Medicines & Healthcare products Regulatory Agency

Early Access to Medicines Scientific Opinion - Public Assessment Report	
Product	**Dostarlimab**
EAMS indication	**Dostarlimab is used in combination with platinum-containing anticancer medicines in adults to treat endometrial cancer (cancer of the lining of the womb) that has a gene abnormality called mismatch repair deficient / microsatellite instability-high and the cancer is at an advanced stage when first diagnosed or has returned after previous treatment.**
Company	**GlaxoSmithKline UK Limited**
EAMS number	**52719/0001**
EAMS Scientific Opinion date	**29/06/2023**

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 dostarlimab?

Dostarlimab is the active substance of a medicine, which is available as a solution concentrate that is further diluted for infusion (drip) into a vein.

What is dostarlimab used to treat?

Dostarlimab is used in combination with other drugs that contain platinum to treat adults who have endometrial cancer (cancer of the lining of the womb) that has a gene abnormality called mismatch repair deficient / microsatellite instability-high and the cancer is at an advanced stage when first diagnosed (called primary advanced) or has returned (called recurrent) after previous treatment.

How is dostarlimab used?

Treatment with dostarlimab must be started and supervised by a doctor experienced in treating cancer.

Dostarlimab is given by infusion (drip) into a vein over 30 minutes. The dose is 500 mg once every 3 weeks for the first 6 doses (each cycle lasts 3 weeks) and then 1,000 mg every 6 weeks (each cycle lasts 6 weeks). Treatment can be continued as long as it continues to work and is well tolerated or for up to 3 years. The doctor may interrupt dostarlimab treatment or stop it altogether if certain side effects occur.

Treatment with other drugs that contain platinum will be given in addition to dostarlimab, and this treatment will be decided by your doctor. For example, you may receive the drugs carboplatin and platinum every 3 weeks for the first 6 cycles.

How does dostarlimab work?

Dostarlimab is a monoclonal antibody, a protein that has been designed to block a receptor (target) called PD-1 on certain cells of the immune system. Some cancers can make proteins that combine with PD-1 to switch off the activity of the immune cells, preventing them from attacking the cancer. By blocking PD-1, dostarlimab stops the cancer switching off these immune cells, thereby increasing the immune system's ability to kill the cancer cells.

How has dostarlimab been studied?

The main study of the effects of dostarlimab in combination with carboplatin/paclitaxel (a type of platinum therapy) enrolled 494 patients with primary advanced or recurrent endometrial cancer. A total of 118 patients had been diagnosed with the gene abnormality called mismatch repair deficient / microsatellite instability-high. The combination of dostarlimab, carboplatin and paclitaxel was compared to treatment with placebo, carboplatin and paclitaxel (essentially carboplatin and paclitaxel).

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

What are the benefits and risks of dostarlimab?

Benefits

When dostarlimab is given in combination with carboplatin/paclitaxel to patients diagnosed with mismatch repair deficient / microsatellite instability-high primary advanced or recurrent endometrial cancer, the proportion of patients without progression of disease at 2 years was 61% compared to 16% in those treated only with carboplatin/paclitaxel. The combination of dostarlimab with carboplatin/paclitaxel also prolonged overall survival as 83% of the patients were still alive at 2 years compared to 59% of the patients who had only received carboplatin/paclitaxel.

Risks

The most common adverse reactions affecting at least 10% of patients, which attributed to dostarlimab when in combination with carboplatin/paclitaxel, were rash, hypothyroidism (low levels of thyroid hormones), abnormal liver tests, fever, and dry skin. Adverse reactions were serious in up to 6% of patients; most serious adverse reactions were immune-related adverse reactions.

Why has dostarlimab been given a positive Early Access to Medicine Scientific opinion?
Endometrial cancer initially diagnosed at an advanced stage (primary advanced) or if returns (first recurrent) after prior treatment carries a poor prognosis with a reduced life expectancy and patients suffer from debilitating symptoms and deterioration in their quality of life. There is currently no treatment licensed for primary advanced or recurrent endometrial cancer and most patients receive platinum therapy (like carboplatin/paclitaxel). In patients with primary advanced or recurrent endometrial cancer that has the gene abnormality called mismatch repair deficient / microsatellite instability-high, the combination of dostarlimab with carboplatin/paclitaxel has been shown to notably slow the progression of cancer and prolong patient survival despite some increase in side effects. These side effects are usually manageable if appropriate measures are in place.

What are the uncertainties?

Data on overall survival are still preliminary. The company that makes dostarlimab will provide additional information when it becomes available.

Are there on-going clinical studies?

The main study evaluating the use of dostarlimab in combination with carboplatin/paclitaxel is still ongoing and further results on the benefits and risks of dostarlimab will be provided once they become available.

What measures are in place to monitor and manage risks?

A risk management plan has been developed to ensure that dostarlimab is used as safely as possible. Based on this plan, the company that makes dostarlimab must ensure that all healthcare professionals expected to use the medicine, as well as patients, are provided with information on the medicine including their side effects and recommendations for preventing or minimising the impact of 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 dostarlimab through the scheme. These safety data will be reviewed and reported to the MHRA on a regular basis by the company.

Healthcare professionals involved in the management of the scheme will receive specific training from the company prior to commencement of patient treatment.

Patients will receive an alert card from their doctor summarising the important risks with the medicine and the details of their treating oncologist. Patients should carry the card with them at all times in case they need treatment or advice from a healthcare professional that is not familiar with dostarlimab treatment.

Other information about dostarlimab – see EAMS Treatment Protocol