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# Summary of the risk management plan (RMP) for Nucala (mepolizumab)

This is a summary of the risk management plan (RMP) for Nucala, which details the measures to be taken in order to ensure that Nucala is used as safely as possible. For more information on RMP summaries, see here.

This RMP summary should be read in conjunction with the EPAR summary and the product information for Nucala, which can be found on Nucala's EPAR page.

## Overview of disease epidemiology

Nucala is an asthma medicine used to treat adults with a particular type of asthma called eosinophilic asthma, when it is severe and does not respond well to other treatments.

Asthma itself is a common, inflammatory disease of the airways that affects children and adults of all ages. It is one of the most common long-term diseases worldwide, and can be life-threatening. Estimates of the prevalence of asthma in European countries range from around 10 to 13% in the UK to 0.28% in Georgia. Its prevalence has considerably increased in recent years, especially in children. Symptoms come and go and include shortness of breath, wheezing, chest tightness and cough. The cause of asthma is unknown; however, a family history of asthma, eczema or allergy makes it more likely that an individual will develop asthma. Across the world, the number of deaths related to asthma is estimated at around 250,000 per year.

Although the majority of patients can be effectively treated with asthma medicines, in about 5-10% of patients asthma does not respond to current standard therapy, and they need treatment with high doses of inhaled or oral corticosteroids (potent anti-inflammatory medicines) and/or medicines that may suppress the immune system. About two-thirds of these are reported to have severe eosinophilic asthma, the type in which Nucala is used. In eosinophilic asthma, symptoms are associated with too many eosinophils (a type of white blood cells) in the blood and in phlegm in the lungs.

## Summary of treatment benefits

Nucala is given by injection under the skin and contains the active substance mepolizumab. The benefits of Nucala in severe eosinophilic asthma that is not well controlled by previous treatment have been shown in three main studies, in which it was compared with a placebo (dummy) injection. The first study involved 616 adults and adolescents given Nucala every 4 weeks for a year, in addition to their regular asthma medicines. The second involved 576 adults and adolescents who were given Nucala every 4 weeks for 28 weeks. The main measure of effectiveness in these studies was the number of severe attacks (exacerbations) of asthma that occurred during treatment, which were reduced by about half in patients who were given Nucala.

The third study involved 135 patients with asthma which was severe enough to need regular treatment by mouth with corticosteroids such as prednisone and prednisolone. The main measure of effectiveness was how much the corticosteroid dose could be reduced using Nucala for 24 weeks compared with

placebo. Over half (37 of 69) of the patients given Nucala were able to reduce their daily corticosteroid dose by more than 50% to a dose of 5 mg or less, and 10 of them were able to stop corticosteroids altogether, compared with about a third of those given placebo (22 of 66, of whom 5 were able to stop corticosteroids).

## Unknowns relating to treatment benefits

Patients in these studies were mostly white and at least 18 years old. There is no evidence to suggest Nucala would work any differently in non-white patients or children. The studies excluded patients who were pregnant or breastfeeding, so there is little information about treatment with Nucala in these patients.

## Summary of safety concerns

***Important identified risks***

| Risk | What is known | Preventability |
|---|---|---|
| Allergic reactions and allergic-like reactions caused by Nucala. | Allergic reactions (including swelling of the face, lips, mouth or tongue; wheezing, difficulty in breathing or shortness of breath; low blood pressure with fainting, dizziness or light-headedness; rash; and itchy raised bumps or hives) have been reported in up to 1 patient in 10 given Nucala but these reactions have also been reported in people given placebo (a dummy injection). | The product information for doctors and patients warns that allergic reactions can occur in patients receiving Nucala. Patients should be told about the symptoms of these reactions and the importance of telling a doctor right away if these symptoms occur. Patients should also be aware that some of these reactions can be serious and that the reactions can begin hours or days after an injection of Nucala. |
| Reactions around the area of the skin where Nucala was injected (injection-site reactions). | Reactions around the area of the skin where the injection of Nucala was given have been reported in 8 out of every 100 patients. These same types of reactions were also reported in 3 out of every 100 patients who got an injection with placebo. The most common symptoms were pain, redness, swelling, itching, and burning. These reactions were not severe and most resolved within a few days. | The product information for doctors and patients warns that reactions can occur around the area of the skin where the shot of Nucala was injected. |

***Important potential risks***

| Risk | What is known |
|---|---|
| Production of antibodies against Nucala by the body's natural defences (immunogenicity) | Like related medicines, the active substance in Nucala, mepolizumab, may trigger the immune system (the body's natural defences) and cause the production of antibodies (a protein that recognises Nucala as 'foreign') against the medicine. These antibodies could decrease the effectiveness of Nucala in controlling asthma and they may increase the chance of side effects such as |

| Risk | What is known |
|---|---|
| | allergic reactions.<br>In studies of Nucala in patients with severe asthma, 6 out of every 100 patients tested positive for such antibodies. However, in most people the presence of these antibodies did not appear to reduce Nucala's effectiveness or cause side effects. |
| Increased infections (infections related to alteration in immune response) | Nucala lowers the body's levels of certain white blood cells, called eosinophils, and patients with low white blood cell counts have a higher chance of developing an infection. Although this may be less likely with lowered eosinophil counts than with some other types of white blood cell, infections (especially serious infections) are a potential concern with medicines like Nucala, particularly as many patients with severe asthma already take other medicines that affect the body's ability to fight infection.<br>In studies with Nucala in patients with severe asthma, overall infections and serious infections occurred in similar numbers among patients given Nucala compared with those given placebo. Infections of the airways (lower respiratory tract), throat (pharyngitis) and urinary tract each occurred in between 3 and 4 people in 100 given the medicine and were slightly more common with Nucala than placebo, but were not serious or severe. |
| Cancers (malignancy) related to alteration in immune response | Certain white blood cells are part of the immune system and help the body to fight cancer. Cancer is therefore a potential concern with medicines such as Nucala that lower eosinophils and affect the body's immune system.<br>Cancers were monitored during the studies that tested Nucala in patients with severe asthma. Cancers occurred in similar numbers among patients who got Nucala compared with those who got placebo and the types of cancers were similar to those occurring generally in people no matter what medicines they take. |
| Side effects on the heart and blood vessels (cardiovascular safety) | Effects on the heart and blood vessels were monitored during the studies that tested Nucala in patients with severe asthma. In general, effects on the heart and blood vessels occurred in similar numbers among patients who got Nucala compared with those who got placebo. In one study of different doses in patients with severe asthma, effects on the heart occurred more often in the patients given Nucala than those who got placebo. This finding was not seen in other studies in patients with severe asthma or other diseases. |
| Worsening of asthma when Nucala treatment is stopped | Worsening of disease symptoms (rebound) when a medicine is stopped is a potential concern and was monitored during the studies that tested Nucala in patients with severe asthma. Asthma worsened after treatment was stopped in similar numbers of patients given Nucala and given placebo. |

***Missing information***

| Risk | What is known |
|---|---|
| Patients who are pregnant or who are currently breastfeeding | There is limited information on the safety of Nucala in pregnant women so it is not known for sure whether it increases the chance of problems with pregnancies or the baby. Animals given Nucala did not have an increase in such problems. A study is planned to collect information on outcomes in women who receive Nucala during their pregnancy, and to compare this with |

| Risk | What is known |
|---|---|
| | outcomes in pregnant women with asthma who do not receive this medicine. Patients should tell their doctor if they think they may be pregnant or are planning to have a baby while taking Nucala. |
| Patients who are less than 18 years of age | Nineteen patients aged 12 to17 years were studied in severe asthma studies with Nucala. The information is limited but the safety of Nucala and how the body handled the medicine in these patients was similar to adult patients. Children with severe asthma under 12 years of age have not been studied. A study in children 6 to 11 years of age is planned to test how the body handles Nucala in this younger age group. |
| Elderly patients | There is limited information on the use of Nucala in patients who are 65 years or older, but the safety of Nucala and how the body handled the drug did not appear to differ based on age. |
| Patients with parasitic infections or at high risk of infection with parasites | As Nucala reduces the number of eosinophils (a type of white blood cells), it may affect how the body fights infections with parasites. Patients infected with parasites were not studied in the severe asthma studies that tested Nucala. Patients infected with parasites should be treated for the infection before getting Nucala. If a patient being treated with Nucala gets a parasite infection, the doctor may temporarily stop Nucala if the parasite infection does not respond to treatment. |
| Limited long-term safety information on the dose of 100 mg given by injection under the skin | There is limited information of the long-term effects of Nucala on patients given the recommended dose of 100 mg by injection under the skin. The average time that patients received this dose was 12 months in studies so far. Some patients have received the dose for up to 17 months. There are studies ongoing in patients with severe asthma to continue to investigate the safety of Nucala for longer periods. |

## Summary of risk minimisation measures by safety concern

All medicines have a summary of product characteristics (SmPC) which provides physicians, pharmacists and other healthcare professionals with details on how to use the medicine, and also describes the risks and recommendations for minimising them. Information for patients is available in lay language in the package leaflet. The measures listed in these documents are known as ‘routine risk minimisation measures’.

The SmPC and the package leaflet are part of the medicine’s product information. The product information for Nucala can be found on Nucala’s EPAR page.

This medicine has no additional risk minimisation measures.

## Planned post-authorisation development plan

***List of studies in post-authorisation development plan***

| Study / activity (including study number) | Objectives | Safety concerns / efficacy issue addressed | Status | Planned date for submission of (interim and) final results |
|---|---|---|---|---|
| Pregnancy | To evaluate | Adverse impact of | Planned | Final report 2Q |

| Study / activity (including study number) | Objectives | Safety concerns / efficacy issue addressed | Status | Planned date for submission of (interim and) final results |
|---|---|---|---|---|
| Surveillance Study | outcomes for pregnant women with asthma and their infants exposed to Nucala. | mepolizumab exposure to pregnancy outcomes and birth defects | | 2022 |
| MEA115666: A multi-centre, open-label, long-term safety study of mepolizumab in asthmatic subjects who participated in the MEA112997 trial | To describe the long-term safety profile of Nucala. | Long-term safety | Ongoing | Final report 2018 |
| 201312: A multi-centre, open-label, study of mepolizumab in a subset of subjects with a history of life threatening/ seriously debilitating asthma who participated in the MEA115661 Trial | To provide extended treatment with Nucala to subjects from study MEA115661 and to further describe long-term safety in these subjects. | Long-term safety | Ongoing | Final report 2018 |
| Study 200862: A randomised, double-blind, placebo-controlled, parallel-group, multi-centre 24-week study to evaluate the efficacy and safety of mepolizumab adjunctive therapy in subjects with severe eosinophilic asthma on markers of asthma control | A study to evaluate the efficacy of Nucala 100 mg subcutaneous injection every 4 weeks versus placebo on health-related quality of life and on $FEV_1$ (a measure of lung function) in adults and adolescents with severe eosinophilic asthma. | To assess the safety and tolerability of mepolizumab compared with placebo in severe asthma | Ongoing | Final report November 2016 |

***Studies which are a condition of the marketing authorisation***

None of the above studies is a condition of the marketing authorisation.

## Summary of changes to the risk management plan over time

### *Major changes to the Risk Management Plan over time*

Not applicable.

This summary was last updated in 11-2015.