Medicines & Healthcare products Regulatory Agency

MHRA

Early Access to Medicines Scientific Opinion - Public Assessment Report	
Product	**Tepotinib**
EAMS indication	**Tepotinib is used for the treatment of adults with advanced non-small cell lung cancer (NSCLC) that has certain abnormal changes in the mesenchymal-epithelial transition factor gene (*MET*).**
Company	**Merck Serono Limited**
EAMS number	**11648/0004**
EAMS Scientific Opinion date	**12 July 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 tepotinib?
Tepotinib is the active substance of a medicine, which is taken by mouth.

What is tepotinib used to treat?
Tepotinib is used to treat a type of lung cancer, called non-small cell lung cancer that has certain abnormal changes in the mesenchymal-epithelial transition factor gene (*MET*) and which has spread and/or cannot be removed by surgery.

How is tepotinib used?

Tepotinib can only be prescribed by specialist doctors experienced in treating cancer.

Tepotinib is a tablet taken by mouth with food or shortly after a meal.

The recommended dose is 2 tablets of tepotinib (450 mg) once daily. In case of side effects, your doctor may advise you to reduce the dose to 1 tablet daily or interrupt the treatment for some days or stop treatment permanently.

How does tepotinib work?

Tepotinib belongs to a group of medicines called protein kinase inhibitors. It blocks an abnormal protein produced by abnormal changes in the mesenchymal-epithelial transition factor gene (*MET*), and in doing so causes the growth of cancer to slow and the cancer to shrink.

How has tepotinib been studied?

The effects of tepotinib were studied in 146 patients whose non-small cell lung cancer has abnormal changes in the mesenchymal-epithelial transition factor gene (*MET*). All patients received the same treatment (single-arm, open label study).

The measures of effectiveness (how well the medicine worked) were the response to treatment by assessing the change in growth of the tumour, the time response lasted for (duration of response), progression-free survival (how long the patients lived without their cancer getting worse) and overall survival (how long the patients lived).

What are the benefits and risks of tepotinib?

Benefits

Tumour shrinkage of at least 30% was seen in 45% of the NSCLC patients treated with tepotinib. For those patients whose tumour shrank, the response lasted about 11 months. At 9 months of follow-up, the proportion of patients without progression of disease was 49%, and the proportion of patients still alive was 69%.

Risks

The most common side effects, affecting at least 20% of patients treated with tepotinib, were swelling caused by fluid build-up in the body (oedema), fatigue (tiredness), nausea (feeling sick), diarrhoea, and shortness of breath. The most common abnormal blood test results were reduced protein levels which may cause swelling, increased creatinine levels and higher than normal liver enzymes which may indicate liver problems. Cases of a serious lung condition (interstitial lung disease) have been reported.

Your doctor may reduce or stop the treatment if side effects are severe.

Why has tepotinib been given a positive Early Access to Medicine Scientific opinion?

The standard treatment of non-small cell lung cancer is chemotherapy and/or immunotherapy when there is no suitable targeted therapy. However, targeted therapy is generally more effective. Tepotinib

is a targeted therapy for non-small cell lung cancer with abnormal changes in the mesenchymal-epithelial transition factor gene (*MET*).
Tepotinib is also convenient to take because it is a tablet, unlike chemotherapy and/or immunotherapy which are given into a vein (intravenously).
The side effects of tepotinib are manageable.

What are the uncertainties?

The number of patients studied was small. Furthermore, tepotinib has not been directly compared with standard treatments. These make it difficult to precisely evaluate the importance of the benefits and side effects.
The company that makes tepotinib will provide additional information when it becomes available.

Are there on-going clinical studies?

The number of patients enrolled in the main trial is being expanded.

What measures are in place to monitor and manage risks?

A risk management plan has been developed to ensure that tepotinib is used as safely as possible. Based on this plan, the company that makes tepotinib must ensure that all healthcare professionals expected to use the medicine, as well as patients, are provided with information on the medicines 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 side effects experienced by patients receiving tepotinib through the scheme. To assist with this, they will receive a physician pack and training prior to commencement of patient treatment. These safety data will be reviewed and reported to the MHRA on a regular basis by the company

Other information about tepotinib – see EAMS Treatment Protocol