SCHEDULING STATUS

Schedule 4

1. NAME OF THE MEDICINE

ZYTIGA® 250 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ZYTIGA® 250 mg tablets

Each tablet contains 250 mg of abiraterone acetate.

Contains sugar (lactose monohydrate).

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

ZYTIGA® 250 mg tablets:

ZYTIGA® 250 mg uncoated tablets are white to off white, oval tablets 16 mm long, debossed with AA250 on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ZYTIGA is indicated with low-dose corticosteroids (prednisone or prednisolone) in adult males for the treatment of:

- high-risk metastatic hormone treatment naïve prostate cancer (mHNPC) or newly diagnosed high-risk metastatic hormone sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (LHRH agonist or surgical castration).

  High-risk is defined as having at least 2 of the following 3 risk factors:

  (1) Gleason score of ≥ 8;

  (2) presence of 3 or more bone lesions;

  (3) presence of measurable visceral (excluding lymph node disease) metastasis.
- metastatic castration resistant prostate cancer with bone metastases who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated.
- metastatic advanced prostate cancer (castration resistant prostate cancer) who have received prior chemotherapy containing docetaxel.

4.2 Posology and method of administration

Posology

The recommended dose of ZYTIGA is 1 g (four 250 mg tablets) as a single daily dose that **must not be taken with food** (see *Method of administration* below). Taking ZYTIGA with food increases systemic exposure to abiraterone (see sections 4.5 and 5.2).

Patients should be maintained on ZYTIGA until radiographic progression and symptomatic/clinical progression and until PSA progression (confirmed 25 % increase over the patient's baseline/nadir).

Dosage of prednisone or prednisolone

For metastatic hormone naïve prostate cancer (mHNPC) or hormone sensitive prostate cancer (mHSPC), ZYTIGA is used with 5 mg prednisone or prednisolone once daily.

For metastatic castration-resistant prostate cancer (mCRPC), ZYTIGA is used with 10 mg prednisone or prednisolone daily.

Recommended monitoring

Serum transaminases and bilirubin should be measured prior to starting treatment with ZYTIGA, every two weeks for the first three months of treatment and monthly thereafter. Blood pressure, serum potassium and fluid retention should be monitored monthly (see section 4.4).

In the event of a missed daily dose of either ZYTIGA, prednisone or prednisolone, treatment should be resumed the following day with the usual daily dose.

Hepatic impairment:

No dose adjustment is necessary for patients with pre-existing mild hepatic impairment, Child-Pugh class A. There are no data on the clinical safety and efficacy of multiple doses of ZYTIGA when administered to patients with moderate or severe hepatic impairment (Child Pugh Class B or C). No dose adjustment can be predicted. ZYTIGA should not be used in patients with moderate to severe hepatic impairment (see section 4.3).

For patients who develop hepatotoxicity during treatment with ZYTIGA (alanine aminotransferase (ALT) or aspartate aminotransferase (AST) increases above 5 times the upper limit of normal or bilirubin increases above 3 times the upper limit of normal), treatment should be withheld immediately until liver function tests normalise (see section 4.4). Re-treatment following return of liver function tests to the patient's baseline may be given at a reduced dose of 500 mg once daily. For patients being re-treated, serum transaminases and

bilirubin 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. Reduced doses should not be taken with food (see previous).

If patients develop severe hepatotoxicity (ALT or AST 20 times the upper limit of normal) anytime while on therapy, ZYTIGA should be discontinued and patients should not be re-treated with ZYTIGA.

Renal impairment:

No dose adjustment is necessary for patients with renal impairment (see section 5.2).

Paediatric population:

There is no relevant use of ZYTIGA in paediatric patients, as prostate cancer is not present in the paediatric population.

Method of administration

ZYTIGA must be taken on an empty stomach, at least one hour before or at least two hours after a meal. The tablets should be swallowed whole with water.

Precautions to be taken before handling or administering ZYTIGA.

Based on its mechanism of action, ZYTIGA may harm a developing foetus; therefore, women (including healthcare professionals), who are pregnant or women who may be pregnant should not handle ZYTIGA 250 mg tablets without protection, e.g. gloves (see section 4.6 and 6.6).

4.3 Contraindications

ZYTIGA is contraindicated in:

- Patients with hypersensitivity to abiraterone acetate or to any of the excipients listed in section 6.1.
- Pregnancy and Lactation (see section 4.6).
- Moderate to severe hepatic impairment (see sections 4.2, 4.4 and 5.2).
- Women should not use ZYTIGA.
- Concomitant administration with rifampicin (see section 4.5).

4.4 Special warnings and precautions for use

Hypertension, hypokalaemia and fluid retention due to mineralocorticoid excess

ZYTIGA may cause hypertension, hypokalaemia and fluid retention (see section 4.8) as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition (see section 5.1). 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 or fluid retention e.g., those with heart failure, recent myocardial infarction or ventricular dysrhythmia.

ZYTIGA should be used with caution in patients with a history of cardiovascular disease. The safety of ZYTIGA in patients with left ventricular ejection fraction < 50 % or NYHA Class III or IV heart failure has not been established.(see section 4.8). Before treatment with ZYTIGA, hypertension must be controlled and hypokalaemia must be corrected. Blood pressure, serum potassium and fluid retention should be monitored at least monthly.

Hepatotoxicity and hepatic impairment

Marked increases in liver enzymes leading to ZYTIGA discontinuation or dose modification occurred in controlled clinical studies (see section 4.8). Serum transaminase and bilirubin levels should be measured prior to starting treatment with ZYTIGA, every two weeks for the

first three 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 upper limit of normal or the bilirubin rises above 3 times the upper limit of normal, treatment with ZYTIGA should be interrupted immediately and liver function closely monitored.

Re-treatment with ZYTIGA may take place only after return of liver function tests to the patient's baseline and at a reduced dose level (see section 4.2).

If patients develop severe hepatotoxicity (ALT or AST 20 times the upper limit of normal) anytime while on therapy, ZYTIGA should be permanently discontinued and patients should not be re-treated with ZYTIGA.

There are no data on the clinical safety and efficacy of multiple doses of ZYTIGA when administered to patients with moderate or severe hepatic impairment (Child Pugh Class B or C). ZYTIGA should not be used in patients with moderate to severe hepatic impairment (see section 4.3*).*

There have been post-marketing reports of acute liver failure and fulminant hepatitis, some with fatal outcome (see section 4.8).

Corticosteroid withdrawal and coverage of stress situations

Caution is advised and monitoring for adrenocortical insufficiency should occur if patients need to be withdrawn from prednisone or prednisolone. If ZYTIGA is continued after corticosteroids are withdrawn, patients should be monitored for symptoms of mineralocorticoid excess (see *previous*).

In patients on prednisone or prednisolone who are subjected to unusual stress, increased dosage 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 ZYTIGA in combination with a glucocorticoid could increase this effect.

Use with chemotherapy

The safety and efficacy of concomitant use of ZYTIGA with cytotoxic chemotherapy has not been established.

Use in combination with radium 223 dichloride

In a randomised clinical trial in patients with asymptomatic or mildly symptomatic bone-predominant metastatic castration resistant prostate cancer, at the time of unblinding, the addition of radium 223 dichloride to ZYTIGA plus prednisone/prednisolone showed an increase in mortality and an increased rate of fracture. Radium 223 dichloride is not recommended for use in combination with ZYTIGA plus prednisone/prednisolone outside of clinical trials.

Lactose

ZYTIGA contains lactose. Patients with rare hereditary problems of galactose intolerance; e.g. galactosaemia the Lapp lactase deficiency or glucose-galactose malabsorption should not take ZYTIGA.

4.5 Interaction with other medicines and other forms of interaction

Effect of food on ZYTIGA:

Administration of ZYTIGA with food significantly increases the absorption of abiraterone acetate. The efficacy and safety of ZYTIGA given with food have not been established. **ZYTIGA must not be taken with food** (see sections 4.2 and 5.2).

Interactions with other medicines

Potential for other medicines to affect ZYTIGA exposures

In a clinical pharmacokinetic interaction study of healthy subjects pretreated with a strong CYP3A4 inducer (rifampicin, 600 mg daily for 6 days) followed by a single dose of ZYTIGA 1 000 mg, the mean plasma AUC∞ of abiraterone was decreased by 55 % *(*see section 4.3*).*

Other strong inducers of CYP3A4 (e.g. phenytoin, carbamazepine, rifabutin, rifapentine, phenobarbitone) during treatment with ZYTIGA are to be avoided.

In a separate clinical pharmacokinetic interaction study of healthy subjects, co-administration of ketoconazole, a strong inhibitor of CYP3A4, had no clinically meaningful effect on the pharmacokinetics of ZYTIGA.

Potential for ZYTIGA to affect exposures to other medicines

ZYTIGA is an inhibitor of the hepatic medicine-metabolising enzymes CYP2D6 and CYP2C8. In a clinical study to determine the effects of abiraterone acetate (plus prednisone) on a single dose of the CYP2D6 substrate dextromethorphan, the systemic exposure (AUC) of dextromethorphan was increased by approximately 200 %. The AUC_{24} for dextrorphan, the active metabolite of dextromethorphan, increased approximately 33 %.

Caution is advised when ZYTIGA is administered with medicines activated by or metabolised by CYP2D6, particularly with medicines that have a narrow therapeutic index. Dose reduction of narrow therapeutic index medicines metabolised by CYP2D6 should be considered (e.g.paroxetine, propafenone, flecainide and haloperidol).

In the same study to determine the effects of ZYTIGA (plus prednisone) on a single dose of the CYP1A2 substrate theophylline, no increase in systemic exposure of theophylline was observed).

In a CYP2C8 interaction trial in healthy subjects, the AUC of pioglitazone was increased by 46 % and the AUCs for M-III and M-IV, the active metabolites of pioglitazone, each decreased by 10 %, when pioglitazone was given together with a single dose of 1 000 mg ZYTIGA. Patients should be monitored for signs of toxicity related to CYP2C8 substrate with a narrow therapeutic index if used concomitantly with ZYTIGA.

Concomitant use with Spironolactone

Spironolactone binds to the androgen receptor and may increase prostate specific antigen (PSA) levels. Use with ZYTIGA is not recommended.

Concomitant use with eplenerone

There is no clinical study data related to concomitant use of eplenerone with ZYTIGA.

4.6 Fertility, pregnancy and lactation

Women should not use ZYTIGA.

Women of childbearing potential

There are no human data on the use of ZYTIGA in pregnancy and ZYTIGA is not for use in women of childbearing potential. Maternal use of a CYP17 inhibitor is expected to produce changes in hormone levels that could affect development of the foetus.

Contraception in males and females

It is not known whether abiraterone or its metabolites are present in semen. 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 until one week after the last dose of ZYTIGA.

Pregnancy

ZYTIGA is contraindicated in women who are or may potentially be pregnant (see section 4.3).

Pregnant women or women of child-bearing potential should handle ZYTIGA uncoated tablets with gloves.

Breastfeeding

ZYTIGA is not for use in women. It is not known if either abiraterone acetate or its metabolites are excreted in human breast milk.

Fertility

In fertility studies in both male and female rats, ZYTIGA reduced fertility, which was completely reversible in 4 to 16 weeks after ZYTIGA was stopped.
It is recommended to store semen before starting treatment with ZYTIGA in patients who might want to father a child.

4.7 Effects on ability to drive and use machines

ZYTIGA has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

Clinical trial data

Summary of the safety profile

In an analysis of adverse reactions of composite Phase 3 studies with ZYTIGA, adverse reactions that were observed in ≥ 10 % of patients were peripheral oedema, hypokalaemia, hypertension, urinary tract infection, and increased alanine aminotransferase and/or increased aspartate aminotransferase.

ZYTIGA may cause hypertension, hypokalaemia and fluid retention as a pharmacodynamic consequence of its mechanism of action. In Phase 3 studies anticipated mineralocorticoid effects were seen more commonly in patients treated with ZYTIGA versus patients treated with placebo: hypokalaemia 18 % versus 8 %, hypertension 22 % versus 16 % and fluid retention (peripheral oedema) 23 % versus 17 %, respectively. In patients treated with ZYTIGA versus patients treated with placebo: Grades 3 and 4 hypokalaemia were observed in 6 % versus 1 %, grades 3 and 4 hypertension were observed in 7 % versus 5 %, and grades 3 and 4 fluid retention oedema were observed in 1 % versus 1 % of patients, respectively. Concomitant use of a corticosteroid reduces the incidence and severity of these adverse reactions (see section 4.4).

Tabulated summary of clinical adverse reactions

In studies of patients with metastatic advanced prostate cancer who were using a LHRH agonist, or were previously treated with orchiectomy, ZYTIGA was administered at a dose of 1 g daily in combination with low dose prednisone or prednisolone (5 - 10 mg daily).

Adverse reactions observed during clinical studies with ZYTIGA are listed below by frequency category. Frequency categories are defined as follows: *very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000) and very rare (< 1/10 000).*

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Table 1: Adverse reactions identified in clinical studies with ZYTIGA	
Infections and infestations	*very common*: urinary tract infection *common: sepsis*
Endocrine disorders	*uncommon*: adrenal insufficiency
Metabolism and nutrition disorders	*very common*: hypokalaemia *common*: hypertriglyceridaemia
Cardiac disorders	*common*: cardiac failure*, angina pectoris, atrial fibrillation, tachycardia *uncommon:* dysrhythmia
Vascular disorders	*very common*: hypertension
Gastrointestinal disorders	*very common:* diarrhoea *common:* dyspepsia
Hepatobiliary disorders	*very common*: increased alanine aminotransferase (ALT) and/or increased aspartate aminotransferase[a] (AST)
Skin and subcutaneous tissue disorders	*common*: rash
Musculoskeletal and connective tissue disorders	*uncommon:* myopathy, rhabdomyolysis *common*: fractures**
Renal and urinary disorders	*common: haematuria*
General disorders and administration site conditions	*very common*: peripheral oedema

* *Cardiac failure also includes congestive heart failure, left ventricular dysfunction and fraction decreased ejection*.

** *Fractures include osteoporosis and all fractures with the exception of pathological fracture.*

[a] *Increased alanine aminotransferase and/or increased aspartate aminotransferase includes increased ALT, increased AST, and abnormal hepatic function.*

The following grade 3 adverse reactions occurred in patients treated with ZYTIGA: hypokalaemia in 5 %; urinary tract infection in 2 %, increased alanine aminotransferase and/or increased aspartate aminotransferase in 4 %, hypertension in 6 %, fractures in 2 %; peripheral oedema, cardiac failure and atrial fibrilliation, in 1 % each. Grade 3 hypertriglyceridaemia and angina pectoris occurred in < 1 % of patients. The overall incidence of fractures was 7 %.

Grade 4 urinary tract infection, increased alanine aminotransferase and/or increased aspartate aminotransferase, hypokalaemia, cardiac failure, atrial fibrillation, and fractures occurred in < 1 % of patients.

Description of selected adverse reactions

Cardiovascular effects

Phase 3 studies conducted with ZYTIGA excluded patients with uncontrolled hypertension, clinically significant heart disease as evidenced by myocardial infarction, arterial thrombotic events in the past 6 months, severe or unstable angina, New York Heart Association Class heart disease or with a cardiac ejection fraction measurement of < 50 %. All patients enrolled (both active and placebo-treated patients) were concomitantly treated with androgen deprivation therapy, predominantly with the use of LHRH agonists, which has been associated with diabetes, myocardial infarction, cerebrovascular accident and sudden cardiac death. The incidence of cardiovascular adverse reactions in the phase 3 studies in patients taking ZYTIGA versus patients taking placebo were as follows: atrial fibrillation 2,6 % vs. 2,0 %, tachycardia 1,9 % vs. 1,0 %, angina pectoris 1,7 % vs. 0,8 %, cardiac failure 0,7 % vs. 0,2 % and dysrhythmia 0,7 % vs. 0,45 %.

Hepatotoxicity

Medicine-associated hepatotoxicity with elevated ALT, aspartate transaminase (AST) and total bilirubin commonly occur in patients treated with ZYTIGA.

Across all clinical studies, hepatotoxicity grades 3 and 4 (eg. ALT or AST increases of > 5 x ULN or bilirubin increases > 1,5 x ULN) were reported in approximately 46 % of patients who received ZYTIGA, typically during the first 3 months after starting treatment. In Study 3011, where N = 1199, grade 3 or 4 hepatotoxicity was observed in 8,4 % of patients treated with ZYTIGA. Ten patients who received ZYTIGA were discontinued because of hepatotoxicity; two had Grade 2 hepatotoxicity, six had Grade 3 hepatotoxicity, and two had Grade 4 hepatotoxicity. No patient died of hepatotoxicity in Study 3011. Patients whose baseline ALT or AST were elevated were more likely to experience liver function test elevations than those beginning with normal values. ALT increase and AST increase was reported in 3,9 % and 2,7 % in the ZYTIGA arm vs. 3,8 % and 1,3 % in the placebo arm respectively.

Hyperbilirubinaemia was reported in 1,3 % in the ZYTIGA arm vs. 1,8 % in the placebo arm. When elevations of either ALT or AST > 5 x ULN, or elevations in bilirubin > 3 x ULN were observed, ZYTIGA was withheld or discontinued. Treatment was withheld or discontinued in 0,8 % of subjects in the ZYTIGA as well as the placebo arms. In two instances marked increases in liver function tests occurred (see section 4.4). These two patients with normal baseline hepatic function, experienced ALT or AST elevations 15 to 40 x ULN and bilirubin elevations 2 to 6 x ULN. Upon discontinuation of ZYTIGA, both patients had normalisation of their liver function tests and one patient was re-treated with ZYTIGA without recurrence of the elevations.

In clinical trials, the risk for hepatotoxicity was mitigated by exclusion of patients with baseline hepatitis or significant abnormalities of liver function tests. Abnormal liver function tests developing in patients participating in clinical trials were managed by requiring

treatment interruption and permitting re-treatment only after return of liver function tests to the patient's baseline (see section 4.2). Patients with elevations of ALT or AST > 20 x ULN were not re-treated with ZYTIGA. The safety of re-treatment in such patients is unknown. The mechanism for hepatotoxicity associated with ZYTIGA is not understood.

Post-marketing data

Table 2 : Adverse reactions identified during post-marketing experience

Cardiac disorders Myocardial infarction, QT prolongation
Respiratory, thoracic and mediastinal disorders Allergic alveolitis
Hepatobiliary disorders Fulminant hepatitis, acute hepatic failure
Musculoskeletal and connective tissue disorders Rhabdomyolysis, myopathy

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine product is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions via "6.04 Adverse Drug Reaction Reporting Form" found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/index/8

Alternatively, suspected adverse reactions may be reported directly to Janssen Pharmaceutica (see section 7 for contact details or visit www.janssen.com).

4.9 Overdose

There is no specific antidote. In the event of an overdose, administration of ZYTIGA should be stopped and general supportive measures undertaken, including monitoring for dysrrhythmias. Liver function should also be assessed. In cases of overdose, side effects may be exacerbated and exaggerated.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification

A.21.12 Hormone inhibitors.

Mechanism of action

Abiraterone acetate is converted in vivo to abiraterone, an androgen biosynthesis inhibitor. Abiraterone selectively inhibits the enzyme 17α hydroxylase/C17,20 lyase (CYP17). This enzyme is expressed in and is required for androgen biosynthesis in testicular, adrenal and prostatic tumour tissues. CYP17 catalyses the conversion of pregnenolone and progesterone into testosterone precursors, DHEA and androstenedione, respectively, by 17α hydroxylation and cleavage of the C17,20 bond. CYP17 inhibition also results in increased mineralocorticoid production by the adrenals (see section 4.4).

Androgen sensitive prostatic carcinoma responds to treatment that decreases androgen levels. Androgen deprivation therapies, such as treatment with luteinising hormone-releasing hormone (LHRH) agonists or orchiectomy, decrease androgen production in the testes but

do not affect androgen production by the adrenals or in the tumour. Treatment with abiraterone acetate decreases serum testosterone to undetectable levels (using commercial assays) when given with LHRH agonists (or orchiectomy).

Pharmacodynamic effects

Prostate specific antigen (PSA) serves as a biomarker in patients with prostate cancer. In a phase 3 clinical study of patients who failed prior chemotherapy with taxanes, 38 % of patients treated with abiraterone acetate, versus 10 % of patients treated with placebo, had at least a 50 % decline from baseline in PSA levels.

5.2 Pharmacokinetic properties

Following administration of abiraterone acetate, the pharmacokinetics of abiraterone and abiraterone acetate have been studied in healthy subjects, patients with metastatic advanced prostate cancer and subjects without cancer with hepatic or renal impairment. Abiraterone acetate is rapidly converted *in vivo* to abiraterone, an androgen biosynthesis inhibitor (see section 5.1).

Absorption

Following oral administration of abiraterone acetate in the fasting state, the time to reach maximum plasma abiraterone concentration is approximately 2 hours.

Administration of abiraterone acetate with food, compared with administration in a fasted state, results in up to a 17-fold increase in mean systemic exposure of abiraterone, depending on the fat content of the meal. Given the normal variation in the content and

composition of meals, taking abiraterone acetate with meals has the potential to result in highly variable exposures. Therefore, **abiraterone acetate must not be taken with food.**

Abiraterone acetate should be taken at least two hours after eating and no food should be eaten for at least one hour after taking ZYTIGA. The tablets should be swallowed whole with water (see section 4.2).

Distribution

The plasma protein binding of ^{14}C-abiraterone in human plasma is 99,8 %. The apparent volume of distribution is approximately 5 630 L, suggesting that abiraterone extensively distributes to peripheral tissues.

Metabolism

Following oral administration of ^{14}C-abiraterone acetate as capsules, abiraterone acetate is hydrolysed to abiraterone, which then undergoes metabolism including sulphation, hydroxylation and oxidation primarily in the liver. The majority of circulating radioactivity (approximately 92 %) is found in the form of metabolites of abiraterone. Of 15 detectable metabolites, 2 main metabolites, abiraterone sulphate and N-oxide abiraterone sulphate, each represents approximately 43 % of total radioactivity.

Elimination

The mean half-life of abiraterone in plasma is approximately 15 hours based on data from healthy subjects. Following oral administration of ^{14}C-abiraterone acetate 1 g, approximately 88 % of the radioactive dose is recovered in faeces and approximately 5 % in urine. The major compounds present in faeces are unchanged abiraterone acetate and abiraterone (approximately 55 % and 22 % of the administered dose, respectively).

Patients with hepatic impairment

The pharmacokinetics of abiraterone acetate was examined in subjects with pre-existing mild or moderate hepatic impairment (Child-Pugh class A and B, respectively) and in healthy control subjects. Systemic exposure to abiraterone after a single oral 1 g dose increased by approximately 11 % and 260 % in subjects with mild and moderate pre-existing hepatic impairment, respectively. The mean half-life of abiraterone is prolonged to approximately 18 hours in subjects with mild hepatic impairment and to approximately 19 hours in subjects with moderate hepatic impairment. No dose adjustment is necessary for patients with pre-existing mild hepatic impairment.

There are no data on the clinical safety and efficacy of multiple doses of abiraterone when administered to patients with moderate or severe hepatic impairment (Child Pugh Class B or C). No dose adjustment can be predicted. Abiraterone acetate should not be used in patients with moderate to severe hepatic impairment (see section 4.3).

For patients who develop hepatotoxicity during treatment with abiraterone acetate, suspension of treatment and dose adjustment may be required (see sections 4.2 and 4.4).

Patients with renal impairment

The pharmacokinetics of abiraterone acetate was compared in patients with end-stage renal disease on a stable haemodialysis schedule versus matched control subjects with normal renal function. Systemic exposure to abiraterone after a single oral 1 g dose did not increase in subjects with end-stage renal disease on dialysis. Administration of abiraterone acetate in patients with renal impairment, including severe renal impairment, does not require dose reduction (see section 4.2).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal anhydrous silica

Croscarmellose sodium

Lactose monohydrate

Magnesium stearate

Microcrystalline cellulose

Povidone

Sodium lauryl sulfate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 30 °C. Keep well closed.

This medicine does not require any special storage conditions.

6.5 Nature and contents of container

ZYTIGA 250 mg tablets are supplied in high density polyethylene round white bottles fitted with a white polypropylene cap and packed into an outer carton. Package size is 120 tablets.

6.6 Special precautions for disposal and other handling

Women who are pregnant or women who may be pregnant should not handle ZYTIGA 250 mg tablets without protection, e.g. gloves (see section 4.6).

Any unused medicine should be returned to the pharmacy to be correctly disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

JANSSEN PHARMACEUTICA (Pty.) Ltd.

(Reg No.: 1980/011122/07)

2 Medical Road,

Halfway House, Midrand, 1648

Tel: +27 (11) 518 7000

RA-JACZA-MedInfo@its.jnj.com

8. REGISTRATION NUMBER

46/21.12/0379

9 DATE OF FIRST AUTHORISATION

Date of registration: 31 July 2014

10 DATE OF REVISION OF THE TEXT

Date of the most recently revised Professional Information as approved by SAHPRA: 03 September 2019