Prescribing Information

Abiraterone Accord 500 mg film-coated tablets

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Presentation: Each tablet contains 500 mg of abiraterone acetate.

Indications: Abiraterone Accord is indicated with prednisone or prednisolone for: the treatment of newly diagnosed high risk metastatic hormone sensitive prostate cancer (mHSPC) in adult men in combination with androgen deprivation therapy (ADT); the treatment of metastatic castration resistant prostate cancer (mCRPC) in adult men who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated; the treatment of mCRPC in adult men whose disease has progressed on or after a docetaxel-based chemotherapy regimen.

Dosage and Administration: this medicinal product should be prescribed by an appropriate healthcare professional. *Posology:* the recommended dose is 1000 mg (two 500 mg tablets) as a single daily dose. *Dosage of prednisone or prednisolone*: for mHSPC, Abiraterone Accord is used with 5 mg prednisone or prednisolone daily. For mCRPC, Abiraterone Accord is used with 10 mg prednisone or prednisolone daily. Medical castration with luteinising hormone releasing hormone (LHRH) analogue should be continued during treatment in patients not surgically castrated. *Recommended monitoring*: serum transaminases should be measured prior to starting treatment, every 2 weeks for the first 3 months of treatment and monthly thereafter. Blood pressure, serum potassium and fluid retention should be monitored monthly. Patients with a significant risk for congestive heart failure should be monitored every 2 weeks for the first three months of treatment and monthly thereafter. In patients with pre-existing hypokalaemia or those that develop hypokalaemia whilst being treated with abiraterone acetate, consider maintaining the patient's potassium level at ≥ 4.0 mM. For patients who develop Grade ≥ 3 toxicities including hypertension, hypokalaemia, oedema and other non-mineralocorticoid toxicities, treatment should be withheld and appropriate medical management should be instituted. Treatment with abiraterone acetate, should not be reinitiated until symptoms of the toxicity have resolved to Grade 1 or baseline. In the event of a missed daily dose of either Abiraterone Accord, prednisone or prednisolone, treatment should be resumed the following day with the usual daily dose. *Hepatotoxicity*: for patients who develop hepatotoxicity during treatment (alanine aminotransferase [ALT] increases or aspartate aminotransferase [AST] increases above 5 times the upper limit of normal [ULN]), treatment should be withheld immediately. Re-treatment following return of liver function tests to the patient's baseline may be given at a reduced dose of 500 mg (one tablet) once daily. For patients being re-treated, serum transaminases should be monitored at a minimum of every two weeks for three months and monthly thereafter. If hepatotoxicity recurs at the reduced dose of 500 mg daily, treatment should be discontinued. If patients develop severe hepatotoxicity (ALT or AST 20 times the ULN) anytime while on therapy, treatment should be discontinued and patients should not be re-treated. *Renal impairment*: no dose adjustment is necessary for patients with renal impairment. There is no clinical experience in patients with prostate cancer and severe renal impairment. Caution is advised in these patients. *Hepatic impairment*: no dose adjustment is necessary for patients with pre-existing mild hepatic impairment, Child-Pugh Class A. Moderate hepatic impairment (Child-Pugh Class B) has been shown to increase the systemic exposure to abiraterone acetate by approximately four-fold following single oral doses of abiraterone acetate 1000 mg. There are no data on the clinical safety and efficacy of multiple doses of abiraterone acetate when administered to patients with moderate or severe hepatic impairment (Child-Pugh Class B or C). No dose adjustment can be predicted. Use should be cautiously assessed in patients with moderate hepatic impairment, in whom the benefit clearly should outweigh the possible risk. It should not be used in patients with severe hepatic impairment. *Paediatric population:* there is no relevant use in the paediatric population. *Method of administration*: for oral use. The tablets should be taken at least 1 hour before or at least 2 hours after eating. These should be swallowed whole with water.

Contraindications: hypersensitivity to the active substance or to any of the excipients; women who are or may potentially be pregnant**;** severe hepatic impairment (Child-Pugh Class

C); abiraterone acetate with prednisone or prednisolone is contraindicated in combination with Ra- 223.

Warnings and Precautions: *Hypertension, hypokalaemia, fluid retention and cardiac failure due to mineralocorticoid excess*: Abiraterone acetate may cause hypertension, hypokalaemia and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition. Co-administration of a corticosteroid suppresses adrenocorticotropic hormone (ACTH) drive, resulting in a reduction in incidence and severity of these adverse reactions. Caution is required in treating patients whose underlying medical conditions might be compromised by increases in blood pressure, hypokalaemia (e.g., those on cardiac glycosides), or fluid retention (e.g., those with heart failure, severe or unstable angina pectoris, recent myocardial infarction or ventricular arrhythmia and those with severe renal impairment). Use with caution in patients with a history of cardiovascular disease. Before treating patients with a significant risk for congestive heart failure, consider obtaining an assessment of cardiac function. Before treatment with abiraterone acetate cardiac failure should be treated and cardiac function optimised. Hypertension, hypokalaemia and fluid retention should be corrected and controlled. During treatment, blood pressure, serum potassium, fluid retention (weight gain, peripheral oedema), and other signs and symptoms of congestive heart failure should be monitored every 2 weeks for 3 months, then monthly thereafter and abnormalities corrected. QT prolongation has been observed in patients experiencing hypokalaemia in association with abiraterone acetate treatment. Assess cardiac function as clinically indicated, institute appropriate management and consider discontinuation of this treatment if there is a clinically significant decrease in cardiac function. *Hepatotoxicity and hepatic impairment*: serum transaminase levels should be measured prior to starting treatment, every 2 weeks for the first 3 months of treatment, and monthly thereafter. If clinical symptoms or signs suggestive of hepatotoxicity develop, serum transaminases should be measured immediately. If at any time the ALT or AST rises above 5 times the ULN, treatment should be interrupted immediately and liver function closely monitored. Re-treatment may take place only after return of liver function tests to the patient's baseline and at a reduced dose level. If patients develop severe hepatotoxicity (ALT or AST 20 times the ULN) anytime while on therapy, treatment should be discontinued and patients should not be re-treated. The use of abiraterone acetate should be cautiously assessed in patients with moderate hepatic impairment, in whom the benefit clearly should outweigh the possible risk. Abiraterone acetate should not be used in patients with severe hepatic impairment. *Corticosteroid withdrawal and coverage of stress situations*: caution is advised and monitoring for adrenocortical insufficiency should occur if patients are withdrawn from prednisone or prednisolone. If abiraterone acetate is continued after corticosteroids are withdrawn, patients should be monitored for symptoms of mineralocorticoid excess. In patients on prednisone or prednisolone who are subjected to unusual stress, an increased dose of corticosteroids may be indicated before, during and after the stressful situation. *Bone density*: decreased bone density may occur in men with metastatic advanced prostate cancer. The use of abiraterone acetate in combination with a glucocorticoid could increase this effect. *Prior use of ketoconazole*: lower rates of response might be expected in patients previously treated with ketoconazole for prostate cancer. *Hyperglycaemia*: the use of glucocorticoids could increase hyperglycaemia, therefore blood sugar should be measured frequently in patients with diabetes. *Hypoglycaemia*: cases of hypoglycaemia have been reported when abiraterone acetate plus prednisone/prednisolone was administered to patients with pre-existing diabetes receiving pioglitazone or repaglinide. Blood sugar should be measured frequently in patients with diabetes. *Use with chemotherapy*: the safety and efficacy of concomitant use of abiraterone acetate with cytotoxic chemotherapy has not been established. *Potential risks*: anaemia and sexual dysfunction may occur in men with metastatic prostate cancer including those undergoing treatment with abiraterone acetate. *Skeletal muscle effects*: cases of myopathy and rhabdomyolysis have been reported in patients treated with abiraterone acetate. Most cases developed within the first 6 months of treatment and recovered after abiraterone acetate withdrawal. Caution is recommended in patients concomitantly treated with medicinal products known to be associated with myopathy/rhabdomyolysis. *Interactions with other medicinal products*: strong inducers of CYP3A4 during treatment are to be avoided unless there is no therapeutic alternative, due to risk of decreased exposure to abiraterone acetate. *Combination of abiraterone and prednisone/prednisolone with Ra-223*: treatment in combination with Ra-223 is contraindicated due to an increased risk of fractures and a trend for increased mortality

among asymptomatic or mildly symptomatic prostate cancer patients as observed in clinical studies. It is recommended that subsequent treatment with Ra-223 is not initiated for at least 5 days after the last administration of abiraterone acetate in combination with prednisone/prednisolone. *Excipients with known effect*: *Lactose:* this medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product. *Sodium:* this medicinal product contains 24 mg sodium per dose of two tablets, equivalent to 1.04 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Fertility, Pregnancy & Lactation: Abiraterone acetate is not for use in women and is contraindicated in women who are or may potentially be pregnant. *Contraception in males and females*: a condom is required if the patient is engaged in sexual activity with a pregnant woman. If the patient is engaged in sex with a woman of childbearing potential, a condom is required along with another effective contraceptive method. *Fertility*: Abiraterone acetate affected fertility in male and female rats, but these effects were fully reversible.

Adverse Events include:
Adverse events which could be considered serious: hypokalaemia, urinary tract infection, hepatotoxicity, fractures, sepsis, anaphylactic reactions, adrenal insufficiency, cardiac failure, angina pectoris, atrial fibrillation, tachycardia, other arrhythmias, myocardial infarction, QT prolongation, hepatitis fulminant, acute hepatic failure, rhabdomyolysis. *Other Very Common adverse events:* hypertension, diarrhoea, alanine aminotransferase increased, aspartate aminotransferase increased, oedema peripheral. *Other Common adverse events:* hypertriglyceridaemia, dyspepsia, rash, haematuria. See SmPC for details of other adverse events.

Presentation and Price: 500mg x 56 £2735.00

Legal Category: POM

Further information is available from: Accord-UK Ltd, Whiddon Valley, Barnstaple, Devon, EX32 8NS.

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard Adverse events should also be reported to Accord-UK LTD on 01271 385257 or email medinfo@accord-healthcare.com.