60-75 GSM MAPLITHO PAPER

242 x 208 mm

- Patients should be informed that in the event of a missed daily dose of Abiraterone acetate or prednisone, they should take their normal dose the following day. If more than one daily dose is skipped, patients should be told to inform their physician.
- Patients should be apprised of the common side effects associated with Abiraterone acetate including peripheral edema, hypokalemia, hypertension, elevated liver function tests, and urinary tract infection. Direct the patient to a complete list of adverse reactions in PATIENT INFORMATION.
- Patients should be advised that their liver function will be monitored using blood tests.
- Patients should be informed that Abiraterone acetate may harm a developing fetus; thus, women who are pregnant or women who may be pregnant should not handle Abiraterone acetate without protection, e.g., gloves. Patients should also be informed that it is not known whether abiraterone or its metabolites are present in semen and they should use a condom if having sex with a pregnant woman. The patient should use a condom and another effective method of birth control if he is having sex with a woman of child-bearing potential. These measures are required during and for one week after treatment with Abiraterone acetate.

PRESENTATION :
Abiraterone acetate tablets IP 250 mg are available in HDPE bottles of 120 tablets.
Abiraterone acetate tablets IP 500 mg are available in HDPE bottles of 60 tablets.

Made in India by:
APRAZER
Aprazer Healthcare Pvt. Ltd.
Vill. Kotla, Barotiwala-174103
Distt. : Solan, Himachal Pradesh
www.aprazerhealthcare.com

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For the use only of an Oncologist or a Hospital or a Laboratory

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Abiraterone Acetate Tablets IP 250 Mg & 500 mg

ABIRAKAST®

WARNINGS AND PRECAUTIONS

Hypertension, Hypokalemia and Fluid Retention Due to Mineralocorticoid Excess :
Abiraterone acetate may cause hypertension, hypokalemia, and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition.

Adrenocortical Insufficiency :
Adrenal insufficiency occurred in the two randomized clinical studies in 0.5% of patients taking Abiraterone acetate and in 0.2% of patients taking placebo. Adrenocortical insufficiency was reported in patients receiving Abiraterone acetate in combination with prednisone, following interruption of daily steroids and/or with concurrent infection or stress. Use caution and monitor for symptoms and signs of adrenocortical insufficiency, particularly if patients are withdrawn from prednisone, have prednisone dose reductions, or experience unusual stress.

Hepatotoxicity :
In the two randomized clinical trials, grade 3 or 4 ALT or AST increases (at least 5× ULN) were reported in 4% of patients who received Abiraterone acetate, typically during the first 3 months after starting treatment. Patients whose baseline ALT or AST were elevated were more likely to experience liver test elevation than those beginning with normal values. Treatment discontinuation due to liver enzyme increases occurred in 1% of patients taking Abiraterone acetate. No deaths clearly related to Abiraterone acetate were reported due to hepatotoxicity events.

Pregnancy :
Abiraterone acetate may harm a developing fetus : thus women who are pregnant or women who may be pregnant should not handle Abiraterone acetate without protection, e.g. gloves. Women of child-bearing potential should avoid becoming pregnant during treatment.

COMPOSITION
ABIRAKAST
Each uncoated Tablet contains:
Abiraterone acetate IP 250 mg
Excipients qs

COMPOSITION
ABIRAKAST
Each uncoated Tablet contains:
Abiraterone acetate IP 500 mg
Excipients qs

DESCRIPTION
Abiraterone acetate is an antiandrogen used in the treatment of Castration-Resistant Prostate Cancer(CRPC).

CLINICAL PHARMACOLOGY
Mechanism of Action
Abiraterone acetate is converted *in vivo* to abiraterone, an androgen biosynthesis inhibitor, that inhibits 17 α-hydroxylase/C17,20-lyase (CYP17). This enzyme is expressed in testicular, adrenal, and prostatic tumor tissues and is required for androgen biosynthesis.

PHARMACOKINETICS
Absorption : Good oral bioavaliability with peak plasma levels seen within 2 hours of administration. Systemic exposure of Abiraterone is increased when administrated with food.
Distribution : Highly plasma protein food(>90%).
Metabolism : Following oral administration, Abiraterone acetate is hydrolyzed to its active metabolite Aberiterone. CYP3A4 and SULT2A1 are the enzymes involved in the metabolism.
Half-life : The mean terminal half-life of Abiraterone is 7 to 17 hours.
Elimination : Mainly excreted in the feces (88%) and approximately 5% in urine.

INDICATIONS AND USAGE
Abiraterone acetate is a CYP17 inhibitor indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer.

DOSAGE AND ADMINISTRATION
Recommended Dosage
The recommended dose of Abiraterone acetate is 1,000 mg (four 250 mg tablets) administered orally once daily in combination with prednisone 5 mg administered orally twice daily.

Administration : Abiraterone acetate must be taken on an empty stomach. No food should be consumed for at least two hours before the dose of Abiraterone acetate is taken and for at least one hour after the dose of Abiraterone Acetate is taken. The tablets should be swallowed whole with water. Do not crush or chew tablets.

Dose modifications :
1) In patients with baseline mild hepatic impairment (Child-Pugh Class A): No dose modifications.
2) In patients with baseline moderate hepatic impairment (Child-Pugh Class B): Use with caution in patients with hepatic impairment. Dose should be reduced to 250 mg PO once daily.
3) In patients with baseline severs hepatic impairment (Child-Pugh Class C) : Should be avoided.
4) In patients who develop severe hepatotoxicity : Should be discontinued.
5) In patients with renal impairment : No dosage modifications are necessary.

DOSAGE FORMS AND STRENGTHS
ABIRAKAST (Abiraterone acetate) is available as 250 mg tablets.

CONTRAINDICATIONS

Abiraterone acetate can cause fetal harm when administered to a pregnant woman. Abiraterone acetate is not indicated for use in women. Abiraterone acetate is contraindicated in women who are or may become pregnant. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, apprise the patient of the potential hazard to the fetus and the potential risk for pregnancy loss

WARNINGS AND PRECAUTIONS
Hypertension, Hypokalemia and Fluid Retention Due to Mineralocorticoid Excess
Abiraterone acetate may cause hypertension, hypokalemia, and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition. Use caution when treating patients whose underlying medical conditions might be compromised by increases in blood pressure, hypokalemia or fluid retention, e.g., those with heart failure, recent myocardial infarction or ventricular arrhythmia. Monitor patients for hypertension, hypokalemia, and fluid retention at least once a month.
Adrenocortical Insufficiency
Adrenal insufficiency occurred in the two randomized clinical studies in 0.5% of patients taking Abiraterone acetate and in 0.2% of patients taking placebo. Adrenocortical insufficiency was reported in patients receiving Abiraterone acetate in combination with prednisone, following interruption of daily steroids and/or with concurrent infection or stress. Use caution and monitor for symptoms and signs of adrenocortical insufficiency, particularly if patients are withdrawn from prednisone, have prednisone dose reductions, or experience unusual stress. Symptoms and signs of adrenocortical insufficiency may be masked by adverse reactions associated with mineralocorticoid excess seen in patients treated with Abiraterone acetate. If clinically indicated, perform appropriate tests to confirm the diagnosis of adrenocortical insufficiency. Increased dosage of corticosteroids may be indicated before, during and after stressful situations.

In the two randomized clinical trials, grade 3 or 4 ALT or AST increases (at least 5× ULN) were reported in 4% of patients who received Abiraterone acetate, typically during the first 3 months after starting treatment. Patients whose baseline ALT or AST were elevated were more likely to experience liver test elevation than those beginning with normal values. Treatment discontinuation due to liver enzyme increases occurred in 1% of patients taking Abiraterone acetate. No deaths clearly related to Abiraterone acetate were reported due to hepatotoxicity events.
Increased Abiraterone exposures with Food
Abiraterone must be taken on an empty stomach. No food should be consumed for at least two hours before the dose of Abiraterone is taken and for at least one hour after the dose of Abiraterone is taken.

ADVERSE EFFECTS:
Serious adverse reactions reported with Abiraterone treatment are described below:

Side effects	major	minor
Musculoskeletal and connective tissue disorder.	Joint swelling. Muscle discomfort	———
General disorder	Edema	———
Vascular disorder	Hot flashes or flush	Hypertension
Gastrointestinal disorder	Diarrhea	Dyspepsia
Infections and Infestations	Urinary tract infection	Upper respiratory tract infection.
Respiratory, thoracic and mediastinal disorder	Cough	———
Renal and urinary disorder	———	Increased urinary frequency. Nocturia
Injury, poisoning and procedural complications	———	Fractures (all types except pathological fractures)

USE IN SPECIFIC POPULATIONS

Pregnancy Category X
Abiraterone acetate can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals. While there are no adequate and well-controlled studies with Abiraterone acetate in pregnant women and Abiraterone acetate is not indicated for use in women, it is important to know that maternal use of a CYP17 inhibitor could affect development of the fetus. Abiraterone acetate caused developmental toxicity in pregnant rats at exposures that were lower than in patients receiving the recommended dose. Abiraterone acetate is contraindicated in women who are or may become pregnant while receiving the drug. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, apprise the patient of the potential hazard to the fetus and the potential risk for pregnancy loss. Advise females of reproductive potential to avoid becoming pregnant during treatment with Abiraterone acetate.

Nursing Mothers
Abiraterone acetate is not indicated for use in women. It is not known if Abiraterone acetate is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from Abiraterone acetate, a decision should be made to either discontinue nursing, or discontinue the drug taking into account the importance of the drug to the mother.
Pediatric Use
Safety and effectiveness of Abiraterone acetate in pediatric patients have not been established.
Geriatric Use
Of the total number of patients receiving Abiraterone acetate in Phase 3 trials, 73% of patients were 65 years and over and 30% were 75 years and over. No overall differences in safety or effectiveness were observed between these elderly patients and younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

OVERDOSAGE
Human experience of overdose with Abiraterone acetate is limited.
There is no specific antidote. In the event of an overdose, stop Abiraterone acetate, undertake general supportive measures, including monitoring for arrhythmias and cardiac failure and assess liver function.

CLINICAL STUDIES
The efficacy and safety of Abiraterone acetate in patients with metastatic castration-resistant prostate cancer (CRPC) that has progressed on androgen deprivation therapy was demonstrated in two randomized, placebo-controlled, multicenter Phase 3 clinical trials. Patients with prior ketoconazole treatment for prostate cancer and a history of adrenal gland or pituitary disorders were excluded from these trials. Concurrent use of spironolactone was not allowed during the study period.
Study 1
Patients with metastatic CRPC who had received prior docetaxel chemotherapy:
A total of 1195 patients were randomized 2:1 to receive either Abiraterone acetate orally at a dose of 1,000 mg once daily in combination with prednisone 5 mg orally twice daily (N=797) or placebo once daily plus prednisone 5 mg orally twice daily (N=398). Patients randomized to either arm were to continue treatment until disease progression (defined as a 25% increase in PSA over the patient's baseline/nadir together with protocol-defined radiographic progression and symptomatic or clinical progression), initiation of new treatment, unacceptable toxicity or withdrawal.
The inhibition of androgen biosynthesis by Abiraterone acetate prolonged overall survival among patients with metastatic Castration-Resistant Prostate Cancer who previously received chemotherapy.

Perameters, Phase III (N=1195)	*Abiraterone acetate + Prednisone (N=797)*	*Placebo + Prednisone (N=398)*
Median Overall survival (months)	14.8	10.9
Time to PSA progression (months)	10.2	6.6
Median Progression-free survival (months)	5.6	3.6
PSA response rate (%)	29	6

Study 2
Patients with metastatic CRPC who had not received prior chemotherapy
In this double-blind study, 1088 patients were randomized 1:1 to received Abiraterone acetate (1000 mg once daily) plus Prednisone 5mg twice daily) or placebo plus Prednisone.
Abiraterone improved radiographic progression-free survival, showed a trend towards improved overall survival and significantly delayed clinical decline and initiation of chemotherapy in patients with metastatic CRPC.

Perameters, Phase III (N=1088)	*Abiraterone acetate + Prednisone (N=546)*	*Placebo + Prednisone (N=542)*
Median radiographic progression-free survival (months)	16.5	8.3

MONITORING PAREMETERS
Monitor patients for hypertension, hypokalemia and fluid relation at least once a month.

Monitor for symptoms and signs of adrenocortical insufficiency, particularly if patients are withdrawn from prednisone, have prednisone dose reductions or experience unusual stress.

Monitor LFTs - serum transminases (ALT and AST) and serum billrubin levels prior to starting treatment with Abiraterone every two weeks for the first three months of treatment and monthly thereafter.
monitor Prostate-specific antigen (PSA).

STORAGE: Store protected from light & moisture, at a temperature not exceeding 30°C.
Keep out of reach of children.

PATIENT COUNSELING INFORMATION
- Patients should be informed that Abiraterone acetate and prednisone are used together and that they should not interrupt or stop either of these medications without consulting their physician.
- Patients receiving GnRH agonists should be informed that they need to maintain this treatment during the course of treatment with Abiraterone acetate and prednisone.
- Patients should be informed that Abiraterone acetate should not be taken with food and that no food should be consumed for at least two hours before the dose of Abiraterone acetate is taken and for at least one hour after the dose of Abiraterone acetate is taken. They should be informed that the tablets should be swallowed whole with water without crushing or chewing. Patients should be informed that taking Abiraterone acetate with food causes increased exposure and this may result in adverse reactions.
- Patients should be informed that Abiraterone acetate is taken once daily and prednisone is taken twice daily according to their physician's instructions.

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