BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.21.243

Section:	Prescription Drugs	**Effective Date:**	April 1, 2026
Subsection:	Antineoplastic Agents	**Original Policy Date:**	June 20, 2025
Subject:	Avmapki Fakzynja Co-pack	**Page:**	1 of 4

Last Review Date: March 6, 2026

Avmapki Fakzynja Co-pack

Description

Avmapki Fakzynja Co-pack (avutometinib/defactinib)

Background
Avmapki Fakzynja Co-pack is a combination of avutometinib and defactinib. Avutometinib is a MEK1 inhibitor which induces the formation of inactive RAF/MEK complexes and prevents phosphorylation of MEK1/2 by RAF. RAF and MEK proteins are regulators of RAS/RAF/MEK/ERK (MAPK) pathway. Avutometinib inhibited MEK1/2 and ERK1/2 phosphorylation and proliferation of tumor cell lines harboring KRAS mutations. Treatment of cancer cells with avutometinib increased the level of phosphorylated focal adhesion kinase (FAK). Defactinib is an inhibitor of FAK and proline-rich tyrosine kinase-2 (Pyk2), the two members of the FAK family of nonreceptor tyrosine kinases. Defactinib inhibited FAK autophosphorylation in cancer cells *in vitro* and in mouse xenograft models. Avutometinib in combination with defactinib enhanced inhibition of cell proliferation *in vitro* and antitumor activity in mouse tumor models including low-grade serious ovarian cancer (LGSOC) (1).

Regulatory Status
FDA-approved indication: Avmapki Fakzynja Co-pack, a combination of avutometinib and defactinib, each kinase inhibitors, is indicated for the treatment of adult patients with *KRAS*-mutated recurrent low-grade serious ovarian cancer (LGSOC) who have received prior systemic therapy (1).

Conduct a comprehensive ophthalmic exam at baseline, prior to cycle 2, and every three cycles thereafter regardless of baseline exam findings, and as clinically indicated (1).

Treatment with Avmapki Fakzynja Co-pack has been associated with ocular toxicities, serious skin toxicities, hepatotoxicity, and rhabdomyolysis. Patients should be monitored for ocular adverse reactions, skin toxicity, liver function tests, and creatinine phosphokinase (CPK). Withhold, reduce, or permanently discontinue Avmapki Fakzynja Co-pack based on severity and duration of adverse reactions (1).

Avmapki Fakzynja Co-pack can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment with Avmapki Fakzynja Co-pack and for 1 month after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception with Avmapki Fakzynja Co-pack and for 4 months after the last dose (1).

The safety and effectiveness of Avmapki Fakzynja Co-pack in pediatric patients less than 18 years of age have not been established (1).

Related Policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Avmapki Fakzynja Co-pack may be considered **medically necessary** if the conditions indicated below are met.

Avmapki Fakzynja Co-pack may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Recurrent low-grade serious ovarian cancer (LGSOC)

AND ALL of the following:

a. Presence of a *KRAS* mutation in tumor specimens
b. Patient has received prior systemic therapy
c. Prescriber agrees to monitor for ocular toxicities
d. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Avmapki Fakzynja Co-pack and for 1 month after the last dose
e. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Avmapki Fakzynja Co-pack and for 4 months after the last dose

Prior – Approval *Renewal* Requirements

Age 18 years of age and older

Diagnosis

Patient must have the following:

1. Recurrent low-grade serous ovarian cancer (LGSOC)

AND ALL of the following:
a. **NO** disease progression or unacceptable toxicity
b. Prescriber agrees to monitor for ocular toxicities
c. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Avmapki Fakzynja Co-pack and for 1 month after the last dose
d. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Avmapki Fakzynja Co-pack and for 4 months after the last dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 3 cartons per 84 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Avmapki Fakzynja Co-pack (avutometinib and defactinib) is indicated for the treatment of recurrent low-grade serous ovarian cancer (LGSOC). Avmapki Fakzynja Co-pack has been associated with ocular toxicity, serious skin toxicities, hepatotoxicity, rhabdomyolysis and embryo-fetal toxicity. The safety and effectiveness of Avmapki Fakzynja Co-pack in pediatric patients less than 18 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Avmapki Fakzynja Co-pack while maintaining optimal therapeutic outcomes.

References

1. Avmapki Fakzynja Co-pack [package insert]. Needham, MA: Verastem, Inc.; May 2025.
2. NCCN Drugs & Biologics Compendium® Avutometinib 2026. National Comprehensive Cancer Network, Inc. Accessed on January 21, 2026.
3. NCCN Drugs & Biologics Compendium® Defactinib 2026. National Comprehensive Cancer Network, Inc. Accessed on January 21, 2026.

Policy History

Date	Action
June 2025	Addition to PA
September 2025	Annual review and reference update
March 2026	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 6, 2026 and is effective on April 1, 2026.