Medicines & Healthcare products Regulatory Agency

MHRA

Early Access to Medicines Scientific Opinion - Public Assessment Report	
Product	**Risankizumab**
EAMS indication	**Risankizumab is indicated for the treatment of adult patients with moderately to severely active Crohn's disease who have had an inadequate response to, lost response to, or were intolerant or contraindicated to tumour necrosis factor-alpha (TNFα) antagonist therapies, vedolizumab and ustekinumab and for the treatment of adolescent patients aged 16 to 17 years with moderately to severely active Crohn's disease who have had an inadequate response to, lost response to, or were intolerant or contraindicated to TNFα antagonist therapies.**
Company	**AbbVie Ltd**
EAMS number	**41042/0007**
EAMS Scientific Opinion date	**13/04/2022**

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 risankizumab?

Risankizumab is the active substance of a medicine, which is given by injection via infusion during the induction phase and under the skin during the maintenance phase. Risankizumab is supplied as vials and as ready to use syringe.

What is risankizumab used to treat?
Risankizumab is a medicine used to treat adults and adolescents aged 16 to 17 years with Crohn's disease (a disease causing inflammation of the digestive tract).

In adults, risankizumab is used to treat moderately to severely active disease when conventional therapy or medicines called TNFα antagonists, vedolizumab and ustekinumab are ineffective, no longer effective, or cannot be tolerated by the patient.
In adolescents aged 16 to 17 years, risankizumab is used to treat moderately to severely active disease when conventional therapy or medicines called TNFα antagonists are ineffective, no longer effective, or cannot be tolerated by the patient.

How is risankizumab used?
Risankizumab is available as a concentrate for solution for infusion (drip) into a vein and as a pre-filled syringe for injection under the skin. It can only be obtained with a prescription and treatment should be supervised by a specialist who has experience in the diagnosis and treatment of Crohn's disease.
The recommended dose by infusion into a vein is 600mg given at the start and at Weeks 4 and 8, followed by 360mg (four 90mg injections) administered under the skin at Week 12, and then every 8 weeks.

How does risankizumab work?
Risankizumab is a monoclonal antibody (a type of protein) that has been designed to block IL-23 to bind to its receptor. By blocking IL-23 from binding to its receptor, risankizumab inhibits IL-23 dependent release of pro-inflammatory cytokines, and thus reduces the inflammation in the gut and the symptoms of these diseases.

How has risankizumab been studied?
Three main studies were conducted to demonstrate the efficacy of risankizumab for the treatment of patients with moderately to severely active Crohn's disease aged 16 years and older. Risankizumab was compared with placebo.

The measures of effectiveness (how well the medicine worked) were the remission of symptoms (stool frequency and abdominal pain) and mucosal inflammation.

When should risankizumab not be given?
Risankizumab may increase the risk of infection and should not be given to patients with clinically important active infections (e.g. active tuberculosis). Risankizumab is contraindicated in patients with hypersensitivity to the active substance or any of the excipients.

What are the benefits and risks of risankizumab?

Benefits
The efficacy of risankizumab was assessed in 1419 subjects with moderately to severely active Crohn's disease.

In one main induction phase study in patients with moderately to severely active Crohn's disease in whom TNFα antagonists or other biologics were ineffective or could not be tolerated, 34.6% (66 out of 191) of patients receiving 600mg of risankizumab showed improved symptoms (stool frequency and abdominal pain) after 12 weeks of treatment, compared with 19.3% (36 out of 187) of patients on placebo.
Risankizumab 600mg also showed improvement of mucosal inflammation in 28% (55 out of 191) compared to placebo 11.2% (21 out of 187) at week 12.

In another main induction phase study in patients with moderately to severely active Crohn's disease in whom conventional therapies or other biologic therapy were ineffective, 43.5% (146 out of 336) of patients receiving 600mg of risankizumab showed improved symptoms (stool frequency and abdominal pain) after 12 weeks compared with 21.7% (38 out of 175) of patients on placebo.
Risankizumab also showed improvement of mucosal inflammation in 40.3% (135 out of 336) compared to placebo 12.0% (21 out of 175).

Similarly, a maintenance study of the effect up to 52 weeks with risankizumab 360mg was more effective than placebo in controlling symptoms (51.8% vs 39%) and in improving mucosal inflammation (46.5% vs 22%).

Risks
The side effects of risankizumab reported in adolescents are comparable to those in adults. Upper respiratory infections are very common. Common adverse events are injection site reactions, tiredness, itching of the skin, headache and tinea infections.

Why has risankizumab been given a positive Early Access to Medicine Scientific opinion?
Crohn's disease is a disease that has a major impact on quality of life and the treatment options available have some limitations in achieving and maintaining clinical remission is some patients.

Risankizumab is being made available to adolescent patients aged 16 to 17 years with the highest need, when the disease is not controlled with the available therapies or where these treatments are not recommended or are not tolerated.

Risankizumab shows meaningful improvement in symptoms compared to placebo in patients that were not responsive or intolerant to current available treatments.

The risks associated with risankizumab can be managed and do not outweigh the benefits.

What are the uncertainties?
The number of adolescents aged 16 to 17 years included in the studies was very small which makes it difficult to precisely evaluate the importance of the benefits and side effects in this age group.
The long-term risks of risankizumab are still unknown.
The company that makes risankizumab will provide additional information when it becomes available.

Are there on-going clinical studies?
A number of clinical studies assessing the efficacy and safety of risankizumab compared to placebo and other treatments are ongoing.

What measures are in place to monitor and manage risks?
A risk management plan has been developed to ensure that risankizumab is used as safely as possible. Based on this plan, the company that make risankizumab 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 side effects experienced by patients receiving risankizumab through the scheme. They will be reminded to report any side effects

each time the medicine is re-supplied. Safety data will be reviewed and reported to the MHRA on a regular basis by the company.

Health care professionals involved in the management of the scheme will receive training from the company, which will ensure that they can recognise, manage and appropriately report adverse events in patients receiving risankizumab.

Other information about risankizumab – see EAMS Treatment Protocol