

Early Access to Medicines Scientific Opinion - Public Assessment Report	
Product	Nivolumab
Condition	Nivolumab is used to treat advanced melanoma (a type of skin cancer affecting cells called melanocytes), which has spread or cannot be removed by surgery
Full indication	Treatment of advanced (unresectable or metastatic) melanoma in adults
Company	Bristol-Myers Squibb Pharmaceutical Limited
EAMS number	15105/0011

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>

On 23 April 2015, the Committee for Medicinal Products for Human Use (CHMP), which is part of the European Medicines Agency (EMA), adopted a positive opinion, recommending the granting of a marketing authorisation in the European Union for the medicinal product Opdivo (nivolumab), which is intended for the treatment of advanced (unresectable or metastatic) melanoma in adults. This can be found here:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/003985/smops/Positive/human_smop_000808.jsp&mid=WC0b01ac058001d127

The marketing authorisation has not been granted at this time.

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.

What is nivolumab used to treat?

Nivolumab is used to treat adults with advanced melanoma (a type of skin cancer affecting cells called melanocytes), which has spread or cannot be removed by surgery.

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 effects of nivolumab have been studied in 418 patients with advanced melanoma who had not received prior therapy; nivolumab was compared with dacarbazine, a type of cancer chemotherapy.

The effects of nivolumab have also been studied in 405 patients with advanced melanoma who had previously received ipilimumab, and where appropriate, a BRAF inhibitor, after this treatment had not worked or had stopped working. Nivolumab was compared with chemotherapy (dacarbazine or carboplatin with paclitaxel).

The measures of effectiveness (how well the medicine worked) were the growth of the tumour, overall survival (how long the patients lived), and progression-free survival (how long the patients lived without their cancer getting worse).

What benefits and risks has nivolumab shown during the studies?

Benefits

Amongst patients who had not received previous therapy, those treated with nivolumab had an increase in overall survival: after 12 months, 73% were alive compared to 42% of those treated with dacarbazine.

Amongst patients who had failed previous therapies, a shrinking of their tumour was observed in 32% of those treated with nivolumab compared to 11% of those treated with chemotherapy.

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, affecting at least 10% of the patients, were fatigue (tiredness), rash,

pruritus (itching), diarrhoea, and nausea (feeling sick).

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

Nivolumab has been shown to slow the progression of cancer and increase patient survival in a condition where other treatments currently have poor results. With regard to the medicine's side effects, the most frequent were mild to moderate in severity. Advanced melanoma is a fatal condition and currently few therapies are available with low to moderate efficacy.

What are the uncertainties?

The results on survival are still preliminary. Certain proteins found on the surface of the cancer cells may predict treatment response and this should be further studied. The company that makes nivolumab has committed to provide this information when it becomes available.

Are there on-going clinical studies?

Apart from the two studies already described, a study comparing nivolumab to ipilimumab and to the combination of nivolumab and ipilimumab in previously untreated patients is on-going.

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 who is not familiar with nivolumab treatment.

Other information about nivolumab – see EAMS Treatment Protocol