CLINICAL UPDATE

Brand Name	Abiraterone
Generic Name	abiraterone
Drug Manufacturer	Janssen Biotech

Clinical Update

TYPE OF CLINICAL UPDATE

New Strength

FDA APPROVAL DATE

October 10, 2020

LAUNCH DATE

N/A

REVIEW DESIGNATION

Standard

TYPE OF REVIEW

New Drug Approval (NDA): 202379

DISPENSING RESTRICTIONS

N/A

Overview

INDICATION(S) FOR USE

Abiraterone acetate tablets are a CYP17 inhibitor indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer (CRPC).

MECHANISMS 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.

CYP17 catalyzes two sequential reactions: 1) the conversion of pregnenolone and progesterone to their 17α-hydroxy derivatives by 17α-hydroxylase activity and 2) the subsequent formation of dehydroepiandrosterone (DHEA) and androstenedione, respectively, by C17, 20-lyase activity. DHEA and androstenedione are androgens and are precursors of testosterone. Inhibition of CYP17 by abiraterone can also result in increased mineralocorticoid production by the adrenals.

Androgen sensitive prostatic carcinoma responds to treatment that decreases androgen levels. Androgen deprivation therapies, such as treatment with GnRH agonists or orchiectomy, decrease androgen production in the testes but do not affect androgen production by the adrenals or in the tumor.

Abiraterone acetate tablets decreased serum testosterone and other androgens in patients in the placebo-controlled clinical trial. It is not necessary to monitor the effect of abiraterone acetate tablets on serum testosterone levels.

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Changes in serum prostate specific antigen (PSA) levels may be observed but have not been shown to correlate with clinical benefit in individual patients.

DOSAGE FORM(S) AND STRENGTH(S)

- Film-Coated Tablets: 500 mg
- Film-Coated Tablets: 250 mg
- Uncoated Tablets: 250 mg

DOSE & ADMINISTRATION

The recommended dose of abiraterone acetate tablets is 1,000 mg (two 500 mg tablets or four 250 mg tablets) orally once daily with prednisone 5 mg orally twice daily.

EFFICACY

The efficacy and safety of abiraterone acetate tablets with prednisone was established in two randomized placebo-controlled international clinical studies. All patients in these studies received a GnRH analog or had prior bilateral orchiectomy. 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.

COU-AA-301: Patients with Metastatic CRPC who had Received Prior Docetaxel Chemotherapy: In COU-AA-301 (NCT00638690), a total of 1195 patients were randomized 2:1 to receive either abiraterone acetate tablets 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.

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Overall Survival of Patients Treated with either Abiraterone Acetate Tablets or Placebo in combination with Prednisone in COU-AA-201 (Intent-to-treat Analysis)

	Abiraterone Acetate Tablets with Prednisone (N = 797)	Placebo with Prednisone (N = 398)
Primary Survival Analysis		
Deaths (%)	333 (42%)	219 (55%)
Median survival (months) (95% CI)	14.8 (14.1, 15.4)	10.9 (10.2, 12.0)
p-value*	< 0.0001	
Hazard ratio (95% CI)‡	0.646 (0.543, 0.768)	
Updated Survival Analysis		
Deaths (%)	501 (63%)	274 (69%)
Median survival (months) (95% CI)	15.8 (14.8, 17.0)	11.2 (10.4, 13.1)
Hazard ratio (95% CI)‡	0.740 (0.638, 0.859)	

* p-value is derived from a log-rank test stratified by ECOG performance status score (0-1 vs. 2), pain score (absent vs. present), number of prior chemotherapy regimens (1 vs. 2), and type of disease progression (PSA only vs. radiographic).

‡ Hazard Ratio is derived from a stratified proportional hazards model. Hazard ratio < 1 favors abiraterone acetate tablets with prednisone.