Medicines & Healthcare products Regulatory Agency

MHRA

Early Access to Medicines Scientific Opinion - Public Assessment Report	
Product	**Nivolumab**
EAMS indication	**Treatment as a single agent of adult patients with advanced oesophageal cancer, which is inoperable or has recurred or spread following cancer chemotherapies**
Company	**Bristol-Myers Squibb Pharmaceuticals Limited**
EAMS number	**15105/0010**
EAMS Scientific Opinion date	**04 June 2020**

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 nivolumab?
Nivolumab is the active substance of a medicine, which is available as a concentrated solution (liquid) that can be diluted for infusion (drip) into a vein. This medicine is already authorised for the treatment of patients with other types of cancer (melanoma, non-small cell lung cancer, renal cell carcinoma, classical Hodgkin lymphoma, squamous cell cancer of the head and neck and urothelial carcinoma) under the name Opdivo®.

What is nivolumab used to treat?
Nivolumab is used to treat adults with advanced oesophageal (gullet) cancer of a certain type (squamous cell carcinoma), which cannot be removed by surgery or has recurred or spread following standard combination chemotherapy.

How is nivolumab used?
Treatment with nivolumab should be started and supervised by a specialist doctor experienced in treating cancer.

The doctor will carry out blood tests to check the patient's liver, kidney and thyroid function before and during treatment.

Nivolumab is given as an infusion into a vein over 30 minutes every two weeks for as long as the patient keeps benefitting from treatment or until it is no longer tolerated. The recommended dose for each infusion is 240 mg.

How does nivolumab work?
Nivolumab is a monoclonal antibody. A monoclonal antibody is a type of protein that has been designed to recognise and attach to a specific structure (called an antigen) that is found in certain cells in the body. Nivolumab has been designed to attach to and block the activity of a protein called PD-1 that is found on the surface of T cells, a type of white blood cell of the immune system able to detect and fight cancer cells. When the PD-1 pathway is active, it stops T cells from attacking cancer cells. By blocking PD-1, nivolumab restores the capacity of T cells to fight cancer cells.

How has nivolumab been studied?
The main study of the effects of nivolumab has enrolled 419 adult patients, aged 64 years on average and with advanced oesophageal cancer that had progressed or recurred after standard combination chemotherapy regimens. Nivolumab was compared with chemotherapy (paclitaxel or docetaxel).

The main measure of effectiveness (how well the medicine worked) was overall survival (how long the patients lived).

What are the benefits and risks of nivolumab?

Benefits
Patients treated with nivolumab had an increase in overall survival. After 12 months, 47% were alive compared to 34% of those receiving chemotherapy. After 18 months, these proportions were 31% and 21%, respectively.

Risks
Nivolumab may be associated with side effects resulting from excessive activity of the immune system, including endocrine abnormalities, diarrhoea/colitis, hepatitis, pneumonitis, nephritis, renal dysfunction and skin adverse reactions. Most will resolve following appropriate treatment or on stopping nivolumab.

The most frequent side effects of nivolumab, affecting at least 10% of the patients, are fatigue (tiredness), skin rash, pruritus (itching), diarrhoea and nausea (feeling sick).

A higher proportion of patients treated with nivolumab died within the first 3 months of treatment 15% compared to 7% of those treated with chemotherapy. The reasons behind this observation are currently not known.

Why has nivolumab been given a positive Early Access to Medicine Scientific opinion?
There is no licensed treatment for oesophageal cancer at this stage of the disease and patients are offered palliative therapy to ease their symptoms. Chemotherapy may be used but does not prolong survival while nivolumab has been shown overall to increase patient survival. With regard to the medicine's side effects, the most frequent were mild to moderate in severity.

What are the uncertainties?
The study supporting the effectiveness of nivolumab was mainly conducted in Asian countries and enrolled fit subjects so that the effectiveness in European and unwell patients has not been fully established.
The company that makes nivolumab will provide additional information when it becomes available.

Are there on-going clinical studies?
There are ongoing studies on nivolumab alone or combined with another cancer therapy (ipilimumab) at different stages of the disease.

What measures are in place to monitor and manage risks?
A risk management plan has been developed to ensure that nivolumab is used as safely as possible. Based on this plan, the company that makes nivolumab 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 nivolumab through the scheme. These safety data will be reviewed and reported to the MHRA on a regular basis by the company.

Patients will also receive an alert card from their doctor summarising the important risks with the medicine and the details of their treating doctor. 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 nivolumab treatment.

Other information about nivolumab – see EAMS Treatment Protocols