mitigate skin toxicities

- **Monitor** for skin-related adverse events[1]
- **Adjust** Avmapki Fakzynja Co-Pack treatment based on severity and persistence[1]

Dose modifications for rash—the most commonly reported skin-related adverse event[1]

Clinical Grading Description[‡]

Grade 1	Grade 2	Grade 3	Grade 4
<10% BSA	10%–30% BSA	>30% BSA	Any % BSA
No impact on ADLs	Limits instrumental ADLs (eg, cooking, shopping)	Limits self-care ADLs (eg, bathing, dressing)	Life-threatening (eg, skin necrosis)

Dose Modification (by severity[‡])

Grade 1	Grade 2	Grade 3	Grade 4
Consider withholding if rash • does not respond to supportive care • recurs after resolution to Grade ≤1 **Reduce** for intolerable Grade 2		**Withhold** until resolved to Grade 2, then resume at reduced dose. If resolved to Grade ≤1, resume at same dose **Discontinue** permanently for recurrent Grade 3 despite dose reduction	**Discontinue** permanently

[‡]As defined by NCI CTCAE, version 5.0.

ADLs, activities of daily living; BSA, body surface area; NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events.

Consider dermatology consultation as appropriate.

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Monitoring and management of skin toxicities (cont'd)

When to expect: Median onset of 14 days after treatment initiation (range, 1 to 500 days)[1]

Management of all other skin-related adverse events[1]

Dose Modification (by severity‡)

Grade 1	Grade 2	Grade 3	Grade 4
	Consider withholding if adverse event • does not respond to supportive care • recurs after resolution to Grade ≤1	***At first occurrence:*** **Withhold** until resolved to baseline or Grade ≤1, then resume at same dose ***At second occurrence:*** **Withhold** until resolved to baseline or Grade ≤1, then resume at reduced dose **Discontinue** permanently for recurrent Grade 3 despite dose reduction	**Discontinue** permanently

‡As defined by NCI CTCAE, version 5.0.

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Skin toxicity management[1]: SEE IT. GRADE IT. ACT.

At treatment initiation (See page 3)

Preventative measures
- Assess dermatologic history
- Administer prophylactic medications at initiation of and during at least the first 2 cycles
- Counsel on skin adverse events and protective measures

After treatment initiation (See pages 4 and 5)

Monitor for skin toxicities
Median onset of 14 days (range, 1 to 500 days)

SEE IT

Skin toxicity observed?

- **No** → **Continue monitoring**
- **Yes** → **Identify type and assess severity (NCI CTCAE Grades)**

GRADE IT

- **Rash** → Refer to rash grading and management (See page 4)
- **Other** → Refer to corresponding grading and management (See page 5)

ACT

Manage based on severity and persistence
Per grading and dose modifications

Throughout management
Consider dermatology consultation as appropriate

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Counsel patients on skin adverse events and proactive management[1]



HCP guidance

Inform patients

- Skin reactions have occurred during treatment with Avmapki Fakzynja Co-Pack

Advise patients

- Use prophylactic topical steroids and oral antibiotics
- Limit unnecessary sunlight exposure with application of daily sunscreen SPF ≥30

Patient actions

Lifestyle adjustments

- Limit sun exposure
- Use sunscreen (SPF ≥30) daily
- Wear protective clothing (eg, hat, long sleeves)
- Take preventative medications

When to contact your HCP

- Sunburn
- Rash
- Progressively worsening skin adverse events
- Blistering of the skin or mouth

HCP, healthcare provider.

Direct patients to watch the video on **managing skin-related side effects**. Help patients see how skin reactions may be managed during treatment.

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IMPORTANT SAFETY INFORMATION (CONT'D)

Warnings and Precautions (Cont'd)

- **Hepatotoxicity:** Monitor liver function tests prior to each cycle, on day 15 of the first 4 cycles, and as clinically indicated. Withhold, reduce or discontinue Avmapki Fakzynja Co-Pack based on severity and persistence of abnormality.
- **Rhabdomyolysis:** Monitor creatine phosphokinase prior to the start of each cycle, on day 15 of the first four cycles, and as clinically indicated. If increased CPK occurs, evaluate patients for rhabdomyolysis or other causes. Withhold, reduce or permanently discontinue Avmapki Fakzynja Co-Pack based on severity and duration of the adverse reaction.
- **Embryo-Fetal Toxicity:** Avmapki Fakzynja Co-Pack can cause fetal harm. Advise patients of the potential risk to a fetus and to use effective contraception.

Adverse Reactions

The most common (≥ 25%) adverse reactions, including laboratory abnormalities, 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.

Drug Interactions

- **Strong and moderate CYP3A4 inhibitors:** Avoid concomitant use with Avmapki Fakzynja Co-Pack.
- **Strong and moderate CYP3A4 inducers:** Avoid concomitant use with Avmapki Fakzynja Co-Pack.
- **Warfarin:** Avoid concomitant use of Avmapki Fakzynja Co-Pack with warfarin and use an alternative to warfarin.
- **Gastric acid reducing agents:** Avoid concomitant use of Avmapki Fakzynja Co-Pack with proton pump inhibitors (PPIs) or H2 receptor antagonists. If use of an acid-reducing agent cannot be avoided, administer Fakzynja 2 hours before or 2 hours after the administration of a locally acting antacid.

Use in Specific Populations

- **Lactation:** Advise not to breastfeed.
- **Fertility:** May impair fertility in males and females.

Please see additional Important Safety Information throughout and click here for full Prescribing Information.

References: 1. Avmapki Fakzynja Co-Pack. Prescribing Information. Verastem Inc; 2025. **2.** Data on file, Verastem Inc. 2025. **3**. US Department of Health and Human Services. Common Terminology Criteria for Adverse Events (CTCAE), version 5. Published November 27, 2017. Accessed May 7, 2026. https://dctd.cancer.gov/research/ctep-trials/for-sites/adverse-events/ctcae-v5-5x7.pdf

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