Early Access to Medicines Scientific Opinion - Public Assessment Report	
Product	**Pembrolizumab**
Condition **Full indication**	**Pembrolizumab is used to treat a type of lung cancer which has spread to other organs and is characterised by non-small cells** **Treatment as monotherapy of adults with metastatic non-small cell lung cancer (NSCLC) whose tumours express PD-L1 as determined by a validated test and who have not received prior systemic therapy and are negative for EGFR sensitising mutation and ALK translocation**
Company	**Merck Sharp & Dohme Limited**
EAMS number	**00025/0001**

Introduction
The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines to UK patients that have a high unmet clinical need. The MHRA scientific opinion provides benefit and risk information to doctors who may wish to prescribe the unlicensed 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 the information supplied to the MHRA on the benefits and risks of a promising new 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 licence such a medicine. The General Medical Council's guidance on prescribing unlicensed medicines can be found here: http://www.gmc-uk.org/mobile/news/14327

What is pembrolizumab?
Pembrolizumab is the active substance of a medicine, which is available as a powder that is made up into a solution for infusion (drip) into a vein. This medicine is already authorised under the name Keytruda® for the treatment of patients with another type of cancer (melanoma) and also for patients previously treated for the type of lung cancer described below.

What is pembrolizumab used to treat?
Pembrolizumab is used as first therapy to treat adults diagnosed with advanced lung cancer of a certain type (i.e. non-small cell lung cancer – "NSCLC"), which has spread to other organs. In addition, the tumour should exhibit a certain level of a protein called programmed death ligand-1 (PD-L1), which is measured in a biopsy by a specialised laboratory.

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

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

Pembrolizumab is given as an infusion into a vein over 30 minutes every three weeks and is continued for as long as the patient keeps benefitting from treatment or until it is no longer tolerated. The recommended dose for each infusion is 2 mg per kilogram body weight.

How does pembrolizumab work?
Pembrolizumab 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. Pembrolizumab 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, pembrolizumab prevents its binding to PD-L1 on the surface of the tumour cells, hence restoring the capacity of T cells to fight cancer cells. Pembrolizumab works best if the tumour exhibits a certain level of PD-L1, which is measured in a biopsy by a specialised laboratory.

How has pembrolizumab been studied?
The effects of pembrolizumab have been looked at in a study that enrolled 550 patients with advanced NSCLC who received several dosing regimens of pembrolizumab. In most patients, disease had progressed following standard chemotherapy. The measures of effectiveness (how well the medicine worked) were the evolution of the tumour size, progression-free survival (how long the patients lived without their cancer getting worse) and overall survival (how long the patients lived).

What benefits and risks has pembrolizumab shown during the studies?

Benefits
If the tumour exhibited PD-L1 above a certain defined level, its shrinking was observed in 47% of the patients that had not received prior treatment and approximately 94% of these patients survived for at least six months.

Risks
Pembrolizumab may be associated with side effects resulting from excessive activity of the immune system, including endocrine abnormalities, pneumonitis, colitis, hepatitis, nephritis and rash. Most will resolve following appropriate treatment or on stopping pembrolizumab.

The most frequent side effects are fatigue (tiredness), diarrhoea, nausea, itching, skin rash and joint pain.

Why has pembrolizumab been given a positive Early Access to Medicine Scientific opinion?
Pembrolizumab has been shown to slow the progression of tumours that exhibits PD-L1 and increase patient survival in a condition where chemotherapy regimens have currently poor results. With regard to the medicine's side effects, the most frequent were mild to moderate in severity. Advanced lung cancer is a fatal condition and currently available chemotherapies used as first treatment have low efficacy.

What are the uncertainties?
The effects of pembrolizumab have not been compared to those of current treatments for advanced lung cancer in the same study, which is needed to measure its effectiveness more precisely, and the results on survival are still preliminary. The company that makes pembrolizumab has committed to provide further data when they become available.

Are there on-going clinical studies?
Several studies with pembrolizumab are ongoing in a number of different cancers, including lung cancer. Only preliminary results are available for a study in advanced NSCLC, which compares the safety and efficacy of pembrolizumab to standard chemotherapy in patients who have not received prior therapy.

What measures are in place to monitor and manage risks?
A risk management plan has been developed to ensure that pembrolizumab is used as safely as possible. Based on this plan, the company that makes pembrolizumab 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 related to the excessive activity of the immune system 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 pembrolizumab 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. Patients should carry the card with them in case they need treatment or advice from a healthcare professional that is not familiar with pembrolizumab treatment.

Other information about pembrolizumab – see EAMS Treatment Protocol