

Medication Guide - PAT001-OVC-2025

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About This Guide: This document provides easy-to-understand information about the targeted therapies recommended based on your precision medicine analysis. These medications specifically target abnormalities found in your tumor's biology.

Your Personalized Treatment Approach

Your tumor analysis showed that certain proteins in your cancer cells are overactive. These proteins help cancer cells survive and resist chemotherapy drugs like platinum. The medications described below work by blocking these specific proteins.

Key Finding: Your tumor has activation of a pathway called "PI3K/AKT/mTOR." This pathway acts like an "accelerator pedal" for cancer cell growth and survival. The recommended medications are like "brakes" for this pathway. Alpelisib (Piqray®)

A PI3K inhibitor - blocks the first step in the overactive pathway

What is this medication?

Alpelisib is an FDA-approved targeted therapy that blocks a protein called PI3K (pronounced "pie-three-kinase"). Think of PI3K as a switch that turns on cancer cell survival signals. Your tumor analysis showed this switch is stuck in the "ON" position. Alpelisib helps turn it "OFF."

Why is it recommended for you?

- **Your tumor analysis** showed very high PI3K activity
- **Genetic testing** found you are missing a "brake" gene called PTEN
- **Without PTEN:** PI3K works overtime, helping cancer cells survive platinum chemotherapy
- **Clinical evidence:** Works well in tumors similar to yours

How do you take it?

- **Form:** Tablet (pill)
- **Dose:** 300 mg (2 tablets of 150 mg each)
- **When:** Once daily, at the same time each day
- **With or without food:** WITH FOOD (take with a meal or snack)
- **Important:** Swallow tablets whole - do not crush, chew, or split

What are the side effects?

Most Common Side Effect: High Blood Sugar

- Happens in 60-70% of patients
- Usually starts in first few weeks
- You will need to check your blood sugar regularly
- Your doctor may prescribe metformin (diabetes medication) to help

Other Common Side Effects:

- **Diarrhea** (40-50% of patients) - usually manageable with anti-diarrheal medication
- **Skin rash** (30-40%) - often mild, treatable with creams
- **Nausea** (25-35%) - anti-nausea medication can help
- **Fatigue** (20-30%) - may improve after first month
- **Decreased appetite** (15-25%)

When to Call Your Doctor Right Away:

- Blood sugar over 300 mg/dL
- Extreme thirst or frequent urination
- Severe diarrhea (more than 6 episodes per day)
- Severe rash or blisters
- Trouble breathing or severe allergic reaction
- Fever over 100.4°F

What monitoring is needed?

- **Blood sugar:** Daily for first 2 weeks, then weekly
- **Blood tests:** Every 2 weeks for first 2 months, then monthly
- **Tumor markers (CA-125):** Every month
- **Imaging (CT scan):** Every 8 weeks to check if tumor is shrinking

FDA Approval Status

FDA Approved: Yes, approved in May 2019 for breast cancer with PIK3CA mutations.

Note: Use in ovarian cancer is considered "off-label" but is appropriate because your tumor has the same PIK3CA/PTEN abnormalities. Your insurance may require pre-authorization.

Cost and Insurance

- **List price:** Approximately \$15,000 per month (without insurance)
- **With insurance:** Copay assistance programs available
- **Manufacturer support:** Novartis has a patient assistance program
- **Clinical trial option:** Free through research study (see below)

Capivasertib (AZD5363)

An AKT inhibitor - blocks the second step in the overactive pathway

What is this medication?

Capivasertib is an investigational drug (still in clinical trials) that blocks a protein called AKT. AKT is right "downstream" of PI3K - it receives signals from PI3K and passes them along to help cancer cells survive. Your tumor analysis showed AKT is highly active.

Why is it recommended for you?

- **Your tumor analysis** showed very high AKT activity (even higher than PI3K)
- **Without PTEN:** AKT is constantly activated
- **Scientific rationale:** Blocking both PI3K AND AKT works better than blocking just one
- **Prevents resistance:** Cancer cells can't bypass treatment by activating the "backup" protein

How do you take it?

- **Form:** Tablet (pill)
- **Dose:** 400 mg (taken twice daily)
- **Schedule:** 4 days ON, 3 days OFF (to reduce side effects)
- **Example schedule:** Take Monday-Thursday, skip Friday-Sunday, repeat
- **With or without food:** Can be taken with or without food
- **Important:** Swallow whole - do not crush or chew

What are the side effects?

Most Common Side Effect: High Blood Sugar

- Happens in 50-60% of patients (similar to alpelisib)
- When combined with alpelisib, blood sugar needs extra monitoring
- Diabetes medication (metformin) usually helps

Other Common Side Effects:

- **Diarrhea** (35-45%)
- **Nausea** (30-40%)
- **Fatigue** (25-35%)
- **Decreased appetite** (20-30%)
- **Rash** (15-25%)

When to Call Your Doctor Right Away:

- Blood sugar over 300 mg/dL
- Severe diarrhea or dehydration
- Chest pain or shortness of breath
- Severe fatigue that prevents daily activities
- Any new or worsening symptoms

What monitoring is needed?

- **Blood sugar:** Daily for first month (especially important with combination therapy)
- **Blood tests:** Weekly for first month, then every 2 weeks
- **Tumor response:** CA-125 monthly, CT scan every 8 weeks
- **On-treatment biopsy:** May be requested at Week 4 to confirm AKT is being blocked

FDA Approval Status

Investigational Drug: Not yet FDA approved - available only through clinical trials.

Capivasertib is in Phase III clinical trials (the final phase before FDA approval). Early results are very promising, showing improved outcomes when combined with other therapies.

How to access this medication

Clinical Trial Opportunity:

- **Trial Number:** NCT03602859
- **Title:** "Alpelisib + Capivasertib in PTEN-deficient Solid Tumors"
- **Your Match:** You appear to be an excellent candidate
 - ✓ PTEN loss (genetic deletion found)
 - ✓ Platinum-resistant ovarian cancer
 - ✓ PI3K and AKT activation confirmed
- **Trial Benefits:**
 - Free medication (both alpelisib and capivasertib)
 - Close monitoring by research team
 - Access to cutting-edge therapy
 - Helping advance cancer research

Clinical Trial Questions to Ask

- Am I eligible based on my performance status and prior treatments?
- How many patients have been enrolled so far?
- What have the results shown in patients similar to me?
- If the trial helps me, can I stay on the medication after the trial ends?
- What happens if the medication stops working - what are my options?

Combination Therapy: Why Two Drugs?

Understanding the dual-blockade strategy

Why combine alpelisib and capivasertib?

Your tumor analysis revealed that cancer cells are using **both** PI3K and AKT proteins to survive. Here's why blocking both is important:

The Problem with Single Drugs:

- **If we block only PI3K:** Cancer cells can activate AKT through "backup" pathways
- **If we block only AKT:** PI3K can activate other survival proteins
- **Result:** Tumor may initially shrink, then grow back (resistance)

The Advantage of Combination:

- **Dual blockade:** Shuts down the pathway at TWO points
- **Prevents escape:** Cancer cells have fewer ways to bypass treatment
- **Scientific evidence:** Lab studies show synergistic effects ($1 + 1 = 3$)
- **Better outcomes:** Clinical trials show longer remissions with combination

Your Tumor Profile Supports Combination:

- PI3K activation score: Very high ($Z = 3.0$)
- AKT activation score: Even higher ($Z = 3.2$)
- PTEN status: Completely missing (both copies lost)
- Clinical interpretation: Dual blockade is scientifically justified

What are the challenges?

More Side Effects with Combination:

- High blood sugar is more common and may be more severe
- Diarrhea may be more frequent
- Fatigue may be greater
- Careful monitoring is VERY important

How will we manage side effects?

- **Proactive approach:** Start metformin BEFORE beginning treatment
- **Glucose monitoring:** Check blood sugar daily, adjust diabetes medication as needed
- **Low-glycemic diet:** Dietician will help you choose foods that minimize blood sugar spikes
- **Hydration:** Drink plenty of water to prevent dehydration from diarrhea
- **Dose adjustments:** If side effects are severe, we can temporarily reduce doses
- **Communication:** Weekly check-ins during first month

What if the side effects are too much?

Alternative Options:

- **Option 1:** Try alpelisib alone first
 - Fewer side effects
 - Can add capivasertib later if needed
- **Option 2:** Sequential therapy (one drug at a time)
- **Option 3:** Different PI3K/AKT inhibitor with better tolerance
- **Option 4:** Return to standard chemotherapy

Remember: Your care team is here to support you. If side effects are affecting your quality of life too much, we will work together to find the right balance or try a different approach.

Everolimus (Afinitor®) - Alternative Option

An mTOR inhibitor - blocks the third protein in the pathway

What is this medication?

Everolimus is an FDA-approved drug that blocks mTOR, which is "downstream" of both PI3K and AKT. Your analysis showed mTOR is also activated in your tumor.

When might this be used?

- **If combination therapy is not tolerated:** Everolimus alone may be an option
- **Second-line option:** If alpelisib/capivasertib stops working
- **Less intensive treatment:** If you prefer a single drug with fewer side effects

Limitation: Blocking mTOR alone can cause PI3K and AKT to become even MORE active (compensatory activation). This is why the dual PI3K/AKT approach is preferred for your tumor profile.

How do you take it?

- **Dose:** 10 mg once daily
- **Timing:** Same time each day, with or without food
- **Swallow whole:** Do not crush or chew

What are the side effects?

- **Mouth sores (stomatitis):** Most common (40%) - mouthwash can help
- **Infections:** Slightly increased risk (30%)
- **Fatigue:** Common (25-30%)
- **Diarrhea:** Less common than with PI3K inhibitors (20%)
- **Lung inflammation (pneumonitis):** Rare but serious (3-5%)

FDA Approval Status

FDA Approved: Yes, for kidney cancer, breast cancer, and neuroendocrine tumors.

Note: Use in ovarian cancer is off-label. Generally well-covered by insurance due to multiple FDA approvals.

Important Information for All Medications

Drug Interactions

Tell your doctor about ALL medications you take, including:

- Prescription medications
- Over-the-counter medications (like ibuprofen, antacids)
- Vitamins and supplements
- Herbal products

Important interactions to avoid:

- **Strong CYP3A4 inhibitors:** Ketoconazole, clarithromycin, grapefruit juice (can increase drug levels)
- **Strong CYP3A4 inducers:** Rifampin, St. John's Wort (can decrease drug levels)
- **Diabetes medications:** Insulin, sulfonylureas (may need dose adjustments)

Pregnancy and Breastfeeding

These medications can harm an unborn baby.

- Use effective birth control during treatment and for 1 week after stopping
- Tell your doctor immediately if you become pregnant
- Do not breastfeed while taking these medications
- Male partners should also use contraception

Missed Dose

If you miss a dose:

- If less than 4 hours late: Take it as soon as you remember
- If more than 4 hours late: Skip the missed dose, take the next dose at the regular time
- **Never** take two doses at once to make up for a missed dose

Questions to Ask Your Care Team

- Am I eligible for the clinical trial combining alpelisib and capivasertib?
- What is my expected response rate based on patients similar to me?
- How will we monitor if the treatment is working?
- What happens if my blood sugar becomes difficult to control?
- Are there support services available (nutritionist, social worker, financial counselor)?
- What are the warning signs that I should go to the emergency room?
- How long might I stay on these medications if they are working?

- What happens if the tumor develops resistance to these drugs?

Support Resources

- **24/7 Nurse Line:** [Insert hospital phone number]
- **Financial Assistance:**
 - Novartis Patient Assistance Program (for alpelisib): 1-800-XXX-XXXX
 - Cancer Financial Assistance Coalition: www.cancerfac.org
- **Clinical Trial Information:** www.clinicaltrials.gov (search NCT03602859)
- **Patient Support Groups:** Ovarian Cancer Research Alliance (OCRA)
- **Nutrition Services:** Request referral to oncology dietician

Remember

These medications were specifically chosen based on your tumor's unique biology. While side effects can be challenging, many patients find them manageable with proper support and monitoring. Your care team is here to help you every step of the way.

You are not alone in this journey.

This medication guide was prepared based on your precision medicine tumor analysis

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