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EPAR summary for the public

Sifrol

pramipexole

This document is a summary of the European Public Assessment Report (EPAR) for Sifrol. 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 Sifrol.

What is Sifrol?

Sifrol is a medicine that contains the active substance pramipexole. It is available as 'immediate-release' white tablets (round: 0.088, 0.7 and 1.1 mg; oval: 0.18 and 0.35 mg) and as 'prolonged-release' white tablets (round: 0.26 and 0.52 mg; oval: 1.05, 1.57, 2.1, 2.62 and 3.15 mg). Immediate-release tablets release the active substance immediately, and prolonged-release tablets release it slowly over a few hours.

What is Sifrol used for?

Sifrol is used to treat the symptoms of the following diseases:

- Parkinson's disease, a progressive brain disorder that causes shaking, slow movement and muscle stiffness. Sifrol can be used either on its own or in combination with levodopa (another medicine for Parkinson's disease), at any stage of disease including the later stages when levodopa starts becoming less effective;
- moderate to severe restless legs syndrome, a disorder where the patient has uncontrollable urges to move the limbs to stop uncomfortable, painful or odd sensations in the body, usually at night. Sifrol is used when a specific cause for the disorder cannot be identified.

The medicine can only be obtained with a prescription.

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How is Sifrol used?

For Parkinson's disease, the starting dose is either one 0.088-mg immediate-release tablet three times a day or one 0.26-mg prolonged-release tablet once a day. The dose should be increased every five to seven days until symptoms are controlled without causing side effects that cannot be tolerated. The maximum daily dose is three 1.1-mg immediate-release tablets or one 3.15-mg prolonged-release tablet. Patients can be switched from the immediate- to the prolonged-release tablets overnight, but the dose might need to be adjusted depending on the patient's response. Sifrol must be given less often in patients who have problems with their kidneys. If treatment is stopped for any reason, the dose should be decreased gradually.

For restless legs syndrome, Sifrol immediate-release tablets should be taken once a day, two to three hours before going to bed. The recommended starting dose is 0.088 mg, but, if needed, this can be increased every four to seven days to reduce symptoms further, to a maximum of 0.54 mg. The patient's response and the need for further treatment should be evaluated after three months. The prolonged-release tablets are not suitable for restless legs syndrome.

Sifrol tablets should be swallowed with water. The prolonged-release tablets must not be chewed, divided or crushed, and should be taken around the same time every day. For more information, see the package leaflet.

How does Sifrol work?

The active substance in Sifrol, pramipexole, is a dopamine agonist (a substance that imitates the action of dopamine). Dopamine is a messenger substance in the parts of the brain that control movement and co-ordination. In patients with Parkinson's disease, the cells that produce dopamine begin to die and the amount of dopamine in the brain decreases. The patients then lose their ability to control their movements reliably. Pramipexole stimulates the brain as dopamine would, so that patients can control their movement and have fewer of the signs and symptoms of Parkinson's disease, such as shaking, stiffness and slowness of movement.

The way pramipexole works in restless legs syndrome is not fully understood. The syndrome is thought to be caused by problems in the way dopamine works in the brain, which may be corrected by pramipexole.

How has Sifrol been studied?

In Parkinson's disease, Sifrol immediate-release tablets have been studied in five main studies. Four studies compared Sifrol with placebo (a dummy treatment): one study in 360 patients with advanced disease who were already taking levodopa that was starting to become less effective, and three studies in a total of 886 patients with early disease who were not receiving levodopa. The main measure of effectiveness was the change in the severity of Parkinson's disease. The fifth study compared Sifrol with levodopa in 300 patients with early disease, and measured the number of patients who had movement symptoms.

To support the use of the prolonged-release tablets, the company presented the results of studies showing that the immediate- and prolonged-release tablets produced the same levels of the active substance in the body. It also presented studies comparing the two tablets in early and advanced Parkinson's disease, and looking at switching patients from immediate- to prolonged-release tablets.

In restless legs syndrome, Sifrol immediate-release tablets have also been studied in two main studies. The first compared Sifrol with placebo over 12 weeks in 344 patients and measured the improvement in symptoms. The second included 150 patients who took Sifrol for six months, and compared the

effects of remaining on Sifrol with switching to placebo. The main measure of effectiveness was the time until symptoms got worse.

What benefit has Sifrol shown during the studies?

In the study of patients with advanced Parkinson's disease, patients taking Sifrol immediate-release tablets had larger improvements after 24 weeks of steady-dose treatment than those taking placebo. Similar results were seen in the first three studies of early Parkinson's disease, with greater improvements after four or 24 weeks. Sifrol was also more effective that levodopa at improving movement symptoms in early disease.

The additional studies showed that the prolonged-release tablets were as effective as the immediate-release tablets in treating Parkinson's disease. They also showed that patients can be safely switched from immediate- to prolonged-release tablets, although dose adjustments were needed in a small number of patients.

In restless legs syndrome, Sifrol immediate-release tablets were more effective than placebo at reducing symptoms over 12 weeks, but the difference between placebo and Sifrol was greatest after four weeks before getting smaller. The results of the second study were insufficient to prove the long-term effectiveness of Sifrol.

What is the risk associated with Sifrol?

The most common side effect with Sifrol (seen in more than 1 patient in 10) is nausea (feeling sick). In patients with Parkinson's disease, the following side effects are also seen in more than 1 patient in 10: dizziness, dyskinesia (difficulty controlling movement) and somnolence (sleepiness). For the full list of all side effects reported with Sifrol, see the package leaflet.

Sifrol should not be used in people who may be hypersensitive (allergic) to pramipexole or any of the other ingredients.

Why has Sifrol been approved?

The CHMP decided that Sifrol's benefits are greater than its risks and recommended that it be given marketing authorisation.

Other information about Sifrol:

The European Commission granted a marketing authorisation valid throughout the European Union for Sifrol to Boehringer Ingelheim International GmbH on 14 October 1997. The marketing authorisation is valid for an unlimited period.

The full EPAR for Sifrol 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 Sifrol, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 10-2010.