Acalabrutinib Fact Sheet

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Generic Name: Acalabrutinib
Trade Name: Calquence® from AstraZeneca

Drug Type: Acalabrutinib is a targeted therapy. Targeted therapy is the result of years of research dedicated to understanding the differences between cancer cells and normal cells. Targeted therapies attack cancer cells while causing minimal damage to the normal cells, leading to fewer side effects. Each type of targeted therapy works a little differently, but all interfere with the ability of the cancer cell to grow, divide, repair and/or communicate with other cells.

As a targeted therapy, acalabrutinib inhibits the function of Bruton's tyrosine kinase (BTK). BTK is a protein inside the cell that may be overexpressed in malignant B-cells. The BTK-specific inhibitor, acalabrutinib, blocks BCR signaling and results in decreased malignant B-cell tumor growth and survival.

What Conditions Are Treated by Acalabrutinib:
Acalabrutinib is currently approved for the treatment of chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) by the US Food and Drug Administration (FDA) in collaboration with the Australian Therapeutic Goods Administration and Health Canada. In the United States, acalabrutinib is also approved for use in previously treated mantle cell lymphoma. The approval for treatment of CLL and SLL was based on studies that demonstrated that acalabrutinib as a single-agent therapy (and combination therapy with obinutuzumab for patients with previously untreated CLL), provides a significant improvement in tolerability as well as progression-free survival compared with standard treatment regimens for these diseases.

Without specific FDA approval for treating WM, acalabrutinib prescribed for patients with WM is given "off-label," signifying that the drug is being prescribed for an unapproved indication or in an unapproved age group, dosage, or route of administration. This ability to prescribe drugs for uses beyond officially approved indications is common in medicine and includes most other drugs used to treat WM, except for ibrutinib and ibrutinib/rituximab combinations. A large single-arm (single-agent), multicenter Phase 2 trial with 19 European and eight US academic institutions provided evidence that acalabrutinib is active as a monotherapy with a manageable safety profile in patients who were previously untreated or had relapsed/refractory WM. Further studies are needed to establish its efficacy against standard treatments and to investigate whether outcomes can be improved with combination therapies.

How Acalabrutinib Is Given:

In the United States, Acalabrutinib is available through specialty pharmacies. The dosage for WM is a 100 mg capsule, taken by mouth twice daily, 12 hours apart at the same times each day, continued until disease progression or unacceptable toxicity is demonstrated. The capsule should be swallowed whole (not crushed, opened, chewed, or dissolved) with at least 8 ounces of water. The drug may be taken with food or on an empty stomach. Acalabrutinib should be taken exactly as prescribed. If a dose of acalabrutinib is missed, it should be taken as soon as remembered, unless it is more than three hours past the usual dose time, in which case the missed dose should be skipped and the next dose should be

taken at the regularly scheduled time. Accordingly, an extra dose should not be taken to make up for the missed dose and the dose should not be changed or the drug stopped unless instructed to do so by a health care provider.

Side Effects Associated with Acalabrutinib:
As a second generation BTK inhibitor, acalabrutinib is more selective for BTK than ibrutinib with less off-target inhibition, so fewer side effects may be seen. However, longer follow-up study is needed to make this determination.

The most common side effects (occurring in greater than 30%) for patients taking acalabrutinib are headache and diarrhea. The less common side effects (occurring in 10-29%) are low blood counts, anemia (low numbers of circulating red blood cells), neutropenia (low numbers of circulating neutrophils, a type of white blood cell), thrombocytopenia (low number of platelets necessary for clotting of the blood), fatigue, bruising, nausea, rash, constipation, abdominal pain (stomach ache), vomiting, upper respiratory tract infection (e.g., the common cold), muscle, pain, and bleeding events (more than bruising), such as hemorrhage. When gastrointestinal side effects (diarrhea, nausea, and vomiting) occur, they are generally mild.

A less common, but potentially serious side effect of acalabrutinib is atrial fibrillation and flutter. This risk may be increased in patients with cardiac risk factors; hypertension (high blood pressure), prior arrhythmias (heart beats with irregular or abnormal rhythm), and acute infection. Patients on acalabrutinib should be regularly monitored for symptoms of arrhythmias (palpitations, dizziness, dyspnea) as well as serious infections, bleeding/hemorrhage, and low blood counts and treated appropriately.

Acalabrutinib can make skin more sensitive to sunlight and may raise the chance of skin cancer; consequently, limit time in the sun, use sunscreen, and wear hats and clothes that cover as much skin as possible while taking acalabrutinib.

Side effects that are very rare, occurring in less than 10% of patients, are not listed here. There is no relationship between the presence and/or severity of side effects and the effectiveness of the medication. The side effects associated with acalabrutinib may be quite manageable, however side effects should always be reported to a health care provider. Most people will not experience all the side effects listed. Side effects are often predictable in terms of their onset, duration, and severity. They are almost always reversible and will go away after therapy is completed.

The FDA advises health care professionals to tell males and females of reproductive age to use effective contraception during treatment and for at least one month after stopping the drug (if told to stop treatment due to disease progression or unmanageable side effects). Women who are pregnant or breastfeeding should not take the drug, as acalabrutinib may cause fetal harm, and it is unknown if the drug is present in breast milk.

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When to Contact Your Doctor or Health Care Provider:
Contact your doctor or health care provider immediately, day or night, if you should experience any of the following symptoms: fever of 100.4° F (38° C) or higher or chills (both are possible signs of infection), shortness of breath or trouble breathing, cough, or any bleeding that won't stop.

The following symptoms also require medical attention but are not an emergency. Contact your doctor or health care provider within 24 hours of noticing any of the following: frequent diarrhea (4-6 episodes in a 24-hour period), black or tarry stools or blood in your stools, long-lasting headache, confusion, change in speech, nausea that interferes with ability to eat and unrelieved with prescribed medication, vomiting more than 4-5 times in a 24-hour period, inability to eat or drink for 24 hours, signs of dehydration (tired, thirst, dry mouth, dark and decreased amount of urine, or dizziness), yellowing of the skin or whites of the eyes, dark or brown (tea colored) urine, pain on the right side of the stomach, easy bleeding or bruising (more than usual), any skin or nail changes (rash, itching, severe dryness, blisters, nail infection, inflammation of the lips), cough with or without mucus, mouth sores, pain or burning with urination, and extreme fatigue (unable to carry on self-care activities).

Always inform your health care provider if you experience any unusual symptoms.

Self-Care Tips While Taking Acalabrutinib:
Do not drink grapefruit juice, eat grapefruit, Seville oranges (often used in marmalades), or starfruit while taking acalabrutinib. These products may increase the amount of acalabrutinib in your blood. Echinacea, a commonly used herbal remedy, may decrease the therapeutic effects of acalabrutinib.

Gastric acid reducing agents may decrease the amount of acalabrutinib in your blood, which may reduce the activity of the drug. Avoid simultaneous use of proton pump inhibitors, such as dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole, or rabeprazole when taking acalabrutinib. Take acalabrutinib two hours before taking acid reducer medications called H2-receptor blockers (e.g., famotidine or ranitidine). Separate taking acalabrutinib from antacids (e.g., calcium carbonate) by at least two hours before and after.

Acalabrutinib may further increase the risk of bleeding in patients taking blood thinner medicines, including aspirin. Any planned surgeries or dental procedures should be discussed with a health care provider. Depending on the bleeding risk, acalabrutinib may need to be discontinued for a short period of time (3-7 days) before and after the procedure.

Acalabrutinib may reduce the efficacy of inactivated (not live) vaccines. Immunizations or vaccinations should not be administered without a health care provider's approval while taking acalabrutinib. Complete all appropriate vaccines at least two weeks before starting the drug. If vaccinated during therapy, revaccinate at least three months after discontinuing the acalabrutinib. Avoid use of live organism vaccines with immunosuppressant therapies such as acalabrutinib. Before starting acalabrutinib, inform your health care provider if you have or had hepatitis B virus (HBV) infection, as serious infections can occur during treatment.

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Stay well hydrated and drink at least 2-3 quarts of fluid every 24 hours, unless you are instructed otherwise.

Wash your hands often and after taking each dose of acalabrutinib.

There is an increased risk of infection, so try to avoid crowds or people with co. Report fever or any other signs of infection immediately to your health care provider.

Make sure you tell your doctor and pharmacist about any other medications you are taking (including prescription, over the counter, vitamins, herbal remedies, etc.), with emphasis on anticoagulants and other medications that affect platelet aggregation.

Use an electric razor and a soft toothbrush to minimize bleeding.

Avoid contact sports or activities that could cause injury.

To help treat/prevent mouth sores while taking acalabrutinib, use a soft toothbrush and rinse mouth three times a day with one teaspoon of baking soda mixed with eight ounces of water.

If you have nausea, ask your health care provider about prescription anti-nausea medication, and eat small, frequent meals to minimize nausea. In general, drinking alcoholic beverages should be kept to a minimum or avoided completely while taking acalabrutinib. This should be discussed with a health care provider.

Eat foods that may help reduce diarrhea:

- Drink plenty of clear fluids (8-10 glasses per day). Examples: Gatorade®, broth, Jello®, water, etc.
- Eat small amounts of soft bland low fiber foods frequently. Examples: banana, rice, noodles, white bread, skinned chicken, turkey or mild white fish.
- Avoid foods such as:
    - Greasy, fatty, or fried foods.
    - Raw vegetables or fruits.
    - Strong spices.
    - Whole grains breads and cereals, nuts, and popcorn.
    - Gas-forming foods and beverages (beans, cabbage, carbonated beverages).
    - Lactose-containing products, supplements, or alcohol.
    - Limit foods and beverages with caffeine and extremely hot or cold beverages.

If you have diarrhea, your doctor can prescribe and/or recommend over-the-counter anti-diarrhea medications, such as loperamide.

Avoid sun exposure. Wear SPF 30 (or higher) sun block and protective clothing.

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While it is always important to get plenty of rest and maintain good nutrition, this is even more important while being treated with acalabrutinib.

Tell all your health care providers that you take acalabrutinib. This includes your doctors, nurses, pharmacists, and dentists. If side effects or symptoms are experienced while being treated with acalabrutinib, tell your health care provider. They can prescribe medications and/or offer suggestions that are effective in managing these problems.

This document does not identify all possible drug interactions.

Monitoring and Testing While Taking Acalabrutinib:
You will be checked regularly by your doctor while you are taking acalabrutinib to monitor side effects and check your response to therapy. Periodic blood work will be obtained to monitor your complete blood count (CBC) as well as the function of other organs (such as your kidneys and liver).

NOTE: The information in this fact sheet is intended to be helpful and educational, but it does not constitute an endorsement by the IWMF and is not meant to be a substitute for professional medical advice. The IWMF strongly encourages discussions with health care professionals about specific medical conditions, side effects, and treatments.

The IWMF acknowledges Dr. Jorge J. Castillo, Dana-Farber Cancer Institute, for his review of this Fact Sheet.

Adapted from the Chemocare website, www.chemocare.com, sponsored by the Cleveland Clinic and Lexicomp© website www.wolterskluwercdi.com/lexicomp-online/