Early Access to Medicines Scientific Opinion - Public Assessment Report

Volanesorsen 300 mg Solution for Injection

As an adjunct to diet for the treatment of adult patients with familial chylomicronaemia syndrome

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EAMS number 47857/0001

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 (as allowed under EU legislation). The General Medical Council's prescribing guidance: Prescribing unlicensed medicines can be found here: https://www.gmc-uk.org/guidance/28349.asp

The 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 neither be regarded as either a licensed indication or a future commitment by the MHRA to licence such a medicine.

Volanesorsen

What is volanesorsen?

Volanesorsen belongs to a class of medicines known as antisense oligonucleotides which can inhibit the production of specific proteins in the body associated with certain diseases. Volanesorsen is given by injection under the skin and is supplied as a ready to use syringe and needle.

What is volanesorsen used to treat?

Volanesorsen, as an adjunct to low fat diet, is used to treat adult patients with familial chylomicronaemia syndrome. This is a rare genetic disease which is characterised by very high levels of certain types of fats in the blood called triglycerides. This can lead to inflammation of the pancreas (pancreatitis) which causes pain and in some cases may be life-threatening.

How is volanesorsen used?

Volanesorsen is given by injection under the skin (also known as subcutaneous injection) once every two weeks. More frequent injections (once every week) may be prescribed in some patients, depending on their weight and their response to therapy. A single syringe and needle delivers one dose. If the patient wishes, either they or a caregiver can administer the injection provided they have received training beforehand from their doctor or nurse. Patients will still need to follow a low fat diet while taking volanesorsen.

How does volanesorsen work?

Volanesorsen action is based on the so-called antisense technology which alters the synthesis of a particular protein that is responsible for a specific disease. Volanesorsen reduces the production of apolipoprotein CIII, a protein produced in the liver that plays a key role in the regulation of triglycerides in the body. By inhibiting the production of apolipoprotein CIII, volanesorsen can lower the levels of

triglycerides in blood.

How has volanesorsen been studied?
Volanesorsen was mainly studied in a clinical trial ("APPROACH" trial) of 66 patients with familial chylomicronaemia syndrome who were on low fat diet, in which volanesorsen alone or given together with other lipid lowering medicines was compared with a placebo (inactive) drug. In this study, the patients received volanesorsen for a period of up to one year. In another study ("COMPASS" trial) volanesorsen was again compared with placebo in 113 patients who had very high triglycerides due to different causes. In this study, the patients received volanesorsen for a period of up to six months. In both studies, the main measure of effectiveness (how well the medicine worked) was the reduction in the levels of triglycerides in blood.

What are the benefits and risks of volanesorsen?
Benefits
Volanesorsen can significantly reduce triglycerides in blood. This, in turn, is expected to lower the risk of pancreatitis in patients with familial chylomicronaemia syndrome.

Risks
During treatment with volanesorsen patients may have a lower than normal number of platelets in blood, a condition called thrombocytopenia. Platelets (thrombocytes) are blood cells that help blood clot. Very low platelet levels may result in increased risk of bleeding but this is rare with volanesorsen. However, in order to early detect any significant problem with platelets, all patients prescribed Volanesorsen will need to have frequent blood tests to check the number of platelets in blood. Depending on the results, some patients may be advised by their doctor to modify their dose or temporarily stop their therapy.

Patients who received volanesorsen in the clinical studies also very frequently reported reactions at the injection site, such as pain, redness, swelling, itching, or a burning feeling.

Why has volanesorsen been given a positive Early Access to Medicine Scientific opinion?
Familial chylomicronaemia syndrome is a chronic disease that has a major impact on quality of life and patients are at high risk of pancreatitis, which is a potentially life-threatening condition. Currently, there are no therapies licensed to treat familial chylomicronaemia syndrome in the UK. The MHRA has considered the benefits and risks of volanesorsen in this difficult to treat condition and concluded that the risks can be effectively managed under the EAMS and do not outweigh the expected benefits.

What are the uncertainties?
As with every rare disease, a relatively small number of patients with familial chylomicronaemia syndrome has been studied in the clinical trials. Therefore, the safety profile of volanesorsen may not be complete and some side effects may not yet be known.

Volanesorsen has also not yet been studied in patients with liver disease, patients with severe renal disease, pregnant women and in children and adolescents. There is also limited experience in patients aged 65 and over.

Are there on-going clinical studies?
There is an ongoing study including patients with familial chylomicronaemia syndrome most of whom participated in the APPROACH and COMPASS trials. This study will provide information about the longer term effects of volanesorsen in these patients. Another ongoing trial is investigating the effects of

volanesorsen in patients with a different lipid disorder.

What measures are in place to monitor and manage risks?
A risk management plan has been developed to ensure that volanesorsen is used as safely as possible. Based on this plan, the company that makes volanesorsen 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 adverse effects experienced by patients receiving volanesorsen 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 and the details of their treating physician. Patients should carry the card with them at all times in case they need treatment or advice from a healthcare professional who is not familiar with volanesorsen treatment.

Other information about Volanesorsen - **See EAMS Treatment Protocols**