Early Access to Medicines Scientific Opinion - Public Assessment Report	
Product	**Nivolumab**
Condition **Full indication**	**Nivolumab is used to treat a type of cancer of the lymph system, which has not responded or come back after transplant of blood forming cells and treatment with brentuximab vedotin** **Treatment as monotherapy of adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL) after autologous stem cell transplant (ASCT) and treatment with brentuximab vedotin**
Company	**Bristol-Myers Squibb Pharmaceuticals Limited**
EAMS number	**15105/0004**

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 nivolumab?
Nivolumab is the active substance of a medicine, which is available as a concentrated solution (liquid) that is diluted for infusion (drip) into a vein. This medicine is already authorised for the treatment of patients with other types of cancer (melanoma, lung and renal cancers) under the name Opdivo®.

What is nivolumab used to treat?
Nivolumab is used to treat adults with classical Hodgkin lymphoma, a certain type of cancer of the lymph system (a part of the immune system) with large abnormal lymphocytes (a type of white blood cell) in the lymph nodes. Nivolumab is used if the tumour has not responded (refractory) or come back (relapsed) after injection of the patient's own blood forming cells (autologous stem cell transplant) and treatment with brentuximab vedotin (Adcetris®).

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 60 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 3 mg per kilogram body weight.

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 studies of the effects of nivolumab have enrolled 95 patients with classical Hodgkin lymphoma that had not responded or come back after transplant of blood forming cells and treatment with brentuximab vedotin.

The measures of effectiveness (how well the medicine worked) were the tumour response (growth or shrinkage), 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 nivolumab shown during the studies?

Benefits
A shrinking of the tumour was observed in 66% of the patients and the proportion of patients alive at 12 months without their cancer getting worse was 57%.

Risks
Nivolumab may be associated with side effects resulting from excessive activity of the immune system, including endocrine abnormalities, diarrhoea/colitis, hepatitis, pneumonitis, nephritis and rash. 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, itching, diarrhoea and nausea (feeling sick).

Why has nivolumab been given a positive Early Access to Medicine Scientific opinion?
Nivolumab has been shown to decrease the tumour size after failure of several treatments which currently constitute standard therapy. With regard to the medicine's side effects, the most frequent are mild to moderate in severity. At this advanced stage, Hodgkin lymphoma is a fatal condition with no effective therapy currently available.

What are the uncertainties?
Further results on survival are being collected. The company that makes nivolumab will provide more information when it becomes available.

Are there on-going clinical studies?
Studies are ongoing in patients with relapsed or refractory Hodgkin lymphoma who have received autologous stem cell transplant with or without prior brentuximab vedotin, and also in combination with other cancer therapies.

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 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 nivolumab 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 nivolumab treatment.

Other information about nivolumab – see EAMS Treatment Protocol