Avutometinib and Defactinib

Patient Education Sheets
Understanding Your Cancer Treatment

Care Team Contact Information: _____

Pharmacy Contact Information: _____

Diagnosis: _____

- This treatment is often used for certain types of ovarian cancer, but it may also be used for other diagnoses.
- Your care team will perform a test for a KRAS gene variant to make sure that avutometinib and defactinib is right for you.

Goal of Treatment: _____

- Treatment may continue until it no longer works or until side effects are no longer controlled.

Treatment Regimen

Treatment Name	How the Treatment Works	How the Treatment is Given
Avutometinib and Defactinib (a-VUE-toe-ME-ti-nib… dee-FAK-ti-nib): Avmapki Fakzynja Co-Pack (ave-MAP-kee Fak-zin-jah koh-pak)	Slows down or stops the growth of cancer cells by blocking a specific protein that helps them survive.	Avutometinib are capsules taken by mouth. Defactinib is a tablet taken by mouth.

Treatment Administration and Schedule: Treatment is typically repeated every 4 weeks. This length of time is called a “cycle”.

- Avutometinib is taken 2 times a ***week*** (on day 1 and day 4 of each week) for the first 3 weeks, followed by 1 week off.
- Defactinib is take 2 times a ***day*** for the first 3 weeks, followed by 1 week off.

Treatment Name	Cycle 1, Day																						Next Cycle
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22-28	1
Avutometinib	✓			✓				✓			✓				✓			✓					✓
Defactinib AM dose	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	**Week-long Break**	✓
Defactinib PM dose	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓

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Treatment Administration and Schedule:

Your avutometinib and defactinib (Avmapki Fakzynja Co-Pack) dose:

_____

_____

_____

- This Co-Pack contains 2 medications: avutometinib (AVMAPKI) and defactinib (FAKZYNJA).
  - Avutometinib is a capsule that comes in 0.8 mg strength.
  - Defactinib is a tablet that comes in 200 mg strength.
  - Your care team will tell how many of each capsule or tablet take. If needed, they may change your dose.
- Your dose might differ, but avutometinib and defactinib is typically taken as:
  - Avutometinib: 3.2 mg (four 0.8 mg capsules) taken by mouth 2 times a week (Day 1 and Day 4), for the first 3 weeks of each 4-week cycle.
  - Defactinib: 200 mg (one 200 mg tablet) taken by mouth 2 times a day at the same time each day, about 12 hours apart, for the first 3 weeks of each 4-week cycle.
  - You will take both medications (avutometinib and defactinib) for the first 21 days (3 weeks) of each cycle, followed by 7 days off treatment (a 1-week break).
- Take avutometinib and defactinib with food.
- **Avutometinib capsules:**
  - Take each dose at the same time.
  - Swallow the avutometinib capsules whole. Do not chew, break, or open the capsules.
  - If you miss a dose of avutometinib by more than 24 hours, skip the missed dose and take the next scheduled dose as prescribed by your care team. Do NOT take 2 doses at the same time to make up for a missed dose.
- **Defactinib tablets:**
  - Swallow the defactinib tablets whole. Do not chew, break, or crush the tablets.
  - If you take antacids, take defactinib tablets 2 hours before or 2 hours after taking the antacid.
  - If you miss a dose of defactinib by more than 6 hours, skip the missed dose and take the next scheduled dose as prescribed by your care team. Do NOT take 2 doses at the same time to make up for a missed dose
- If you vomit after taking avutometinib capsules or defactinib tablets, do NOT take an additional dose. Take the next scheduled dose as prescribed by your care team

Storage and Handling of Avutometinib and Defactinib

- Store avutometinib and defactinib in the refrigerator at 36°F to 46°F (2°C to 8°C) in their original bottles.
- Do NOT remove the desiccant from the avutometinib bottle.
- Keep avutometinib and defactinib out of the reach of children and pets.
- Ask your care team how to safely throw away any unused avutometinib or defactinib.

Appointments: Appointments may include regular check-ups with your care team, lab visits, and imaging tests. It's important to keep your appointments whenever you can. If you miss any appointments, call your care provider as soon as possible to reschedule your appointment.

Supportive Care to Prevent and Treat Side Effects

Description	Supportive Care Taken at Home
To help prevent or treat nausea or vomiting	
To help prevent skin reactions	
Other	

Common Side Effects

Side Effect	Important Information
Low White Blood Cell (WBC) Count and Increased Risk of Infection	Description: WBCs help protect the body against infections. If you have a low WBC count, you may be at a higher risk of infection. Recommendations: • Wash your hands and bathe regularly. • Avoid crowded places. • Stay away from people who are sick. Talk to your care team if you have: • Fever of 100.4 °F (38°C) or higher • Chills • Cough • Sore throat • Painful urination • Tiredness that is worse than normal • Skin infections (red, swollen, or painful areas)
Low Red Blood Cell (RBC) Count and Hemoglobin (Hgb)	Description: RBCs and Hgb help bring oxygen to your body's tissues and take away carbon dioxide. If you have low RBC counts or Hgb, you may feel weak, tired, or look pale. Recommendations: • Get 7 to 8 hours of sleep each night. • Avoid operating heavy machinery when tired. • Balance work and rest, staying active but resting when needed. Talk to your care team if you have: • Shortness of breath • Dizziness • Fast or abnormal heartbeats • Severe headache
Low Platelet Count	Description: Platelets help the blood clot and heal wounds. If you have low platelet counts, you are at a higher risk of bruising and bleeding. Recommendations: • Blow your nose gently and avoid picking it. • Brush your teeth gently with a soft toothbrush and maintain good oral hygiene. • Use an electric razor for shaving and a nail file instead of nail clippers. • Avoid over-the-counter medications that may increase the risk of bleeding, such as NSAIDs. • Talk with your care team or dentist before medical or dental procedures, as you may need to pause your treatment. Talk to your care team if you have: • Nosebleed lasting over 5 minutes despite pressure • Cut that continues to bleed • Significant gum bleeding when flossing or brushing • Severe headaches • Blood in your urine or stool • Blood in your spit after a cough

Nausea and Vomiting	Description: Nausea is an uncomfortable feeling in your stomach or the need to throw up. This may or may not cause vomiting. Recommendations: • Eat smaller, more frequent meals. • Avoid fatty, fried, spicy, or highly sweet foods. • Eat bland foods at room temperature and drink clear liquids. • If you vomit, start with small amounts of water, broth, or other clear liquids when you are ready to eat again. If that stays down, then try soft foods (such as gelatin, plain cornstarch pudding, yogurt, strained soup, or strained cooked cereal). Slowly work up to eating solid food. • Your care provider may prescribe medicine for these symptoms. Talk to your care team if you have: • Vomiting for more than 24 hours • Vomiting that's nonstop • Signs of dehydration (like feeling very thirsty, having a dry mouth, feeling dizzy, or having dark urine) • Blood or coffee-ground-like appearance in your vomit • Bad stomach pain that doesn't go away after vomiting
Diarrhea	Description: Diarrhea is when you have loose, watery bowel movements more often than usual. The need to use the bathroom may occur urgently. Recommendations: • Keep track of how many times you go to the bathroom each day. • Drink 8 to 10 glasses of water or other fluids every day, unless your doctor tells you otherwise. • Eat small meals of mild, low-fiber foods like bananas, applesauce, potatoes, chicken, rice, and toast. • Stay away from foods with high fiber (like raw vegetables, fruits, and whole grains), foods that cause gas (like broccoli and beans), dairy foods (like yogurt and milk), and spicy, fried, and greasy foods. • Your care team may recommend a medicine (such as loperamide) for diarrhea. Talk to your care team if you have: • 4 or more bowel movements than normal in 24 hours • Dizziness or lightheadedness while having diarrhea • Bloody diarrhea
Constipation	Description: Constipation means having a hard time passing stools or not going to the bathroom often. Your stools might feel hard and dry, which can make you uncomfortable or hurt. Recommendations: • Keep track of how many times you move your bowels every day. • Drink 8 to 10 glasses of water or other fluids each day, unless your doctor tells you otherwise. • Try to stay active and get some exercise if you can. • Eat high-fiber foods like raw fruits and vegetables. • Your care team may recommend a medicine (such as polyethylene glycol 3350 or senna) to help move your bowels. Talk to your care team if you have: • Constipation that lasts 3 or more days • Constipation after 48 hours, even after using a laxative

Stomach (Abdominal) Pain	Description: Abdominal pain is when you feel discomfort or pain in the belly area. Talk to your care team if you have: • Severe abdominal pain
Liver Problems	Description: Treatment can harm your liver. This may cause nausea, stomach pain, and bleeding or bruising. It can also turn your skin and eyes yellow and make your urine dark. Lab tests may be performed to monitor liver function. Talk to your care team if you have: • Yellowing of your skin or the whites of your eyes • Severe nausea or vomiting • Pain on the right side of your stomach area (abdomen) • Dark urine (tea colored) • Bleeding or bruising more easily than normal
Heartburn	Description: Heartburn happens when stomach acid moves up into your throat or chest. This can cause a burning feeling in your chest, sour taste in your mouth, or discomfort after eating. Recommendations: • Eat smaller meals more often instead of large meals. • Avoid lying down for at least 2 to 3 hours after eating. • Limit foods that can make heartburn worse, such as spicy foods, fried foods, caffeine, alcohol, or citrus. • Raise the head of your bed with extra pillows or a wedge if heartburn happens at night. • Your care team may prescribe medicine to help reduce stomach acid. Talk to your care team if you have: • Heartburn that happens often or does not get better with the changes above. • Trouble swallowing. • Chest pain that is severe or different than usual. • Throwing up blood or material that looks like coffee grounds • Black or bloody stools
Mouth Irritation and Sores	Description: This treatment can irritate the lining of the mouth. In some cases, this can cause redness, sores, pain, and swelling. Recommendations: • Rinse your mouth after meals and at bedtime, and more often if sores develop. • Brush your teeth with a soft toothbrush or cotton swab after meals. • Use a mild, non-alcohol mouth rinse at least four times daily (after meals and at bedtime). A simple mixture is 1/8 teaspoon salt and 1/4 teaspoon baking soda in 8 ounces of warm water. • Avoid acidic, hot, spicy, or rough foods and drinks that may irritate your mouth. • If you have mouth sores, avoid tobacco, alcohol, and alcohol-based mouthwashes. • Your care team may prescribe medicine for these symptoms. Talk to your care team if you have: • Pain or sores in your mouth or throat

<table>
<tr><td>Fatigue</td><td>Description: Fatigue is a constant and sometimes strong feeling of tiredness.

Recommendations:
Routine exercise has been shown to decrease levels of fatigue. Work with your care team to find the right type of exercise for you.
Ask your family and friends for help with daily tasks and emotional support.
Try healthy ways to feel better, like meditation, writing in a journal, doing yoga, and using guided imagery to lower anxiety and feel good.
Make a regular sleep schedule and limit naps during the day so you can sleep better at night, aiming for 7 to 8 hours of sleep.
Don't use heavy machines or do things that need your full attention if you're very tired to avoid accidents.
Talk to your care team if you have:
Tiredness that affects your daily life
Tiredness all the time, and it doesn't get better with rest
Dizziness and weakness, along with being tired</td></tr>
<tr><td>Swelling of Lower Legs and Hands</td><td>Description: Swelling and fluid retention can occur in different areas of the body, like the legs or hands. You might notice areas feel puffy or tighter than usual.
Recommendations:
Keep a daily log of swelling and note any changes in size or location.
Elevate swollen limbs when resting.
Limit salt intake.
Stay active with regular, gentle exercises.
Avoid prolonged periods of sitting or standing without movement.
Talk to your care team if you have:
Swelling that suddenly worsens or spreads to other areas
Pain, redness, or warmth in the affected area
Signs of shortness of breath or difficulty breathing
Swelling is persistent and does not improve with home management
Unexpected weight gain
Note: You care team may ask you to contact them if your weight increases by a certain amount over a certain time period.</td></tr>
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Muscle or Joint Pain or Weakness	Description: Muscle pain feels like soreness, aches, cramps, or stiffness in one or more muscles. It may also include tenderness or weakness. Joint pain happens where two bones come together and can feel sharp, dull, throbbing, or burning. It often causes stiffness, swelling, and difficulty moving. Recommendations: • Track your pain levels, areas of discomfort, and any activities that worsen or improve your symptoms. • Engage in gentle exercises like walking, stretching, or yoga to maintain mobility and strength, but consult your care team before starting any new exercise routine. • Apply a warm compress to relax stiff muscles or use cold packs to reduce swelling and numb pain in affected areas. • Your care team may prescribe or recommend medications, including over-the-counter pain relievers. Talk to your care team if you have: • Persistent or worsening muscle or joint pain that does not improve with home treatments • New symptoms, such as swelling, redness, or warmth in the joints • Weakness that affects your ability to perform daily activities
Eye problems	Description: Eye problems are common with this treatment and can sometimes be serious. These include blurred vision, new floaters (spots or lines in your vision), flashes of light, or changes affecting the retina (the back of the eye). These conditions may affect your ability to see clearly. Recommendations: • You will need a full eye exam before starting treatment, before cycle 2, and every 3 cycles during treatment. • Your care team will also send you for an eye exam right away if you have any new or worsening eye problems. • Wear sunglasses outdoors to reduce light sensitivity. • Use good lighting for reading and close work to reduce eye strain. • Avoid driving at night or in low light if you have vision changes. Talk to your care team if you have: • Blurred vision or double vision • New floaters (spots, lines, or shapes across your vision) • Flashes of light or sensitivity to light • Eye pain, redness, or swelling • Loss of part of your vision (shadow or curtain) • Any sudden or new change in vision
Skin Problems	Description: Treatment can cause a rash with itchy, dry, red, or puffy skin. Recommendations: • Keep your skin soft and moisturized with lotions or creams. • Wear loose, comfortable clothes. • Don’t use perfumes and colognes. • Stay out of the sun, especially between 10 AM and 4 PM. • Wear long-sleeved shirts with UV protection and a wide hat to block the sun. • Use sunscreen with at least SPF 30 and put on lip balm with SPF too. • Don't use tanning beds. • Your care team may suggest taking certain medicines or applying special creams. Talk to your care team if you have: • Rash or itching that continues to worsen

Hair Loss	Description: Hair loss or hair thinning can start days to a few weeks after treatment begins, but it usually grows back later. It might be a different texture or color when it comes back and may not look the same as before. Recommendations: • You can wear scarves, hats, or wigs, and think about getting a short haircut before treatment. • Keep your head covered to protect it from the sun and keep it warm. • If your scalp isn't covered outside, remember to put sunscreen on it. Talk to your care team if you would like a wig prescription.
High Triglyceride Levels	Description: Triglycerides are a type of fat found in your blood. Some cancer treatments can cause triglyceride levels to go up. High triglycerides usually do not cause symptoms, but very high levels may increase your risk for pancreatitis (inflammation of the pancreas) or heart problems over time. Recommendations: • Increase physical activity as recommended by your care team. • Eat a healthy diet that is low in fried foods, sweets, and high-fat meats. • Your care team may check your blood with regular lab tests to monitor triglyceride levels. • Limit alcohol, which can raise triglyceride levels. Talk to your care team if you have: • Nausea or vomiting that is new or worsening • Severe stomach pain that does not go away • Loss of appetite • Fever or chills

Select Rare Effects

Side Effect	Talk to Your Care Team if You Have Any of These Signs or Symptoms	
Nerve Problems	• New or worsening numbness or tingling in your hands or feet	• Muscle weakness
Lung Problems	• Cough • Shortness of breath	• Chest pain

Before starting treatment, ask your care team when to call 9-1-1 or seek emergency help.
If you experience any new, worsening, or uncontrolled side effects, contact your care team immediately.

Intimacy, Fertility, Pregnancy, and Breastfeeding

- Treatment may **change how you feel about intimacy and your body.** However, physical closeness—such as holding hands and hugging—remains safe. It is common to have questions about intimacy. If needed, talk to your care team for guidance.
- Treatment may **affect your ability to have children**. It may damage your reproductive organs or stop them from working. If you are worried about fertility, talk to your care team before starting treatment.
- Treatment may **harm an unborn baby**.
    - If you might get pregnant, take a pregnancy test before starting treatment.
    - Use an effective method of birth control during treatment and for 1 month after your last dose.
    - If you think you might be pregnant or if you become pregnant, tell your care team right away.
    - If your partners could become pregnant, use an effective method of birth control—such as condoms—during treatment and for 4 months after your last dose.
- **Do NOT breastfeed** during treatment and for 2 weeks after your last dose.

Additional Information

- **Tell your care team about all the medicines you take**.
  This includes prescriptions, over-the-counter drugs, vitamins, and herbal products. Before starting any new medicine, supplement, or vaccine, ask your care team first.
- **Avoid using this medicine with gastric acid reducing medications**, including proton pump inhibitors (PPIs) or H2 receptor antagonists. If taking both this medication and the acid reducing medications cannot be avoided, take defactinib 2 hours before or 2 hours after taking the gastric acid reducing medications.
- **Taking avutometinib and defactinib with warfarin increases the risk of bleeding.**
  Taking avutometinib and defactinib with warfarin can cause changes in how fast your blood clots and can cause bleeding.
    - Before taking avutometinib and defactinib, tell your care team if you are taking warfarin as they may recommend a different blood thinner medicine for your care.
    - Your care team may do blood tests more often, to check how fast your blood clots during and after you stop treatment with avutometinib and defactinib.
    - Tell your care team right away if you develop any signs or symptoms of bleeding.
- The most common **severe change in laboratory** test result was increased creatine phosphokinase (CPK).
- **This Patient Education Sheet may not describe all possible side effects.**
  Call your healthcare provider for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

Notes

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Important notice: The Association of Cancer Care Centers (ACCC), Hematology/Oncology Pharmacy Association (HOPA), Network for Collaborative Oncology Development & Advancement, Inc. (NCODA), and Oncology Nursing Society (ONS) have collaborated in gathering information for and developing this patient education guide. This guide represents a brief summary of the medication derived from information provided by the drug manufacturer and other resources.

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