hikma.

Press Release

Hikma launches Abiraterone Acetate Tablets

London, 14 February 2019 – Hikma Pharmaceuticals PLC (Hikma, Group) (LSE: HIK) (NASDAQ Dubai: HIK) (OTC: HKMPY) (rated Ba1 Moody's / BB+ S&P, both stable) announces that Hikma Pharmaceuticals USA Inc., formerly known as West-Ward Pharmaceuticals Corp., has launched Abiraterone Acetate Tablets, 250mg, the generic equivalent to Zytiga®.[1] Abiraterone acetate tablets are a CYP17 inhibitor indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer (CRPC).

In October 2018, the United States District Court for the District of New Jersey's invalidated a key Zytiga® patent. On 20 November 2018, the United States Court of Appeals for the Federal Circuit denied the patent holder's request to prevent Hikma's launching Abiraterone Acetate Tablets pending appeal. Hikma was one of the first ANDA applicants to submit an ANDA with a Paragraph IV certification challenging the validity of certain patents listed for Zytiga® tablets, 250mg, and therefore is eligible for 180 days of generic drug exclusivity.

According to IQVIA, US sales of Abiraterone Acetate Tablets were approximately $1,793 million in the 12 months ending December 2018.

Brian Hoffmann, President, Generics Division, said, "We are adding Abiraterone Acetate Tablets to our oncology portfolio, improving patients access to this life-saving product. This launch continues to demonstrate our ability to successfully litigate paragraph IV products, which is an important element of our portfolio strategy."

-- ENDS --

Enquiries
Hikma Pharmaceuticals PLC

Susan Ringdal	+44 (0)20 7399 2760/ +44 7776 477050
EVP, Strategic Planning and Global Affairs	uk-investors@hikma.uk.com

FTI Consulting

Ben Atwell/Andrew Ward	+44 (0)20 3727 1000

[1] Zytiga® is a registered trademark of Janssen Biotech, Inc.

hikma.

About Hikma

Hikma helps put better health within reach every day for millions of people in more than 50 countries around the world. For more than 40 years, we've been creating high-quality medicines and making them accessible to the people who need them. Headquartered in the UK, we're a global company with a local presence across the United States (US), the Middle East and North Africa (MENA) and Europe, and we use our unique insight and expertise to transform cutting-edge science into innovative solutions that transform people's lives. We're committed to our customers, and the people they care for, and by thinking creatively and acting practically, we provide them with a broad range of branded and non-branded generic medicines. Together, our 8,500 colleagues are helping to shape a healthier world that enriches all our communities. We are a leading licensing partner in the MENA region, and through our venture capital arm, are helping bring innovative health technologies to people around the world. For more information, please visit www.hikma.com.

Important Safety Information for Abiraterone Acetate Tablets, 250mg:

Administration
Important Administration Instructions
Patients receiving abiraterone acetate tablets should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy. Abiraterone acetate tablets must be taken on an empty stomach, either one hour before or two hours after a meal. The tablets should be swallowed whole with water. Do not crush or chew tablets.

Dose Modification Guidelines in Hepatic Impairment and Hepatotoxicity
Hepatic Impairment
In patients with baseline moderate hepatic impairment (Child-Pugh Class B), reduce the recommended dose of abiraterone acetate tablets to 250 mg once daily. In patients with moderate hepatic impairment monitor ALT, AST, and bilirubin prior to the start of treatment, every week for the first month, every two weeks for the following two months of treatment and monthly thereafter. If elevations in ALT and/or AST greater than 5X upper limit of normal (ULN) or total bilirubin greater than 3X ULN occur in patients with baseline moderate hepatic impairment, discontinue abiraterone acetate tablets and do not re-treat patients with abiraterone acetate tablets.

Do not use abiraterone acetate tablets in patients with baseline severe hepatic impairment (Child-Pugh Class C).

Hepatotoxicity
For patients who develop hepatotoxicity during treatment with abiraterone acetate tablets (ALT and/or AST greater than 5X ULN or total bilirubin greater than 3X ULN), interrupt treatment with abiraterone acetate tablets. Treatment may be restarted at a reduced dose of 750 mg once daily following return of liver function tests to the patient's baseline or to AST and ALT less than or equal to 2.5X ULN and total bilirubin less than or equal to 1.5X ULN. For patients who resume treatment, monitor serum transaminases and bilirubin at a minimum of every two weeks for three months and monthly thereafter.

If hepatotoxicity recurs at the dose of 750 mg once daily, re-treatment may be restarted at a reduced dose of 500 mg once daily following return of liver function tests to the patient's baseline or to AST and ALT less than or equal to 2.5X ULN and total bilirubin less than or equal to 1.5X ULN.

If hepatotoxicity recurs at the reduced dose of 500 mg once daily, discontinue treatment with abiraterone acetate tablets.

Permanently discontinue abiraterone acetate tablets for patients who develop a concurrent elevation of ALT greater than 3 x ULN and total bilirubin greater than 2 x ULN in the absence of biliary obstruction or other causes responsible for the concurrent elevation.

Dose Modification Guidelines for Strong CYP3A4 Inducers
Avoid concomitant strong CYP3A4 inducers (e.g., phenytoin, carbamazepine, rifampin, rifabutin, rifapentine, phenobarbital) during abiraterone acetate tablets treatment.

If a strong CYP3A4 inducer must be co-administered, increase the abiraterone acetate tablets dosing frequency to twice a day only during the co-administration period (e.g., from 1,000 mg once daily to 1,000 mg twice a day). Reduce the dose back to the previous dose and frequency, if the concomitant strong CYP3A4 inducer is discontinued.

Important Safety Information

Contraindications
Pregnancy
Abiraterone acetate tablets can cause fetal harm and potential loss of pregnancy.

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. Monitor patients for hypertension, hypokalemia and fluid retention at least once a month. Control hypertension and correct hypokalemia before and during treatment with Abiraterone acetate.

Closely monitor patients whose underlying medical conditions might be compromised by increases in blood pressure, hypokalemia or fluid retention, such as those with heart failure, recent myocardial infarction, cardiovascular disease or ventricular arrhythmia. The safety of abiraterone acetate in patients with left ventricular ejection fraction <50% or New York Heart Association (NYHA) Class III or IV heart failure (in COU-AA-301) or NYHA Class II to IV heart failure (in COU-AA-302) has not been established because these patients were excluded from these randomized clinical trials.

Adrenocortical Insufficiency
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. Monitor patients 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. Perform appropriate tests, if clinically indicated, to confirm adrenocortical insufficiency. Increased dosage of corticosteroids may be indicated before, during and after stressful situations.

Hepatotoxicity
In postmarketing experience, there have been abiraterone acetate-associated severe hepatic toxicity, including fulminant hepatitis, acute liver failure and deaths. Measure serum transaminases (ALT and AST) and bilirubin levels prior to starting treatment with abiraterone acetate, every two weeks for the first three months of treatment, and monthly thereafter. In patients with baseline moderate hepatic impairment receiving a reduced abiraterone acetate dose of 250 mg, measure ALT, AST and bilirubin prior to the start of treatment, every week for the first month, every two weeks for the following two months of treatment and monthly thereafter. Promptly measure serum total bilirubin, AST and ALT if clinical symptoms or signs suggestive of hepatotoxicity develop. Elevations of AST, ALT or bilirubin from the patient's baseline should prompt more frequent monitoring. If at any time AST or ALT rise above five times the upper limit of normal (ULN) or the bilirubin rises above three times the ULN, interrupt abiraterone acetate treatment and closely monitor liver function. Re-treatment with abiraterone acetate at a reduced dose level may take place only after return of liver function tests to the patient's baseline or to AST and ALT less than or equal to 2.5X ULN and total bilirubin less than or equal to 1.5X ULN.

Permanently discontinue abiraterone acetate for patients who develop a concurrent elevation of ALT greater than 3X ULN and total bilirubin greater than 2X ULN in the absence of biliary obstruction or other causes responsible for the concurrent elevation.

The safety of abiraterone acetate re-treatment of patients who develop AST or ALT greater than or equal to 20X ULN and/or bilirubin greater than or equal to 10X ULN is unknown.

Adverse Reactions
The most common adverse reactions (≥10%) are fatigue, arthralgia, hypertension, nausea, edema, hypokalemia, hot flush, diarrhea, vomiting, upper respiratory tract infection, cough and headache.

The most common laboratory abnormalities (>20%) are anemia, elevated alkaline phosphatase, hypertriglyceridemia, lymphopenia, hypercholesterolemia, hyperglycemia and hypokalemia.

Drug Interactions
Based on *in vitro* data, abiraterone acetate is a substrate of CYP3A4. In a dedicated drug interaction trial, co-administration of rifampin, a strong CYP3A4 inducer, decreased exposure of abiraterone by 55%. Avoid concomitant strong CYP3A4 inducers during abiraterone acetate treatment. If a strong CYP3A4 inducer must be co-administered, increase the abiraterone acetate dosing frequency. In a dedicated drug interaction trial, co-administration of ketoconazole, a strong inhibitor of CYP3A4, had no clinically meaningful effect on the pharmacokinetics of abiraterone.

Abiraterone acetate is an inhibitor of the hepatic drug-metabolizing enzymes CYP2D6 and CYP2C8. Avoid co-administration with CYP2D6 substrates with a narrow therapeutic index. If alternative treatments cannot be used, consider a dose reduction of the CYP2D6 substrate drug. In a CYP2C8 drug-drug interaction trial in healthy subjects, the AUC of pioglitazone (CYP2C8 substrate), was increased by 46% when pioglitazone was given together with a single dose of 1,000 mg abiraterone acetate. Monitor patients closely for signs of toxicity related to a CYP2C8 substrate with a narrow therapeutic index if used concomitantly with abiraterone acetate.

Use in Specific Populations
Pregnancy and Lactation
Based on findings from animal studies and the mechanism of action, abiraterone acetate is contraindicated for use in pregnant women because the drug can cause fetal harm and potential loss of pregnancy. Abiraterone acetate is not indicated for use in females.

Females and Males of Reproductive Potential
Advise males with female partners of reproductive potential to use effective contraception during treatment and for 3 weeks after the final dose of abiraterone acetate.

Infertility
Based on animal studies, abiraterone acetate may impair reproductive function and fertility in males of reproductive potential.

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

For more information, please see the full Prescribing Information, including Patient Information.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit http://www.fda.gov/medwatch, or call 1-800-FDA-1088.

Manufactured by: The Arab Pharmaceuticals Manufacturing Company, P.O. Box 41, Sahab - Jordan
Distributed by: West-Ward Pharmaceuticals Corp., Eatontown, NJ 07724

Document Identification Number: WW30014