ໃບຕົ້ວ 25
PHOLORLA 25

ສ່ວນປະກອບ:
ໃນ 1 ເມັດ ປະກອບດ້ວຍ Lorlatinib 25 mg.

ຂໍ້ບ່ຽວຄຸມ:
ໃຊ້ປິ່ນປົວ ມະເຮັ້ງປອດ ທີ່ບໍ່ແມ່ນເຊວຂະໜາດນ້ອຍ (NSCLC) ທີ່ເປັນ ALK-Positive.

ຂະໜາດ, ວິທີໃຊ້ ແລະ ຄຳເຕືອນ:
-ປະລິມານປະຈຳວັນທີ່ແນະນຳແມ່ນ ວັນລະ 1 ຄັ້ງ, ຄັ້ງລະ 4 ເມັດ. ສາມາດກິນຮ່ວມ ຫຼື ບໍ່ຮ່ວມກັບອາຫານກໍ່ໄດ້, ແຕ່ຄວນກິນໃນເວລາດຽວກັນຂອງທຸກໆວັນ;
-ຫ້າມຫຍໍ້, ບິດ ຫຼື ຫ້າມເມັດຢາ.

ຜົນຂ້າງຄຽງເມື່ອໃຊ້ຢາ:
ໃນເວລາໃຊ້ຢາ ຈະພົບເຫັນອາການດັ່ງລຸ່ມນີ້:
-ແຂບ, ມື, ຂາ ຫຼື ຕີນ ມີອາການບວມ;
-ນ້ຳໜັກເພີ່ມຂຶ້ນ;
-ມີອາການເມື່ອຍລ້າ, ອ່ອນເພຍ;
-ຖອກທ້ອງ;
-ປວດຂໍ້.

ຂະໜາດການປັບຈຸ:
ປັບຈຸໃນຂວດຜລາສຕິກ ຈຳນວນ 30 ເມັດ, ໃສ່ໃນກັບເຈ້ຍ ກັບລະ 1 ຂວດ.

ການເກັບຮັກສາ:
ເກັບມ້ຽນປ່ອນແຫ້ງບ່ໍມີແສງແດດສ່ອງເຖິງ ແລະ ໃນອຸນຫະພູມ 15-30 ອົງສາ, ເກັບໄວ້ໃນທີ່ຫ່າງໄກຈາກມືເດັກນ້ອຍ.

ຜະລິດ ແລະ ຈຳໜ່າຍໂດຍ:
ໂຮງງານຜະລິດຢາເລກ 2 ວຽງຈັນ
ຕຸ້ ປ.ນ 2580, ຖະໜົນລາວໄທ, ໂສກປ່າຫຼວງ, 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
PHOLORLA® is indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) whose disease has progressed on
- crizotinib and at least one other ALK inhibitor for metastatic disease; or
- alectinib as the first ALK inhibitor therapy for metastatic disease; or
- ceritinib as the first ALK inhibitor therapy for metastatic disease.

This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

2 DOSAGE AND ADMINISTRATION
2.1Recommended Dosage
The recommended dosage of PHOLORLA is 100 mg orally once daily, with or without food, until disease progression or unacceptable toxicity.
Swallow tablets whole. Do not chew, crush or split tablets. Do not ingest if tablets are broken, cracked, or otherwise not intact.
Take PHOLORLA at the same time each day. If a dose is missed, then take the missed dose unless the next dose is due within 4 hours. Do not take 2 doses at the same time to make up for a missed dose.
Do not take an additional dose if vomiting occurs after PHOLORLA but continue with the next scheduled dose.
2.2Dosage Modifications for Adverse Reactions
The recommended dose reductions are:
- First dose reduction: PHOLORLA 75 mg orally once daily
- Second dose reduction: PHOLORLA 50 mg orally once daily

Permanently discontinue PHOLORLA in patients who are unable to tolerate 50 mg orally once daily.
Dosage modifications for adverse reactions of PHOLORLA are provided in Table 1.

Table 1 Recommended PHOLORLA Dosage Modifications for Adverse Reactions

Adverse Reaction[a]	Dosage Modifications
Central Nervous System Effects	
Grade 1	Continue at the same dose or withhold the dose until recovery to baseline. Resume PHOLORLA at the same dose or at a reduced dose.
Grade 2 OR Grade 3	Withhold dose until Grade 0 or 1. Resume PHOLORLA at a reduced dose.
Grade 4	Permanently discontinue PHOLORLA.
Hyperlipidemia	
Grade 4 hypercholesterolemia OR Grade 4 hypertriglyceridemia	Withhold PHOLORLA until recovery of hypercholesterolemia and/or hypertriglyceridemia to less than or equal to Grade 2. Resume PHOLORLA at the same dose. If severe hypercholesterolemia and/or hypertriglyceridemia recurs, resume PHOLORLA at a reduced dose.
Atrioventricular (AV) Block	
Second-degree AV block	Withhold PHOLORLA until PR interval is less than 200 ms. Resume PHOLORLA at a reduced dose.
First occurrence of complete AV block	Withhold PHOLORLA until • pacemaker placed OR • PR interval less than 200 ms. If a pacemaker is placed, resume PHOLORLA at the same dose. If no pacemaker is placed, resume PHOLORLA at a reduced dose.
Recurrent complete AV block	Place pacemaker or permanently discontinue PHOLORLA.
Interstitial Lung Disease (ILD)/Pneumonitis	
Any Grade treatment–related ILD/Pneumonitis	Permanently discontinue PHOLORLA.
Other Adverse Reactions	
Grade 1 OR Grade 2	Continue PHOLORLA at same dose or reduced dose.
Grade 3 OR Grade 4	Withhold PHOLORLA until symptoms resolve to less than or equal to Grade 2 or baseline. Resume PHOLORLA at reduced dose.

Abbreviation: AV=atrioventricular.
[a]Grade based on National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

2.3Concomitant Use of Strong or Moderate CYP3A Inducers
PHOLORLA is contraindicated in patients taking strong CYP3A inducers. Discontinue strong CYP3A inducers for 3 plasma half-lives of the strong CYP3A inducer prior to initiating PHOLORLA. Avoid concomitant use of PHOLORLA with moderate CYP3A inducers.
2.4Dosage Modification for Strong CYP3A Inhibitors
Avoid concomitant use of PHOLORLA with strong CYP3A inhibitors. If concomitant use with a strong CYP3A inhibitor cannot be avoided, reduce the starting dose of PHOLORLA from 100 mg orally once daily to 75 mg orally once daily. In patients who have had a dose reduction to 75 mg orally once daily due to adverse reactions and who initiate a strong CYP3A inhibitor, reduce the PHOLORLA dose to 50 mg orally once daily.
If concomitant use of a strong CYP3A inhibitor is discontinued, increase the PHOLORLA dose (after 3 plasma half-lives of the strong CYP3A inhibitor) to the dose that was used before starting the strong inhibitor.

3 DOSAGE FORMS AND STRENGTHS
Tablets:
- 25 mg: round, film-coated
- 100 mg: oval, film-coated

4 CONTRAINDICATIONS
PHOLORLA is contraindicated in patients taking strong CYP3A inducers, due to the potential for serious hepatotoxicity.

5 WARNINGS AND PRECAUTIONS
5.1Risk of Serious Hepatotoxicity with Concomitant Use of Strong CYP3A Inducers
Severe hepatotoxicity occurred in 10 of 12 healthy subjects receiving a single dose of PHOLORLA with multiple daily doses of rifampin, a strong CYP3A inducer. Grade 4 alanine aminotransferase (ALT) or aspartate aminotransferase (AST) elevations occurred in 50% of subjects, Grade 3 ALT or AST elevations occurred in 33% and Grade 2 ALT or AST elevations occurred in 8%. ALT or AST elevations occurred within 3 days and returned to within normal limits after a median of 15 days (7 to 34 days); the median time to recovery was
18 days in subjects with Grade 3 or 4 ALT or AST elevations and 7 days in subjects with Grade 2 ALT or AST elevations.
PHOLORLA is contraindicated in patients taking strong CYP3A inducers. Discontinue strong CYP3A inducers for 3 plasma half-lives of the strong CYP3A inducer prior to initiating PHOLORLA.
Avoid concomitant use of PHOLORLA with moderate CYP3A inducers. If concomitant use of moderate CYP3A inducers cannot be avoided, monitor AST, ALT, and bilirubin 48 hours after initiating PHOLORLA and at least 3 times during the first week after initiating PHOLORLA.
Depending upon the relative importance of each drug, discontinue PHOLORLA or the CYP3A inducer for persistent Grade 2 or higher hepatotoxicity.
5.2Central Nervous System Effects
A broad spectrum of central nervous system (CNS) effects can occur in patients receiving PHOLORLA. These include seizures, hallucinations, and changes in cognitive function, mood (including suicidal ideation), speech, mental status, and sleep. Overall, CNS effects occurred in 54% of patients receiving PHOLORLA. Cognitive effects occurred in 29% of the 332 patients who received PHOLORLA at any dose in Study B7461001; 2.1% of these events were severe (Grade 3 or 4). Mood effects occurred in 24% of patients; 1.8% of these events were severe. Speech effects occurred in 14% of patients; 0.3% of these events were severe. Hallucinations occurred in 7% of patients; 0.6% of these events were severe. Mental status changes occurred in 2.1% of patients; 1.8% of these events were severe. Seizures occurred in 3% of patients, sometimes in conjunction with other neurologic findings. Sleep effects occurred in 10% of patients. The median time to first onset of any CNS effect was 1.2 months (1 day to 1.7 years). Overall, 1.5% of patients required permanent discontinuation of PHOLORLA for a CNS effect; 9% required temporary discontinuation and 8% required dose reduction.
Withhold and resume at the same dose or at a reduced dose or permanently discontinue PHOLORLA based on severity.
5.3Hyperlipidemia
Increases in serum cholesterol and triglycerides can occur in patients receiving PHOLORLA. Grade 3 or 4 elevations in total cholesterol occurred in 17% and Grade 3 or 4 elevations in triglycerides occurred in 17% of the 332 patients who received PHOLORLA in Study B7461001. The median time to onset was 15 days for both hypercholesterolemia and hypertriglyceridemia. Approximately 7% of patients required temporary discontinuation and 3% of patients required dose reduction of PHOLORLA for elevations in cholesterol and in triglycerides. Eighty percent of patients required initiation of lipid-lowering medications, with a median time to onset of start of such medications of 21 days.
Initiate or increase the dose of lipid-lowering agents in patients with hyperlipidemia. Monitor serum cholesterol and triglycerides before initiating PHOLORLA, 1 and 2 months after initiating PHOLORLA, and periodically thereafter. Withhold and resume at the same dose for the first occurrence; resume at the same or a reduced dose of PHOLORLA for recurrence based on severity.
5.4Atrioventricular Block
PR interval prolongation and atrioventricular (AV) block can occur in patients receiving PHOLORLA. In 295 patients who received PHOLORLA at a dose of 100 mg orally once daily in Study B7461001 and who had a baseline electrocardiography (ECG), 1% experienced AV block and 0.3% experienced Grade 3 AV block and underwent pacemaker placement.
Monitor ECG prior to initiating PHOLORLA and periodically thereafter. Withhold and resume at a reduced dose or at the same dose in patients who undergo pacemaker placement. Permanently discontinue for recurrence in patients without a pacemaker.
5.5Interstitial Lung Disease/Pneumonitis
Severe or life-threatening pulmonary adverse reactions consistent with interstitial lung disease (ILD)/pneumonitis can occur with PHOLORLA. ILD/pneumonitis occurred in 1.5% of patients who received
PHOLORLA at any dose in Study B7461001, including Grade 3 or 4 ILD/pneumonitis in 1.2% of patients. One patient (0.3%) discontinued PHOLORLA for ILD/pneumonitis.
Promptly investigate for ILD/pneumonitis in any patient who presents with worsening of respiratory symptoms indicative of ILD/pneumonitis (e.g., dyspnea, cough, and fever). Immediately withhold PHOLORLA in patients with suspected ILD/pneumonitis. Permanently discontinue PHOLORLA for treatment-related ILD/pneumonitis of any severity.
5.6Embryo-Fetal Toxicity
Based on findings from animal studies and its mechanism of action, PHOLORLA can cause fetal harm when administered to a pregnant woman. Administration of lorlatinib to pregnant rats and rabbits by oral gavage during the period of organogenesis resulted in malformations, increased post-implantation loss, and abortion at maternal exposures that were equal to or less than the human exposure at the recommended dose of 100 mg once daily based on area under the curve (AUC).
Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use an effective non-hormonal method of contraception, since PHOLORLA can render hormonal contraceptives ineffective, during treatment with PHOLORLA and for at least 6 months after the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with PHOLORLA and for 3 months after the final dose.

6 ADVERSE REACTIONS

The following adverse reactions are described elsewhere in the labeling:

- Risk of Serious Hepatotoxicity with Concomitant Use of Strong CYP3A Inducers
- Central Nervous System Effects
- Hyperlipidemia
- Atrioventricular Block
- Interstitial Lung Disease/Pneumonitis

7 DRUG INTERACTIONS

7.1 Effect of Other Drugs on PHOLORLA

Effect of CYP3A Inducers

Concomitant use of PHOLORLA with a strong CYP3A inducer decreased lorlatinib plasma concentrations, which may decrease the efficacy of PHOLORLA. The effect of concomitant use of PHOLORLA with a moderate CYP3A inducer on lorlatinib plasma concentrations has not been studied.

Severe hepatotoxicity occurred in healthy subjects receiving PHOLORLA with rifampin, a strong CYP3A inducer. In 12 healthy subjects receiving a single 100 mg dose of PHOLORLA with multiple daily doses of rifampin, Grade 3 or 4 increases in ALT or AST occurred in 83% of subjects and Grade 2 increases in ALT or AST occurred in 8%. A possible mechanism for hepatotoxicity is through activation of the pregnane X receptor (PXR) by PHOLORLA and rifampin, which are both PXR agonists. The risk of hepatotoxicity with concomitant use of PHOLORLA and moderate CYP3A inducers that are also PXR agonists is unknown.

PHOLORLA is contraindicated in patients taking strong CYP3A inducers. Discontinue strong CYP3A inducers for 3 plasma half-lives of the strong CYP3A inducer prior to initiating PHOLORLA.

Avoid concomitant use of PHOLORLA with moderate CYP3A inducers. If concomitant use of moderate CYP3A inducers cannot be avoided, monitor ALT, AST, and bilirubin as recommended.

Effect of Strong CYP3A Inhibitors

Concomitant use with a strong CYP3A inhibitor increased lorlatinib plasma concentrations, which may increase the incidence and severity of adverse reactions of PHOLORLA. Avoid the concomitant use of PHOLORLA with a strong CYP3A inhibitor. If concomitant use cannot be avoided, reduce PHOLORLA dose as recommended.

7.2 Effect of PHOLORLA on Other Drugs

CYP3A Substrates

Concomitant use of PHOLORLA decreases the concentration of CYP3A substrates, which may reduce the efficacy of these substrates. PHOLORLA is considered a moderate CYP3A inducer. Avoid concomitant use of PHOLORLA with CYP3A substrates, for which minimal concentration changes may lead to serious therapeutic failures. If concomitant use is unavoidable, increase the CYP3A substrate dosage in accordance with approved product labeling.

P-glycoprotein (P-gp) Substrates

Concomitant use of PHOLORLA decreases the concentration of P-gp substrates, which may reduce the efficacy of these substrates. PHOLORLA is considered a moderate P-gp inducer. Avoid concomitant use of PHOLORLA with P-gp substrates for which minimal concentration changes may lead to serious therapeutic failures. If concomitant use is unavoidable, increase the P-gp substrate dosage in accordance with approved product labeling.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on findings from animal studies and its mechanism of action, PHOLORLA can cause embryo-fetal harm when administered to a pregnant woman. There are no available data on PHOLORLA use in pregnant women. Administration of lorlatinib to pregnant rats and rabbits by oral gavage during the period of organogenesis resulted in malformations, increased post-implantation loss, and abortion at maternal exposures that were equal to or less than the human exposure at the recommended dose of 100 mg once daily based on AUC (see Data). Advise a pregnant woman of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies are 2 to 4% and 15 to 20%, respectively.

8.2 Lactation

Risk Summary

There are no data on the presence of lorlatinib or its metabolites in either human or animal milk or its effects on the breastfed infant or on milk production. Because of the potential for serious adverse reactions in breastfed infants, instruct women not to breastfeed during treatment with PHOLORLA and for 7 days after the final dose.

8.3 Females and Males of Reproductive Potential

Pregnancy Testing

Verify pregnancy status in females of reproductive potential prior to initiating PHOLORLA.

Contraception

PHOLORLA can cause embryo-fetal harm when administered to a pregnant woman.

Females

Advise female patients of reproductive potential to use effective non-hormonal contraception during treatment with PHOLORLA and for at least 6 months after the final dose. Advise females of reproductive potential to use a non-hormonal method of contraception, because PHOLORLA can render hormonal contraceptives ineffective.

Males

Based on genotoxicity findings, advise males with female partners of reproductive potential to use effective contraception during treatment with PHOLORLA and for at least 3 months after the final dose.

Infertility

Males

Based on findings from animal studies, PHOLORLA may transiently impair male fertility.

8.4 Pediatric Use

The safety and effectiveness of PHOLORLA in pediatric patients have not been established.

8.5 Geriatric Use

Of the 295 patients in Study B7461001 who received 100 mg PHOLORLA orally once daily, 18% of patients were aged 65 years or older. Although data are limited, no clinically important differences in safety or efficacy were observed between patients aged 65 years or older and younger patients.

8.6 Hepatic Impairment

No dose adjustment is recommended for patients with mild hepatic impairment (total bilirubin ≤ upper limit of normal [ULN] with AST > ULN or total bilirubin >1 to 1.5 × ULN with any AST). The recommended dose of PHOLORLA has not been established for patients with moderate or severe hepatic impairment.Renal Impairment

No dose adjustment is recommended for patients with mild or moderate renal impairment (creatinine clearance [CLcr] 30 to 89 mL/min estimated by Cockcroft-Gault). The recommended dose of PHOLORLA has not been established for patients with severe renal impairment.

9 HOW SUPPLIED/STORAGE AND HANDLING

25mg and 100mg tablets are supplied as:

HDPE bottle packaging ,30tablets/bottle.

Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

10 PATIENT COUNSELING INFORMATION

Risk of Serious Hepatotoxicity with Concomitant Use of Strong CYP3A Inducers

Inform patients of the potential risk of hepatoxicity with the concomitant use of strong CYP3A inducers.

Advise patients to inform their healthcare providers of all medications they are taking, including prescription medicines, over-the-counter drugs, vitamins, and herbal products (e.g,. St. John's wort).

Central Nervous System (CNS) Effects

Advise patients to notify their healthcare provider if they experience new or worsening CNS symptoms.

Hyperlipidemia

Inform patients that serum cholesterol and triglycerides will be monitored during treatment. Advise patients that initiation or an increase in the dose of lipid-lowering agents may be required.

Atrioventricular (AV) Block

Inform patients of the risks of AV block. Advise patients to contact their healthcare provider immediately to report new or worsening cardiac symptoms.

Interstitial Lung Disease (ILD)/Pneumonitis

Inform patients of the risks of severe ILD/pneumonitis. Advise patients to contact their healthcare provider immediately to report new or worsening respiratory symptoms.

Embryo-Fetal Toxicity

Advise females of reproductive potential of the potential risk to a fetus. Advise females to inform their healthcare provider of a known or suspected pregnancy.

Advise females of reproductive potential to use effective non-hormonal contraception during treatment with PHOLORLA and for at least 6 months after the final dose.

Advise male patients with female partners of reproductive potential to use effective contraception during treatment with PHOLORLA and for at least 3 months after the final dose.

Lactation

Advise women not to breastfeed during treatment with PHOLORLA and for 7 days after the final dose.

Infertility

Advise males of reproductive potential that PHOLORLA may transiently impair fertility.

PATIENT INFORMATION
PHOLORLA (lor-BREN-ah)
(lorlatinib)
tablets

What is the most important information I should know about PHOLORLA?
PHOLORLA may cause serious side effects, including:

- **Liver problems due to interactions with other medicines.** It is important to know what medicines should not be taken with PHOLORLA.
- **Problems with brain (central nervous system [CNS]) function.** Many patients experienced problems with brain function including problems with thinking (such as forgetfulness or confusion), mood (such as depression), speech, seeing or hearing things that are not real (hallucinations), and seizures during treatment with PHOLORLA. In some patients, these problems are severe and your healthcare provider may need to have you stop taking PHOLORLA.
- **Increases in the cholesterol and triglycerides (lipid) levels in your blood.** Most patients will have an increase in the lipid levels in your blood during treatment with PHOLORLA.
  - If you have increases in the lipid levels in your blood during treatment with PHOLORLA, your healthcare provider may need to start you on a medicine to lower the levels. If you are already taking a medicine to lower the lipid levels in your blood, your healthcare provider may need to increase your dose of that medicine.
  - Your healthcare provider should do blood tests to check the lipid levels in your blood before starting treatment, 1 to 2 months after starting treatment, and during treatment with PHOLORLA.
- **Heart problems.** PHOLORLA may cause very slow or abnormal heartbeats. Your healthcare provider should check your heart rhythm (electrocardiogram [EKG]) before starting and during treatment with PHOLORLA. Tell your healthcare provider right away if you feel dizzy or faint or have abnormal heartbeats. In some patients, these problems are severe and your healthcare provider may need to have you stop taking PHOLORLA or have a pacemaker placed.
- **Lung problems.** PHOLORLA may cause severe or life-threatening swelling (inflammation) of the lungs during treatment that can lead to death. Symptoms may be similar to those from lung cancer. Tell your healthcare provider right away if you have any new or worsening symptoms of lung problems, including trouble breathing, shortness of breath, cough, or fever.

In some patients, these problems are severe and your healthcare provider may need to have you stop taking PHOLORLA. **See "What are possible side effects of PHOLORLA?" for more information about side effects.**

What is PHOLORLA?

PHOLORLA is a prescription medicine that is used to treat people with non-small cell lung cancer (NSCLC)

- that is caused by an abnormal anaplastic lymphoma kinase (ALK) gene **and,**
- that has spread to other parts of your body **and,**
- who have taken the medicine alectinib or ceritinib or who have taken both the medicine crizotinib and at least 1 other medicine to treat NSCLC that is caused by the ALK gene, **and**
- their NSCLC is no longer responding to these treatments. It is not known if PHOLORLA is safe and effective in children.

Do not take PHOLORLA if you take certain other medicines called strong CYP3A inducers. Ask your healthcare provider for a list of these medicines if you are not sure.

Before taking PHOLORLA, tell your healthcare provider about all of your medical conditions, including if you:

- are taking other medications
- have had episodes of depression or seizures
- have high levels of cholesterol or triglycerides in your blood
- have problems with your heart beat
- have lung or breathing problems
- are pregnant or plan to become pregnant. PHOLORLA can harm your unborn baby.
  - Your healthcare provider will do a pregnancy test before you start treatment with PHOLORLA.
  - oTell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with PHOLORLA.
- are breastfeeding or plan to breastfeed. It is not known if PHOTRAME passes into your breast milk.
  - Do not breastfeed during treatment and for 4 months after your last dose of PHOTRAME. Talk to your healthcare provider about the best way to feed your baby during this time.

—Females who are able to become pregnant should use effective non-hormonal birth control during treatment with PHOLORLA and for at least 6 months after the final dose of PHOLORLA. Birth control pills (oral contraceptives) and other hormonal forms of birth control may not be effective if used during treatment with PHOLORLA. Talk to your healthcare provider about birth control choices that are right for you during this time.

—Males who have female partners who are able to become pregnant should use effective birth control during treatment with PHOLORLA and for at least 3 months after the final dose of PHOLORLA.

- are breastfeeding or plan to breastfeed. It is not known if PHOLORLA passes into your breast milk. Do not breastfeed during treatment with PHOLORLA and for 7 days after the final dose. Talk to your healthcare provider about the best way to feed your baby during this time.

Tell your healthcare provider about all the medicines you take, including prescription medicines, over-the-counter medicines, vitamins, and herbal supplements.

How should I take PHOLORLA?

- Take PHOLORLA exactly as your healthcare provider tells you to take it. Do not change your dose or stop taking PHOLORLA unless your healthcare provider tells you to.
- Your healthcare provider may change your dose, temporarily stop, or permanently stop treatment with PHOLORLA if you develop side effects.
- Swallow PHOLORLA tablets whole. Do not chew, crush, or split PHOLORLA tablets. Do not take PHOLORLA tablets if they are broken, cracked, or not intact.
- Take PHOLORLA at approximately the same time each day.
- You may take PHOLORLA with or without food.
- If you miss a dose, take it as soon as you remember. However, if it is close to the time of your next dose (within 4 hours), just take your next dose at your regular time.
- If you vomit after taking a dose of PHOLORLA, do not take an extra dose. Take your next dose at your regular time.

What are the possible side effects of PHOLORLA?

- **See "What is the most important information I should know about PHOLORLA?"**

The most common side effects of PHOLORLA include:

- swelling in your arms, legs, hands and feet (edema)
- numbness and tingling feeling in your joints or arms and legs (peripheral neuropathy)
- difficulty thinking or confusion
- difficulty breathing
- tiredness (fatigue)
- weight gain
- pain in your joints
- changes in mood, feeling sad or anxious
- diarrhea

PHOLORLA may cause decreased fertility in males. In males, this could affect your ability to father a child. Talk to your healthcare provider if you have concerns about fertility.

These are not all of the possible side effects of PHOLORLA. For more information, ask your healthcare provider or pharmacist.

Call your healthcare provider for medical advice about side effects.

How should I store PHOLORLA?

- Store PHOLORLA at room temperature between 68°F to 77°F (20°C to 25°C).

Keep PHOLORLA and all medicines out of the reach of children.

General information about the safe and effective use of PHOLORLA

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use PHOLORLA for a condition for which it was not prescribed. Do not give PHOLORLA to other people, even if they have the same symptoms that you have. It may harm them. You can ask your healthcare provider or pharmacist for more information about PHOLORLA that is written for health professionals.