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**EPAR summary for the public**

# Nuedexta

Dextromethorphan / quinidine



This is a summary of the European public assessment report (EPAR) for Nuedexta. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Nuedexta.

## What is Nuedexta and what is it used for?

Nuedexta is a medicine that contains two active substances, dextromethorphan and quinidine. It is used to treat the symptoms of pseudobulbar affect (PBA) in adults. PBA is a condition where damage to certain areas of the brain results in sudden and uncontrollable episodes of crying or laughing that do not relate to the patient's real emotional state.

## How is Nuedexta used?

Nuedexta is available as capsules (15 mg or 23 mg dextromethorphan and 9 mg quinidine) and can only be obtained with a prescription.

Treatment should be started with one lower strength capsule (15mg/9mg) once a day (in the morning), which is increased after one week to twice a day (in the morning and evening, 12 hours apart). In patients whose response is inadequate after four weeks, the higher strength capsule (23mg/9mg) may be used twice a day.

## How does Nuedexta work?

Although the exact cause of PBA is unclear, it is believed that it affects the way signals are transmitted between brain cells by 'neurotransmitters', chemicals that allow nerve cells to communicate with each other.

Although the exact way dextromethorphan works in PBA is unclear, it attaches to several different nerve cell receptors in the brain such as NMDA receptors and sigma-1 receptors for the neurotransmitter glutamate as well as receptors for the neurotransmitter serotonin. Since these

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neurotransmitters are involved in the control of emotions, dextromethorphan helps to normalise its activity in the brain, reducing the symptoms of PBA.

The role of quinidine is to prevent dextromethorphan from being broken down early in the body and thereby it prolongs the action of dextromethorphan in the body.

## What benefits of Nuedexta have been shown in studies?

Nuedexta has been studied in one main study involving 326 patients with PBA due to multiple sclerosis or amyotrophic lateral sclerosis. Nuedexta was compared with placebo (a dummy treatment) for 12 weeks. The main measure of effectiveness was based on the reduction in the number of episodes of laughing or crying. Treatment with Nuedexta was effective in reducing patients' PBA episodes which were reduced by nearly 50% more than in patients treated with placebo. The study also measured the change in the patients' symptoms, assessed in several ways including using a standard scale (called a CNS-LS score which ranges from 7 to 35). A decrease in the total score indicates an improvement in PBA symptoms. After 12 weeks of treatment with Nuedexta, the CNS-LS score decreased by 8.2 points, compared with a decrease of 5.7 points for placebo.

## What is the risk associated with Nuedexta?

The most common side effects with Nuedexta (which may affect up to 1 in 10 people) are diarrhoea, nausea (feeling sick), dizziness, headache, somnolence (sleepiness) and fatigue (tiredness). Serious side effects reported include muscle spasticity (excessive stiffness of muscles), respiratory depression (inhibition of breathing) and decreased oxygen saturation (lower-than-normal levels of oxygen) in the blood. For the full list of all side effects reported with Nuedexta, see the package leaflet.

Nuedexta must not be used in patients:

- who are already being treated with the medicines quinidine, quinine or mefloquine or who have previously developed certain serious problems such as thrombocytopenia (low platelet counts) due to the use of these medicines;
- with 'prolonged QT interval' (a disruption of the electrical activity of the heart);
- with or at high risk of complete AV block (a type of heart rhythm disorder);
- with a history suggestive of torsades de pointes ventricular tachycardia (abnormal heart rhythms);
- who are taking the medicine thioridazine used for mental illness;
- who are taking or have taken within the last 14 days medicines for depression called monoamine oxidase inhibitors (MAOI).

For the full list of restrictions, see the package leaflet.

## Why has Nuedexta been approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) decided that Nuedexta's benefits are greater than its risks and recommended that it be approved for use in the EU. The CHMP concluded that Nuedexta is effective in treating the symptoms of PBA based on the studies in patients with PBA caused by multiple sclerosis and amyotrophic lateral sclerosis. The CHMP also noted that there is currently no treatment available for this distressing condition. Regarding its safety, the CHMP decided that dextromethorphan and quinidine have been marketed as medicines for a number of years and their safety and interactions with other medicines are relatively well known. The main safety issues were considered manageable and adequately addressed by risk minimisation measures.

## What measures are being taken to ensure the safe use of Nuedexta?

A risk management plan has been developed to ensure that Nuedexta is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Nuedexta, including the appropriate precautions to be followed by healthcare professionals and patients.

In addition, the company that makes Nuedexta must ensure that all healthcare professionals who are expected to use Nuedexta receive an information pack and a patient alert card with key safety information. The company will also carry out a study on the use of Nuedexta and a study to monitor Nuedexta's safety including its effects on the heart and potential for interactions with other medicines.

## Other information about Nuedexta

The European Commission granted a marketing authorisation valid throughout the European Union for Nuedexta on 24 June 2013.

The full EPAR for Nuedexta can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports. For more information about treatment with Nuedexta, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

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