GlaxoSmithKline (GSK) today announced that the European Medicines Agency (EMA) has agreed to remove the conditional status of the marketing authorisation for Votrient (pazopanib) and convert it to a full marketing authorisation. Pazopanib was granted a conditional licence in the European Union in June 2010. The specific obligations of the conditional approval included a non-inferiority study to evaluate the efficacy and safety of pazopanib versus sunitinib¹ (COMPARZ: COMparing the efficacy, sAfety and toleRability of paZopanib vs. sunitinib).

The COMPARZ results were first presented at the European Society of Medical Oncology (ESMO) Congress 2012² by the study's lead investigator, Robert J Motzer, MD of the Memorial Sloan Kettering Cancer Centre, and will be published in a peer-reviewed journal. The study met its primary endpoint demonstrating non-inferiority of pazopanib to sunitinib (Sutent®, Pfizer) in terms of progression-free survival (intent-to-treat population by independent review; hazard ratio 1.047 [95% CI: 0.898-1.220]).²

These results and data from other ongoing studies of pazopanib in advanced renal cell carcinoma (RCC) were reviewed by the Committee for Medicinal Products for Human Use (CHMP), a scientific advisory committee to the EMA, which issued a positive opinion to grant full approval of pazopanib’s marketing authorisation.³ This decision was ratified by the European Commission on 14th June 2013.

Dr Paul Nathan, Consultant Medical Oncologist at The Mount Vernon Cancer Centre, Northwood, commented: “We welcome the EMA’s decision to convert the marketing authorisation for pazopanib to a full approval, which is based on emerging clinical data that supports doctors, nurses and patients to make informed choices in the treatment of advanced renal cell carcinoma”.

The most common adverse events (≥ 30%, all grades) in the COMPARZ study for pazopanib compared to sunitinib, respectively, included: diarrhoea (63% vs. 57%); fatigue (55% vs. 63%); hypertension (46% vs. 41%); nausea (45% vs. 46%); decreased appetite (37% vs. 37%); ALT increase (31% vs. 18%); hair colour changes (30% vs. 10%); hand-foot syndrome (29% vs. 50%); taste alteration (26% vs. 36%); and, thrombocytopenia (10% vs. 34%).²

Erik van Snippenberg, General Manager of GSK UK commented: “GSK is delighted that the EMA has lifted the conditional nature of pazopanib’s licence. This is based on the strength of the COMPARZ head-to-head results, which demonstrate that pazopanib is not less effective than sunitinib with a differentiated tolerability profile.”

Pazopanib is available on the NHS in England and Wales having received a positive Technology Appraisal Guidance in February 2011 from the National Institute of Health and Care Excellence (NICE).⁴ Pazopanib is also available on NHS Scotland following advice issued by the Scottish Medicines Consortium (SMC) in March 2011.⁵

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FURTHER INFORMATION

About VOTRIENT® (pazopanib)

Votrient® (pazopanib) received conditional marketing authorisation in the EU in June 2010 for the first line treatment of advanced Renal Cell Carcinoma (RCC) and for patients who have received prior cytokine therapy for advanced disease.6

Pazopanib is a targeted therapy, known as a tyrosine kinase inhibitor (TKI). TKIs inhibit receptors such as the vascular endothelial growth factor receptor (VEGFR) that controls tumour angiogenesis (the growth of new blood vessels), which is the process that supports the development and progression of tumours. Pazopanib inhibits angiogenesis, thereby slowing tumour growth and the spread of cancer to another part of the body.7,8

COMPARZ was a non-inferiority study designed to show that pazopanib was not less effective than sunitinib with a primary endpoint of progression-free survival (PFS) in the intent-to-treat population by independent review. The criterion for non-inferiority defined in the protocol was the upper bound of a two-sided 95% confidence interval (CI) for the PFS hazard ratio (HR) of <1.25. The non-inferiority margin stipulated by the European Medicines Agency (EMA) was the upper bound of a two-sided 95% CI for the HR of ≤1.22.

The most common adverse events associated with pazopanib (all grades, incidence ≥20%) seen in patients treated for advanced RCC are: diarrhoea, hair colour change, hypertension, nausea, fatigue and decreased appetite.6

The most important serious adverse reactions identified in the RCC trials were transient ischaemic attack, ischaemic stroke, myocardial ischaemia, myocardial and cerebral infarction, cardiac dysfunction, gastrointestinal perforation and fistula, QT prolongation and pulmonary, gastrointestinal and cerebral haemorrhage, all adverse reactions being reported in <1% of treated patients. Fatal events that were considered possibly related to pazopanib included gastrointestinal haemorrhage, pulmonary haemorrhage/haemoptysis, abnormal hepatic function, intestinal perforation and ischemic stroke.6

Please refer to the Summary of Product Characteristics for further information.

About a Conditional Marketing Authorisation

A conditional marketing authorisation is granted to a medicinal product for which the balance between risks and benefits is assessed to be positive, based on the evidence available and that fulfils an unmet medical need, and when the benefit to public health of immediate availability outweighs the risk inherent in the fact that additional data are still required. For a conditional marketing authorisation to be granted, it is also necessary that the applicant will be able to provide comprehensive data. A conditional marketing authorisation is valid for one year, subject to renewal. When the European Medicines Agency (EMA) is satisfied with the additional data provided, the conditional marketing authorisation may be converted into a full marketing authorisation.

References:

2. Motzer RJ, Hutson TE, Reeves J, et al. Randomized, open label, phase III trial of pazopanib versus sunitinib in first-line treatment of patients with metastatic renal cell carcinoma (mRCC); Results of the COMPARZ trial. Abstract and oral presentation at European Society of Medical Oncology Congress 2013. Abstract no. LBA8_PR.
5. SMC. Pazopanib (Votrient). Advice no. 676/11 www.scottishmedicines.org.uk/SMC_Advice/Advice/676_11_pazopanib_Votrient/pazopanib_Votrient

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