LINPARIB® (OLAPARIB) F. C. TABLET

LINPARIB®
OLAPARIB

LINPARIB® (OLAPARIB) F. C. TABLET FOR ORAL USE
Read this patient information carefully before you start taking Linparib® because it answers some common questions about Linparib®. This medication is prescribed for your current condition, therefore do not use it in similar cases and do not recommend it to others.
To report SUSPECTED ADVERSE REACTIONS, contact Noavaran Daroui Kimia Co. at +982166433514 or send email to medical@kimia-pharma.co

Read this patient information carefully before you start taking Linparib® because it contains important information for you. This leaflet does not take the place of talking with your healthcare provider about your medical condition or treatment.

Composition
Each film-coated tablet Linparib® 100 mg contains: Olaparib 100 mg.
Each film-coated tablet Linparib® 150 mg contains: Olaparib 150 mg.

Mechanism of action
Olaparib is an inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, including PARP1, PARP2, and PARP3.

Pharmacokinetic
Absorption
Following oral administration of Linparib®, the median time to peak plasma concentration is 1.5 hours.

Distribution
The mean (± standard deviation) apparent volume of distribution of Linparib® is 158 ± 136 L following a single 300 mg dose of Linparib®. The protein binding of Linparib® is approximately 82% in vitro.

Metabolism
Linparib® is metabolized by cytochrome P450 (CYP) 3A in vitro.

Elimination
The mean (± standard deviation) terminal plasma half-life of Linparib® is 14.9 ± 8.2 hours and the apparent plasma clearance is 7.4 ± 3.9 L/h following a single 300 mg dose of Linparib®.

Excretion
Following a single dose of radiolabeled Linparib®, 86% of the dosed radioactivity was recovered within a 7-day collection period, 44% via the urine and 42% via the feces. The majority of the material was excreted as metabolites.

Indication
Linparib® is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated:

Ovarian cancer
- for the maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic BRCA-mutated advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for Linparib®.
- in combination with bevacizumab for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with homologous recombination deficiency (HRD)-positive status defined by either:
  - a deleterious or suspected deleterious *BRCA* mutation, and/or
  - genomic instability.

  Select patients for therapy based on an FDA-approved companion diagnostic for Linparib®.
- for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in complete or partial response to platinum-based chemotherapy.

Breast cancer
- for the adjuvant treatment of adult patients with deleterious or suspected deleterious g*BRCA*m human epidermal growth factor receptor 2 (HER2)-negative high risk early breast cancer who have been treated with neoadjuvant or adjuvant chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for Linparib®.
- for the treatment of adult patients with deleterious or suspected deleterious g*BRCA*m, HER2-negative metastatic breast cancer who have been treated with chemotherapy in the neoadjuvant, adjuvant or metastatic setting. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy. Select patients for therapy based on an FDA-approved companion diagnostic for Linparib®.

Pancreatic cancer
- for the maintenance treatment of adult patients with deleterious or suspected deleterious g*BRCA*m metastatic pancreatic adenocarcinoma whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen. Select patients for therapy based on an FDA-approved companion diagnostic for Linparib®.

Prostate cancer
- for the treatment of adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC) who have progressed following prior treatment with enzalutamide or abiraterone. Select patients for therapy based on an FDA-approved companion diagnostic for Linparib®.

It is not known if Linparib® is safe and effective in children.

Dosage and Administration
- Recommended dosage is 300 mg taken orally twice daily with or without food.
- Patients receiving Linparib® for mCRPC should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy.
- For moderate renal impairment (CLcr 31-50 mL/min), reduce Linparib® dosage to 200 mg orally twice daily.

Side effects / Adverse reactions
It should be noted that these side effects do not occur in all patients. These are not all the possible side effects of Linparib®. For more information, ask your healthcare provider or pharmacist.

Linparib® may cause serious side effects including:
- **Bone marrow problems called Myelodysplastic Syndrome (MDS) or Acute Myeloid Leukemia (AML).** Some people who have ovarian cancer or breast cancer and who have received previous treatment with chemotherapy, radiotherapy or certain other medicines for their cancer have developed MDS or AML during treatment with Linparib®. MDS or AML may be life-threatening. If you develop MDS or AML, your healthcare provider will stop treatment with Linparib®.

  Symptoms of low blood cell counts are common during treatment with Linparib®, but can be a sign of serious bone marrow problems, including MDS or AML. Symptoms may include:
  - blood in urine or stool
  - shortness of breath
  - frequent infections
  - weakness
  - weight loss
  - bruising or bleeding more easily
  - fever
  - feeling very tired

  Your healthcare provider will do blood tests to check your blood cell counts:
  - before treatment with Linparib®
  - every month during treatment with Linparib®
  - weekly if you have low blood cell counts that last a long time. Your healthcare provider may stop treatment with Linparib® until your blood cell counts improve.
- **Lung problems (pneumonitis).** Tell your healthcare provider if you have any new or worsening symptoms of lung problems, including shortness of breath, fever, cough, or wheezing. Your healthcare provider may do a chest x-ray if you have any of these symptoms. Your healthcare provider may temporarily or completely stop treatment if you develop pneumonitis. Pneumonitis may be life-threatening.
- **Blood clots (Venous Thromboembolic Events).** Some people may develop a blood clot in a deep vein, usually in the leg (venous thrombosis) or a clot in the lung (pulmonary embolism) which may be severe or life-threatening. Tell your healthcare provider right away if you have any symptoms such as pain or swelling in an extremity, shortness of breath, chest pain, breathing that is more rapid than normal (tachypnea), or heart beats faster than normal (tachycardia). Your healthcare provider will monitor you for these symptoms and may prescribe blood thinner medicine.

Call your healthcare provider right away if you have any of aforementioned symptoms.

The most common side effects of Linparib® are:
- nausea or vomiting. Tell your healthcare provider if you get nausea or vomiting. Your healthcare provider may prescribe medicines to treat these symptoms.
- tiredness or weakness
- low red blood cell counts
- loss of appetite
- shortness of breath
- low white blood cell counts
- changes in the way food tastes
- dizziness
- indigestion or heartburn
- diarrhea
- cough
- headache
- low platelet counts

Drug interaction
- **Use with Anticancer Agents**
  Clinical studies of Linparib® with other myelosuppressive anticancer agents, including DNA damaging agents, indicate a potentiation and prolongation of myelosuppressive toxicity.
- **Strong and Moderate CYP3A Inhibitors**
  Coadministration of CYP3A inhibitors (strong inhibitors e.g. itraconazole, telithromycin, clarithromycin, protease inhibitors boosted with ritonavir or cobicistat, boceprevir, telaprevir or moderate inhibitors e.g. erythromycin, diltiazem, fluconazole, verapamil) can increase Linparib® concentrations, which may increase the risk for adverse reactions. Avoid coadministration of strong or moderate CYP3A inhibitors. If the strong or moderate inhibitor must be coadministered, reduce the dose of Linparib®.
- **Strong and Moderate CYP3A Inducers**
  Concomitant use with a strong or moderate CYP3A inducer (e.g. phenytoin, rifampicin, rifapentine, carbamazepine, nevirapine, phenobarbital and St John's Wort) decreased Linparib® exposure, which may reduce Linparib® efficacy. Avoid coadministration of strong or moderate CYP3A inducers.

Warnings
Before taking Linparib®, tell your healthcare provider about all of your medical conditions, including if you:
- have lung or breathing problems
- have kidney problems
- are pregnant, become pregnant, or plan to become pregnant. Linparib® can harm your unborn baby and may cause loss of pregnancy (miscarriage).
- are breastfeeding or plan to breastfeed.

Do not take Linparib® if you are allergic to Linparib® or any of the other ingredients of this medicine.

Tell your healthcare provider about all the medicines you take, including prescription medicines and over-the-counter medicines, vitamins, and herbal supplements. Taking Linparib® and certain other medicines may affect how Linparib® works and may cause side effects.

Missed dose
If you miss a dose of Linparib®, take your next dose at your usual scheduled time. Do not take an extra dose to make up for a missed dose.

Overdose
If you take too much Linparib®, call your healthcare provider or go to the nearest hospital emergency room right away.

Pregnancy and lactation
Linparib® can harm your unborn baby and may cause loss of pregnancy (miscarriage).
- If you are able to become pregnant, your healthcare provider may do a pregnancy test before you start treatment with Linparib®.
- **Females** who are able to become pregnant should use effective birth control (contraception) during treatment with Linparib® and for 6 months after the last dose of Linparib®. Talk to your healthcare provider about birth control methods that may be right for you. Tell your healthcare provider right away if you become pregnant or think you might be pregnant following treatment with Linparib®.
- **Males** with female partners who are pregnant or able to become pregnant should use effective birth control (contraception) during treatment with Linparib® and for 3 months after the last dose of Linparib®.
- Do not donate sperm during treatment with Linparib® and for 3 months after your final dose.

It is not known if Linparib® passes into your breast milk. Do not breastfeed during treatment with Linparib® and for 1 month after receiving the last dose of Linparib®. Talk to your healthcare provider about the best way to feed your baby during this time.

Patient information
- Take Linparib® tablets exactly as your healthcare provider tells you.
- Do not change your dose or stop taking Linparib® unless your healthcare provider tells you to. Your healthcare provider may temporarily stop treatment with Linparib® or change your dose of Linparib® if you experience side effects.
- Your healthcare provider will decide how long you stay on treatment.
- **Do not take more than 4 Linparib® tablets in 1 day.** If you have any questions about Linparib®, please talk to your healthcare provider or pharmacist.
- Take Linparib® by mouth 2 times a day.
- Each dose should be taken about 12 hours apart.
- Swallow Linparib® tablets whole. Do not chew, crush, dissolve, or divide the tablets.
- Take Linparib® with or without food.
- If you are taking Linparib® for early breast cancer and you have hormone receptor-positive disease, you should continue to take hormonal therapy during your treatment with Linparib®.
- If you are taking Linparib® for prostate cancer and you are receiving gonadotropin-releasing hormone (GnRH) analog therapy, you should continue with this treatment during your treatment with Linparib® unless you have had a surgery to lower the amount of testosterone in your body (surgical castration).
- Avoid grapefruit, grapefruit juice, Seville oranges and Seville orange juice during treatment with Linparib® since they may increase the level of Linparib® in your blood.
- Linparib® may influence your ability to drive and use machines. If you feel dizzy, weak or tired while taking Linparib® do not drive or use tools or machines.

Storage
- Keep away from light and moisture. Store below 30°C.
- Keep out of the reach of children.
- Store Linparib® in the original bottle to protect it from moisture.
- Keep the desiccant in the bottle. do not eat or throw away desiccant pack.
- Safely throw away medicine that is out of date or that you no longer need. Ask your pharmacist how to safely throw away Linparib® tablets.
- Use appropriate precautions for handling and disposal of cytotoxic drugs.

Packaging
Bottle of 30 F. C. Tablets

MANUFACTURED BY:
Noavaran Daroui Kimia Co., Tehran, Iran.
Telefax: +982166437014
www.kimia-pharma.co

References
https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208558s024lbl.pdf
https://www.ema.europa.eu/en/documents/product-information/lynparza-epar-product-information_en.pdf
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