Medicines & Healthcare products Regulatory Agency

MHRA

Early Access to Medicines Scientific Opinion - Public Assessment Report	
Product	**Pemigatinib**
EAMS indication	**Treatment of adult patients with cholangiocarcinoma (cancer of the bile ducts) that has spread locally or to other parts of the body and has a specific genetic abnormality (fibroblast growth factor receptor 2 fusion or rearrangement) and has returned after or not responded to treatment with chemotherapy.**
Company	**Incyte Biosciences UK Ltd**
EAMS number	**42338/0002**
EAMS Scientific Opinion date	**15/01/2021**

Introduction
The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines and medicines used outside their licence, to UK patients that have a high unmet clinical need. The MHRA scientific opinion provides benefit and risk information to physicians who may wish to prescribe the EAMS medicine under their own responsibility. More information about the scheme can be found here:
http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm

The scientific opinion is based on assessment of the information supplied to the MHRA on the benefits and risks of the medicine. As such this is a scientific opinion and should not be regarded as a medicine licensed by the MHRA or a future commitment by the MHRA to license such a medicine, nor should it be regarded as an authorisation to sell or supply such a medicine. A positive scientific opinion is not a recommendation for use of the medicine and should not be interpreted as such. Under EAMS the risk and legal responsibility for prescribing a 'special' remains with the physician, and the opinion and EAMS documentation published by the MHRA are intended only to inform physicians' decision making and not to recommend use. An EAMS scientific opinion does not affect the civil liability of the manufacturer or any physician in relation to the product.

The General Medical Council's guidance on prescribing unlicensed medicines can be found here:
https://www.gmc-uk.org/guidance/ethical_guidance/14327.asp

What is pemigatinib?

Pemigatinib is the active substance of a medicine, which is a tablet, taken orally.

What is pemigatinib used to treat?
Pemigatinib is used to treat a type of bile duct cancer (cholangiocarcinoma) with a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement that has spread locally or distantly and is not responding to or has worsened after treatment with a least one course of chemotherapy treatment.

How is pemigatinib used?

Pemigatinib treatment should be started only by a doctor experienced in the diagnosis and treatment of patients with biliary tract cancer. FGFR2 fusion or rearrangement must be confirmed in a tumour specimen by an appropriate diagnostic test before pemigatinib therapy is started.
The recommended dose is 13.5mg pemigatinib tablet taken orally once daily for 14 days followed by 7 days off therapy. The tablet should be swallowed whole and can be taken with or without food. Treatment should be continued as long as the patient does not show evidence of disease progression or unacceptable toxicity.

How does pemigatinib work?
Permanent activation of FGFR signalling can encourage the growth and survival of malignant cells. In experiments in cancer cells with FGFR amplifications and fusions that lead to constant FGFR signalling, pemigatinib prevents phosphorylation of FGFR, interfering with signalling in the cell and reducing cell survival.

How has pemigatinib been studied?
Pemigatinib has been studied in 107 patients with locally advanced unresectable or metastatic cholangiocarcinoma that had progressed after at least one previous chemotherapy treatment and had an FGFR2 fusion or rearrangement. The main measure of effectiveness (how well the medicine worked) was the reduction in the size of the tumour, specifically whether the tumour shrank by more than 30% (partial response) or disappeared (complete response) and how long this response lasted for (duration of response).

When should pemigatinib not be given?
Pemigatinib should not be given to patients taking St John's wort, as this reduces the level of pemigatinib in the body so that it might not be effective against the tumour.

What are the benefits and risks of pemigatinib?
Benefits
In the 107 patients with cholangiocarcinoma and FGFR2 fusion or rearrangement, the tumour disappeared in 3 patients and shrank by more than 30% in 35 patients, meaning that 38 patients (35.5%) responded. The duration of response was at least 6 months in 24 responders (63%) and at least 12 months in 7 responders (18%).

Risks
The most common side effect is increased levels of phosphate in the blood (hyperphosphataemia), which affected over half of the patients in the study. Other very common side effects (which may affect more than 1 in 10 people) include change in taste, dry eyes, nausea, diarrhoea, constipation, low levels of sodium in the blood and high levels of creatinine in the blood. Common side effects (may affect up to 1 in 10 people) include nail changes and a build-up of fluid at the back of the eye which can cause the light sensitive layer to become separated (serous retinal detachment). Specialist eye examinations are needed before starting treatment with pemigatinib and at regular intervals during pemigatinib treatment. Pemigatinib can harm the unborn child; effective contraception is required.

Why has pemigatinib been given a positive Early Access to Medicine Scientific opinion?
Cholangiocarcinoma is a rare cancer with a poor prognosis and less than 10% of patients with advanced disease survive for 5 years. There are no licenced treatments for patients with advanced disease that has progressed after an initial course of chemotherapy or for cholangiocarcinoma with FGFR2 fusion or rearrangements. Available chemotherapy options give a response in 8% to 12% of patients. The response with pemigatinib in 35.5% of patients is a meaningful improvement over these other possible therapies. The risks associated with pemigatinib can be managed and do not outweigh the benefits.

What are the uncertainties?
The study did not compare pemigatinib to another treatment for cholangiocarcinoma. Therefore, it is not known by how much overall survival is improved or how much longer people treated with pemigatinib live before their disease gets worse (progression free survival) compared to if they received treatment with

chemotherapy. The company that makes pemigatinib will provide additional information when it becomes available.

Are there on-going clinical studies?
There is a study of pemigatinib compared to chemotherapy in patients with advanced or metastatic cholangiocarcinoma with FGFR2 rearrangement that have not received any previous chemotherapy treatment for their advanced disease. The company that makes pemigatinib will provide additional information when it becomes available.

What measures are in place to monitor and manage risks?
A risk management plan has been developed to ensure that pemigatinib is used as safely as possible. Based on this plan, the company that makes pemigatinib must ensure that all healthcare professionals expected to use the medicine, as well as patients, are provided with information on the medicine, including the side effects and recommendations for minimising these side effects.

Information will be collected about patients before they enter the scheme. Healthcare professionals will be asked by the company to report adverse effects experienced by patients receiving pemigatinib through the scheme. These safety data will be reviewed and reported to the MHRA on a regular basis by the company.

Patients in the Early Access to Medicines Scheme will also receive an alert card from their doctor summarising the important risks with the medicine and the details of their treating physician. Patients should carry the card with them at all times in case they need treatment or advice from a healthcare professional who is not familiar with pemigatinib treatment.

Other information about pemigatinib – see EAMS Treatment Protocol