**ໂພອາຄາ**
**PHOACA**

**ສ່ວນປະກອບ:**
ໃນ 1 ເມັດແຄັບຊຸນ ປະກອບດ້ວຍ Acalabrutinib 100 mg.

**ຂໍ້ບ່ຊີ້ບັງ:**
-ສຳລັບປິ່ນປົວ ມະເຮັງຕ່ອມນ້ຳເຫຼືອງ (MCL) ໃນຜູ້ປ່ວຍທີ່ໄດ້ຮັບການປິ່ນປົວດ້ວຍເຄມີບຳບັດແລ້ວຢ່າງໜ້ອຍ 1 ຄັ້ງ;
-ສຳລັບປິ່ນປົວ ມະເຮັງເມັດເລືອດຂາວ ຊະນິດຊ້ຳເຣື້ອ (CLL) ຫຼື ຊະນິດເຊວຂະໜາດນ້ອຍ (SLL).

**ຂະໜາດ, ວິທີໃຊ້ ແລະ ຄຳເຕືອນ:**
-ປະລິມານປະຈຳວັນທີ່ແນະນຳແມ່ນ ວັນລະ 2 ຄັ້ງ, ຄັ້ງລະ 1 ເມັດ, ຮັບປະທານຫ່າງກັນ 12 ຊມ;
-ຮັບປະທານຮ່ວມ ຫຼື ບໍ່ຮ່ວມກັບອາຫານ;
-ຄວນຮັບປະທານ ໃນເວລາດຽວກັນຂອງທຸກໆວັນ;
-ຫ້າມຫຍໍ້, ບິດ ຫຼື ຫັກເມັດຢາ;
-ຖ້າລືມໃຫ້ກິນທັນທີເມື່ອນຶກໄດ້ພາຍໃນ 6 ຊມ ກ່ອນກິນຢາຄັ້ງຕໍ່ໄປ. ແຕ່ຖ້າເກີນ 6 ຊມ ແມ່ນໃຫ້ກິນໃນວັນຖັດໄປຕາມເວລາເດີມ (ຫ້າມບໍ່ໃຫ້ກິນເພີ່ມເປັນ 2 ເທົ່າ).

**ຜົນຂ້າງຄຽງເມື່ອໃຊ້ຢາ:**
ໃນເວລາໃຊ້ຢາ ຈະພົບເຫັນອາການດັ່ງລຸ່ມນີ້:
-ເຈັບຫົວ;
-ປວດກ້ຳມເນື້ອ;
-ຖອກທ້ອງ;
-ອ່ອນເພຍ.

**ຂະໜາດການບັນຈຸ:**
ບັນຈຸໃນຂວດພລາສຕິກ ຈຳນວນ 60 ເມັດ, ໃສ່ໃນກັບເຈ້ຍ ກັບລະ 1 ຂວດ.

**ການເກັບຮັກສາ:**
ເກັບມ້ຽນບ່ອນແຫ້ງບໍ່ມີແສງແດດສ່ອງເຖິງ ແລະ ໃນອຸນຫະພູມ 15-30 ອົງສາ, ເກັບໄວ້ໃນທີ່ຫ່າງໄກຈາກມືເດັກນ້ອຍ.

**ຜະລິດ ແລະ ຈຳໜ່າຍໂດຍ:**
ໂຮງງານຜະລິດຢາເລກ 2 ວຽງຈັນ
ຕູ້ ປ.ນ 2580, ຖະໜົນລາວໄທ, ໂສກປ່າໝວງ, ນະຄອນຫຼວງວຽງຈັນ, ສປປ ລາວ.
ໂທ: (856-21) 315 293, 351 586, 030 526 4122.
ແຟກ: (856-21) 314 722, 263 246, 351 866.

## FULL PRESCRIBING INFORMATION

**1 INDICATIONS AND USAGE**
**1.1 Mantle Cell Lymphoma**
PHOACA is indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.
This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.
**1.2 Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma**
PHOACA is indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

**2 DOSAGE AND ADMINISTRATION**
**2.1Recommended Dosage**
PHOACA as Monotherapy
For patients with MCL, CLL, or SLL, the recommended dose of PHOACA is 100 mg taken orally approximately every 12 hours until disease progression or unacceptable toxicity.
PHOACA in Combination with Obinutuzumab
For patients with previously untreated CLL or SLL, the recommended dose of PHOACA is 100 mg taken orally approximately every 12 hours until disease progression or unacceptable toxicity. Start PHOACA at Cycle 1 (each cycle is 28 days). Start obinutuzumab at Cycle 2 for a total of 6 cycles and refer to the obinutuzumab prescribing information for recommended dosing. Administer PHOACA prior to obinutuzumab when given on the same day.
Advise patients to swallow capsule whole with water. Advise patients not to open, break or chew the capsules. PHOACA may be taken with or without food. If a dose of PHOACA is missed by more than 3 hours, it should be skipped and the next dose should be taken at its regularly scheduled time. Extra capsules of PHOACA should not be taken to make up for a missed dose.
**2.2Recommended Dosage for Hepatic Impairment**
Avoid administration of PHOACA in patients with severe hepatic impairment.
Dose modifications are not required for patients with mild or moderate hepatic impairment.
**2.3Recommended Dosage for Drug Interactions**
Dose Modifications for Use with CYP3A Inhibitors or Inducers
These are described in Table 1.

**Table 1. Recommended Dose Reductions for PHODABRA for Adverse Reactions**

| CYP3A | Co-administered Drug | Recommended PHOACA use |
|---|---|---|
| Inhibition | Strong CYP3A inhibitor | Avoid concomitant use.<br>If these inhibitors will be used short-term (such as anti-infectives for up to seven days), interrupt PHOACA. |
| | Moderate CYP3A inhibitor | 100 mg once daily. |
| Induction | Strong CYP3A inducer | Avoid concomitant use.<br>If these inducers cannot be avoided, increase PHOACA dose to 200 mg approximately every 12 hours. |

Concomitant Use with Gastric Acid Reducing Agents
*Proton Pump Inhibitors:* Avoid concomitant use.
*H2-Receptor Antagonists:* Take PHOACA 2 hours before taking a H2-receptor antagonist.
Antacids: Separate dosing by at least 2 hours.
**2.4Dose Modifications for Adverse Reactions**
Recommended dose modifications of PHOACA for Grade 3 or greater adverse reactions are provided in Table 2.

**Table 2: Recommended Dose Modifications for Adverse Reactions**

| Event | Adverse Reaction Occurrence | Dose Modification (Starting dose = 100 mg approximately every 12 hours) |
|---|---|---|
| Grade 3 or greater non-hematologic toxicities,<br>Grade 3 thrombocytopenia with bleeding,<br>Grade 4 thrombocytopenia | First and Second | Interrupt PHOACA.<br>Once toxicity has resolved to Grade 1 or baseline level, PHOACA may be resumed at 100 mg approximately every 12 hours. |
| **Event** | **Adverse Reaction Occurrence** | **Dose Modification** (Starting dose = 100 mg approximately every 12 hours) |
| or<br>Grade 4 neutropenia lasting longer than 7 days | Third | Interrupt PHOACA.<br>Once toxicity has resolved to Grade 1 or baseline level, PHOACA may be resumed at a reduced frequency of 100 mg once daily. |
| | Fourth | Discontinue PHOACA. |

Adverse reactions graded by the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE).
Refer to the obinutuzumab prescribing information for management of obinutuzumab toxicities.

**3 DOSAGE FORMS AND STRENGTHS**
100 mg capsules.

**4 CONTRAINDICATIONS**
None.

**5 WARNINGS AND PRECAUTIONS**
**5.1Serious and Opportunistic Infections**
Fatal and serious infections, including opportunistic infections, have occurred in patients with hematologic malignancies treated with PHOACA.
Serious or Grade 3 or higher infections (bacterial, viral, or fungal) occurred in 19% of 1029 patients exposed to PHOACA in clinical trials, most often due to respiratory tract infections (11% of all patients, including pneumonia in 6%). These infections predominantly occurred in the absence of Grade 3 or 4

neutropenia, with neutropenic infection reported in 1.9% of all patients. Opportunistic infections in recipients of PHOACA have included, but are not limited to, hepatitis B virus reactivation, fungal pneumonia, *Pneumocystis jiroveci* pneumonia, Epstein-Barr virus reactivation, cytomegalovirus, and progressive multifocal leukoencephalopathy (PML). Consider prophylaxis in patients who are at increased risk for opportunistic infections. Monitor patients for signs and symptoms of infection and treat promptly.

**5.2Hemorrhage**

Fatal and serious hemorrhagic events have occurred in patients with hematologic malignancies treated with PHOACA. Major hemorrhage (serious or Grade 3 or higher bleeding or any central nervous system bleeding) occurred in 3.0% of patients, with fatal hemorrhage occurring in 0.1% of 1029 patients exposed to PHOACA in clinical trials. Bleeding events of any grade, excluding bruising and petechiae, occurred in 22% of patients.

Use of antithrombotic agents concomitantly with PHOACA may further increase the risk of hemorrhage. In clinical trials, major hemorrhage occurred in 2.7% of patients taking PHOACA without antithrombotic agents and 3.6% of patients taking PHOACA with antithrombotic agents. Consider the risks and benefits of antithrombotic agents when co-administered with PHOACA. Monitor patients for signs of bleeding. Consider the benefit-risk of withholding PHOACA for 3-7 days pre- and post-surgery depending upon the type of surgery and the risk of bleeding.

**5.3Cytopenias**

Grade 3 or 4 cytopenias, including neutropenia (23%), anemia (8%), thrombocytopenia (7%), and lymphopenia (7%), developed in patients with hematologic malignancies treated with PHOACA. Grade 4 neutropenia developed in 12% of patients. Monitor complete blood counts regularly during treatment. Interrupt treatment, reduce the dose, or discontinue treatment as warranted.

**5.4Second Primary Malignancies**

Second primary malignancies, including skin cancers and other solid tumors, occurred in 12% of 1029 patients exposed to PHOACA in clinical trials. The most frequent second primary malignancy was skin cancer, reported in 6% of patients. Monitor patients for skin cancers and advise protection from sun exposure.

**5.5Atrial Fibrillation and Flutter**

Grade 3 atrial fibrillation or flutter occurred in 1.1% of 1029 patients treated with PHOACA, with all grades of atrial fibrillation or flutter reported in 4.1% of all patients. The risk may be increased in patients with cardiac risk factors, hypertension, previous arrhythmias, and acute infection. Monitor for symptoms of arrhythmia (e.g., palpitations, dizziness, syncope, dyspnea) and manage as appropriate.

## 6 ADVERSE REACTIONS

The following clinically significant adverse reactions are discussed in greater detail in other sections of the labeling:

Serious and Opportunistic Infections
Hemorrhage
Cytopenias
Second Primary Malignancies
Atrial Fibrillation and Flutter

## 7 DRUG INTERACTIONS

| | | |
|---|---|---|
| Strong CYP3A Inhibitors | | |
| *Clinical Impact* | Co-administration of PHOACA with a strong CYP3A inhibitor (itraconazole) increased acalabrutinib plasma concentrations. Increased acalabrutinib concentrations may result in increased toxicity. | |
| *Prevention or Management* | Avoid co-administration of strong CYP3A inhibitors with PHOACA. Alternatively, if the inhibitor will be used short-term, interrupt PHOACA. | |
| Moderate CYP3A Inhibitors | | |
| *Clinical Impact* | Co-administration of PHOACA with a moderate CYP3A inhibitor may increase acalabrutinib plasma concentrations. Increased acalabrutinib concentrations may result in increased toxicity. | |
| *Prevention or Management* | When PHOACA is co-administered with moderate CYP3A inhibitors, reduce acalabrutinib dose to 100 mg once daily. | |
| Strong CYP3A Inducers | | |
| *Clinical Impact* | Co-administration of PHOACA with a strong CYP3A inducer (rifampin) decreased acalabrutinib plasma concentrations. Decreased acalabrutinib concentrations may reduce PHOACA activity. | |
| *Prevention or Management* | Avoid co-administration of strong CYP3A inducers with PHOACA. If a strong CYP3A inducer cannot be avoided, increase the acalabrutinib dose to 200 mg approximately every 12 hours. | |
| Gastric Acid Reducing Agents | | |
| *Clinical Impact* | Co-administration of PHOACA with a proton pump inhibitor, H2-receptor antagonist, or antacid may decrease acalabrutinib plasma concentrations. Decreased acalabrutinib concentrations may reduce PHOACA activity. If treatment with a gastric acid reducing agent is required, consider using a H2- receptor antagonist (e.g., ranitidine or famotidine) or an antacid (e.g., calcium carbonate). | |
| *Prevention or Management* | Antacids | Separate dosing by at least 2 hours. |
| | H2-receptor antagonists | Take PHOACA 2 hours before taking the H2-receptor antagonist. |
| | Proton pump inhibitors | Avoid co-administration. Due to the long-lasting effect of proton pump inhibitors, separation of doses may not eliminate the interaction with PHOACA. |

## 8 USE IN SPECIFIC POPULATIONS

**8.1Pregnancy**

Risk Summary

Based on findings in animals, PHOACA may cause fetal harm and dystocia when administered to a pregnant woman. There are no available data in pregnant women to inform the drug-associated risk. In animal reproduction studies, administration of acalabrutinib to animals during organogenesis resulted in dystocia in rats and reduced fetal growth in rabbits at maternal exposures (AUC) 2 times exposures in patients at the recommended dose of 100 mg approximately every 12 hours (*see Data*). Advise pregnant women of the potential risk to a fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

**8.2Lactation**

Risk Summary

No data are available regarding the presence of acalabrutinib or its active metabolite in human milk, its effects on the breastfed child, or on milk production. Acalabrutinib and its active metabolite were present in the milk of lactating rats. Due to the potential for adverse reactions in a breastfed child from PHOACA, advise lactating women not to breastfeed while taking PHOACA and for at least 2 weeks after the final dose.

**8.3Females and Males of Reproductive Potential**

Pregnancy

Pregnancy testing is recommended for females of reproductive potential prior to initiating PHOACA therapy. Contraception

*Females*

PHOACA may cause embryo-fetal harm and dystocia when administered to pregnant women. Advise female patients of reproductive potential to use effective contraception during treatment with PHOACA and for at least 1 week following the last dose of PHOACA. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be informed of the potential hazard to a fetus.

**8.4Pediatric Use**

The safety and efficacy of PHOACA in pediatric patients have not been established.

**8.5Geriatric Use**

Of the 929 patients with CLL or MCL in clinical trials of PHOACA, 68% were 65 years of age or older, and 24% were 75 years of age or older. Among patients 65 years of age or older, 59% had Grade 3 or higher adverse reactions and 39% had serious adverse reactions. Among patients younger than age 65, 45% had Grade 3 or higher adverse reactions and 25% had serious adverse reactions. No clinically relevant differences in efficacy were observed between patients ≥ 65 years and younger.

**8.6Hepatic Impairment**

Avoid administration of PHOACA in patients with severe hepatic impairment. The safety of PHOACA has not been evaluated in patients with moderate or severe hepatic impairment.

## 9 HOW SUPPLIED/STORAGE AND HANDLING

HDPE bottle packaging , 60 capsules/bottle.

Storage

Store at 20°C-25°C (68°F-77°F); excursions permitted to 15°C-30°C (59°F-86°F)

## 10 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Serious and Opportunistic Infections

Inform patients of the possibility of serious infection and to report signs or symptoms suggestive of infection.

Hemorrhage

Inform patients to report signs or symptoms of bleeding. Inform patients that PHOACA may need to be interrupted for major surgeries.

Cytopenias

Inform patients that they will need periodic blood tests to check blood counts during treatment with PHOACA.

Second Primary Malignancies

Inform patients that other malignancies have been reported in patients who have been treated with PHOACA, including skin cancer and other solid tumors. Advise patients to use sun protection.

Atrial Fibrillation and Flutter

Counsel patients to report any signs of palpitations, dizziness, fainting, chest discomfort, and shortness of breath.

Pregnancy Complication

PHOACA may cause fetal harm and dystocia. Advise women to avoid becoming pregnant during treatment and for at least 1 week after the last dose of PHOACA.

Lactation

Advise females not to breastfeed during treatment with PHOACA and for at least 2 weeks after the final dose.

Dosing Instructions

Instruct patients to take PHOACA orally twice daily, about 12 hours apart. PHOACA may be taken with or without food. Advise patients that PHOACA capsules should be swallowed whole with a glass of water, without being opened, broken, or chewed.

Missed Dose

Advise patients that if they miss a dose of PHOACA, they may still take it up to 3 hours after the time they would normally take it. If more than 3 hours have elapsed, they should be instructed to skip that dose and take their next dose of PHOACA at the usual time. Warn patients they should not take extra capsules to make up for the dose that they missed.

Drug Interactions

Advise patients to inform their healthcare providers of all concomitant medications, including over-the-counter medications, vitamins and herbal products.