

Avutometinib and Defactinib (Avmapki Fakzynja Co-Pack)

About This Medicine

AVUTOMETINIB AND DEFACTINIB ((AH-voo-toe-ME-tin-ib and deh-FAK-tin-ib) treat ovarian cancer. They work together to block a protein that causes cancer cells to grow and multiply. This helps to slow or stop the spread of cancer cells. They are given orally (by mouth).

These medicines may be used for other purposes; ask your care team if you have questions.

Possible Side Effects

- Bone marrow suppression. This is a decrease in the number of white blood cells, red blood cells, and platelets. This may raise your risk of infection, make you tired and weak, and raise your risk of bleeding.
- Blurred vision or other changes in eyesight
- Eye problems such eye swelling, retinal detachment (thin membrane that covers the back of the eye separates from the eyeball) and blockage of small veins in the retina.
- Soreness of the mouth and throat. You may have red areas, white patches, or sores that hurt.
- Nausea and vomiting (throwing up)
- Diarrhea (loose bowel movements)
- Constipation (not able to move bowels)
- Pain in your abdomen
- Indigestion
- Tiredness
- Swelling of the hands, feet, or any other part of the body
- Muscle and bone pain
- Increase in creatine phosphokinase (CPK), which can sometimes be the result of muscle inflammation or damage. You may have muscle aching and/or cramping.
- Urinary tract infection
- Changes in your liver function
- Increase in your triglyceride levels
- Trouble breathing
- Cough
- Dry skin and itching
- Rash

- Pimple like rash

Note: Each of the side effects above was reported in 25% or greater of people treated with avutometinib and defactinib. All possible side effects are not included. Your side effects may be different depending on your cancer diagnosis, condition, or if you are receiving other medicines in combination. Please discuss any concerns or questions with your care team.

Warnings and Precautions

- Severe eye problems
- Severe allergic skin reaction. You may develop blisters on your skin that are filled with fluid or a severe red rash all over your body that may be painful. Sometimes, a serious and life-threatening reaction to this medicine can happen that can cause a skin rash, along with problems with your organs, swollen lymph nodes, fever and higher than normal white blood cells.
- Severe changes in your liver function
- Rhabdomyolysis- damage to your muscles which may release proteins in your blood and affect how your kidneys work, which may be life-threatening. You may have severe muscle weakness and/or pain, or dark urine.

Note: Some of the side effects above are very rare. If you have concerns and/or questions, please discuss them with your care team.

Important Information

- You will need an eye exam before treatment, during treatment, and for any new or worsening eye problems.
- Your care team will prescribe you an oral antibiotic and a corticosteroid cream to decrease your risk of skin reactions. You should apply the cream to your face, scalp, neck, upper chest and upper back as directed by your care team. Call your care team if you get a rash so they can give you further instructions.
- Sensitivity to sunlight/light. You may get a skin rash/reaction if you are in the sun or are exposed to sun lamps and tanning beds.

How to Take Your Medicine

Note: Avutometinib and Defactinib are taken on different schedules, so be sure to follow the instructions for each medicine carefully.

- **Avutometinib:** Swallow capsules whole with food. Take the capsules at approximately the same time on days it is scheduled. Do not chew, break, or open the capsules.
- **Missed dose:** If you miss a dose by more than 24 hours, skip the missed and go back to your normal schedule. Do not take 2 doses at the same time or extra doses to make up for a missed dose.

- Do not replace a vomited dose.
- **Defactinib:** Swallow tablets whole with food. Take the tablets at approximately the same time each day. Do not chew, break, or crush the tablets.
- **Missed dose:** If you miss a dose by more than 6 hours, skip the missed and go back to your normal schedule. Do not take 2 doses at the same time or extra doses to make up for a missed dose.
- Do not replace a vomited dose.
- **Overdosage:** If you think you have taken too much of this medicine contact a poison control center or emergency room at once.
- **Handling:** Wash your hands after handling your medicine. Your caretakers should not handle your medicine with bare hands and should wear latex gloves.
- This medicine may be present in the urine, stool and other body fluids such as blood, vomit, semen, and vaginal fluids. Take precautions to prevent others from coming in contact with your medicine or your body fluids. Follow safety precautions during your treatment and for as long as directed by your care team after your treatment. If you take a pill each day, follow these precautions every day.
- **Storage:** Store these medicines in the original package in the refrigerator, between 36°F to 46°F (2°C to 8°C). Keep out of the reach of children and pets.
- **Disposal of unused medicine:** Do not flush any expired and/or unused medicine down the toilet or drain unless you are specifically instructed to do so on the medicine label. Some facilities have take-back programs and/or other options. If you do not have a take-back program in your area, then please discuss with your care team how to dispose of unused medicine.

Treating Side Effects

- Manage tiredness by pacing your activities for the day.
- Be sure to include periods of rest between energy-draining activities.
- Get regular exercise, with your care team's approval. If you feel too tired to exercise vigorously, try taking a short walk.
- To help decrease the risk of infection, wash your hands regularly.
- Avoid close contact with people who have a cold, the flu, or other infections.
- Take your temperature as your care team tells you, and whenever you feel like you may have a fever.
- To help decrease the risk of bleeding, use a soft toothbrush. Check with your care team before using dental floss.
- Be very careful when using knives or tools.
- Use an electric shaver instead of a razor.
- Drink enough fluids to keep your urine pale yellow.
- If you throw up or have diarrhea, you should drink more fluids so that you do not become dehydrated (lack of water in the body from losing too much fluid).
- Mouth care is very important. Your mouth care should consist of routine, gentle cleaning of your teeth or dentures and rinsing your mouth with a mixture of 1/2 teaspoon of salt in 8 ounces of water or 1/2 teaspoon of baking soda in 8 ounces of water. This should be done at least after each meal and at bedtime.
- If you have mouth sores, avoid mouthwash that has alcohol. Also avoid alcohol and smoking because they can bother your mouth and throat. To help with nausea and vomiting, eat small, frequent meals instead of three large meals a day. Choose foods and drinks that are at room

temperature. Ask your care team about other helpful tips and medicine that is available to help stop or lessen these symptoms.

- If you are not able to move your bowels, check with your care team before you use enemas, laxatives, or suppositories.
- If you have diarrhea, eat low-fiber foods that are high in protein and calories and avoid foods that can irritate your digestive tracts or lead to cramping.
- Ask your care team about medicines that are available to help stop or lessen constipation and/or diarrhea.
- Keeping your pain under control is important to your well-being. Please tell your doctor or care team if you are experiencing pain.
- To help with dry skin and itching, moisturize your skin several times a day.
- Avoid sun exposure and apply sunscreen routinely when outdoors.
- Use sunscreen with SPF 30 or higher when you are outdoors even for a short time. Cover up when you are out in the sun. Wear wide-brimmed hats, long-sleeved shirts, and pants. Keep your neck, chest, and back covered.
- Wear dark sunglasses when in the sun or bright lights.
- If you get a rash do not put anything on it unless your care team says you may. Keep the area around the rash clean and dry. Ask your care team for medicine if your rash bothers you.

Food and Medicine Interactions

- This medicine may interact with grapefruit and grapefruit juice. Talk to your care team as this could make side effects worse.
- Check with your care team about all other prescription medicines and over-the-counter medicines and dietary supplements (vitamins, minerals, herbs, and others) you are taking before starting this medicine as there are known medicine interactions with avutometinib and defactinib. Also, check with your care team before starting any new prescription or over-the-counter medicines, or dietary supplements to make sure that there are no interactions.
- This medicine may interact with St. John's Wort and may lower the levels of the medicine in your body, which can make it less effective.
- Medicines that treat heartburn and stomach upset may lower the effect of your cancer treatment if taken with avutometinib and defactinib. Ask your care team what medicine you can take to help with heartburn or stomach upset.
- There are known interactions of avutometinib and defactinib with blood thinning medicine such as warfarin. Ask your care team what precautions you should take.

When to Call Your Care Team

Call your care team if you have any of these symptoms and/or any new or unusual symptoms:

- Fever of 100.4° F (38° C) or higher
- Chills
- Tiredness that interferes with your daily activities
- Feeling dizzy or lightheaded



- Easy bleeding or bruising
- Dry eyes
- Sensitivity to light
- Eye swelling, redness and/or itching
- Flashes of light and/or dark areas in your field of vision, colored dots, or halos
- Blurred vision or other changes in eyesight such as a loss of vision
- Pain in your mouth or throat that makes it hard to eat or drink
- Pain in your abdomen that does not go away
- Nausea that stops you from eating or drinking and/or is not relieved by prescribed medicines
- No bowel movement in 3 days or when you feel uncomfortable
- Diarrhea, 4 times in one day or diarrhea with lack of strength or a feeling of being dizzy
- Signs of possible liver problems: dark urine, pale bowel movements, pain in your abdomen, feeling very tired and weak, unusual itching, or yellowing of the eyes or skin
- Signs of rhabdomyolysis such as decreased or very dark urine, muscle pain in the shoulders, thighs, or lower back; muscle weakness or trouble moving arms and legs.
- Unexplained muscle pain, tenderness, or weakness
- Weight gain of 5 pounds in one week (fluid retention)
- Swelling of the hands, feet, or any other part of the body
- Signs of a urinary tract infection such as burning or pain when you pass urine, trouble urinating, smelly and/or cloudy urine, pain in your lower abdomen or lower/side of your back.
- Cough that is bothersome
- Wheezing and/or trouble breathing
- Flu-like symptoms: fever, headache, muscle and joint aches, and tiredness
- Swollen lymph nodes in your neck and/or armpits
- New rash and/or itching or a rash that is not relieved by prescribed medicines
- Dry skin and/or itching that is bothersome
- Develop sensitivity to sunlight/light

Reproduction Warnings

- **Pregnancy warning:** This medicine can cause serious birth defects. If you can become pregnant, use birth control while taking this medicine and for 1 month after the last dose. If you can get your partner pregnant, use birth control while taking this medicine and for 4 months after the last dose. Tell your care team right away if you think you might be pregnant or think your partner might be pregnant.
- **Breastfeeding warning:** Do not breastfeed while taking this medicine and for 2 weeks after the last dose.
- **Fertility warning:** This medicine may affect your ability to have children in the future. If you plan to have children, talk with your care team.

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