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Withdrawal of application to change the marketing authorisation for Sialanar (glycopyrronium bromide)

Proveca Pharma Limited withdrew its application for the use of Sialanar in the treatment of severe drooling in children aged 2 to 3 years old.

The company withdrew the application on 6 September 2024.

What is Sialanar and what is it used for?

Sialanar is a medicine for treating severe saliva drooling in children and adolescents aged 3 years and above with chronic (long-term) conditions affecting the nervous system, such as cerebral palsy, epilepsy and neurodegenerative diseases (diseases where cells of the central nervous system stop working or die).

Sialanar has been authorised in the EU since September 2016.

It contains the active substance glycopyrronium bromide and is available as a solution to be taken by mouth.

Further information on Sialanar's current uses can be found on the Agency's website: ema.europa.eu/en/medicines/human/EPAR/sialanar.

What change had the company applied for?

The company applied to extend the use of Sialanar to children from 2 years of age with chronic conditions affecting the nervous system.

How does Sialanar work?

The active substance in Sialanar, glycopyrronium bromide, blocks receptors in the salivary glands known as muscarinic receptors. When activated by nerves from the brain, these receptors trigger the production of saliva. By blocking the receptors, the medicine is expected to help reduce the amount of saliva produced by the glands and so reduce drooling.

In children from 2 years old, Sialanar was expected to work in the same way as it does in children aged 3 years and above.

What did the company present to support its application?

The company provided data from a clinical trial involving 87 children aged 3 to 17 years with severe drooling due to chronic neurological disorders. In this study, the effectiveness of Sialanar in treating severe drooling was compared with placebo (a dummy treatment), with both treatments being used alongside the standard of care (treatment that medical experts consider most appropriate). The severity of drooling was measured using the Drooling Impact Scale (DIS), a score that measures how much drooling affects a person's daily life and well-being.

The company also submitted data from a real-world study involving 39 children under 3 years of age with severe drooling, who were treated with glycopyrronium bromide given enterally (by mouth or through a tube that goes directly to the stomach or intestine).

Further data were submitted from two studies published in the scientific literature. The first used the DIS and another score called the Drooling Rating Scale (DRS) to compare the safety and effectiveness of different treatments for drooling in 483 children and adolescents from 20 months to 19 years old, 150 of whom received glycopyrronium bromide enterally. The second study involved 18 children under 3 years of age who were given glycopyrronium bromide tablets to treat severe drooling; glycopyrronium bromide treatment was not compared with any other treatment or placebo and its effect was measured using the DIS.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the European Medicines Agency had evaluated the information from the company and had prepared questions for the company. The company had not responded to the questions at the time of the withdrawal.

What did the Agency recommend at that time?

Based on the review of the information, at the time of the withdrawal, the Agency had some concerns and its provisional opinion was that Sialanar could not have been authorised for the treatment of severe drooling in children aged 2 to 3 years with chronic conditions affecting the nervous system.

The Agency had concerns about the safety and effectiveness of Sialanar in 2- to 3-year-old children due to uncertainties relating to the design and methodology of the studies and the quality of the data provided. In particular, the study comparing Sialanar with placebo did not include children under 3 years of age and the other studies did not provide specific data for children aged 2 to 3 years. It was therefore not possible to compare data from these studies. There was also a lack of information about the form of glycopyrronium bromide used in the studies and whether this was sufficiently similar to Sialanar. In addition, there were uncertainties regarding the safety of the medicine in children under 3 years of age.

Therefore, at the time of the withdrawal, the Agency's opinion was that the company had not provided enough information to support the application for a change to the marketing authorisation of Sialanar.

What were the reasons given by the company for withdrawing the application?

In its letter notifying the Agency of the withdrawal of application, the company stated that the withdrawal is based on the CHMP's consideration that the Committee will not be able to conclude that the benefits outweigh the risks on the basis of the data provided.

Does this withdrawal affect patients in clinical trials or compassionate use programmes?

The company informed the Agency that there are no consequences for patients in clinical trials or in compassionate use programmes using Sialanar.

If your child is in a clinical trial or compassionate use programme and you need more information about their treatment, speak with their clinical trial doctor.

What is happening with Sialanar for the treatment of children aged 3 years and older with a chronic condition affecting the nervous system?

Sialanar continues to be authorised in children 3 years old and above who have a chronic condition affecting the nervous system.