EMA/317132/2010
EMEA/H/C/573

EPAR summary for the public

Xeristar

duloxetine

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

What is Xeristar?

Xeristar is a medicine that contains the active substance duloxetine. It is available as gastroresistant capsules (white and blue: 30 mg; green and blue: 60 mg). 'Gastroresistant' means that the capsules' contents pass through the stomach without being broken down until they reach the intestine. This prevents the active substance from being destroyed by the acid in the stomach.

What is Xeristar used for?

Xeristar is used to treat adults (aged 18 years or over) with the following diseases:

- major depression;
- pain due to diabetic peripheral neuropathy (damage to the nerves in the extremities that can occur in patients with diabetes);
- generalised anxiety disorder (long-term anxiety or nervousness about everyday matters).

The medicine can only be obtained with a prescription.

How is Xeristar used?

For major depression, the recommended dose of Xeristar is 60 mg once a day. A response is usually seen in two to four weeks. In patients who respond to Xeristar, treatment should continue for several

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

months to prevent the disease coming back, or for longer in patients who have had repeated periods of depression in the past.

For diabetic neuropathic pain, the recommended dose is 60 mg per day but some patients may need a higher dose of 120 mg per day. The response to treatment should be assessed regularly.

For generalised anxiety disorder, the recommended starting dose is 30 mg once a day, but the dose can be increased to 60, 90 or 120 mg depending on the patient's response. Most patients will need to take 60 mg per day. Patients who also have major depression should start with 60 mg once a day. In patients who respond to Xeristar, treatment should continue for several months, to prevent the disorder coming back.

The dose of Xeristar should be reduced gradually when stopping treatment.

How does Xeristar work?

The active substance in Xeristar, duloxetine, is a serotonin-noradrenaline re-uptake inhibitor. It works by preventing the neurotransmitters 5-hydroxytryptamine (also called serotonin) and noradrenaline from being taken back up into nerve cells in the brain and spinal cord. Neurotransmitters are chemicals that allow nerve cells to communicate with one another. By blocking their re-uptake, duloxetine increases the amount of these neurotransmitters in the spaces between these nerve cells, increasing the level of communication between the cells. Since these neurotransmitters are involved in maintaining high mood and reducing the sensation of pain, blocking their re-uptake into nerve cells can improve the symptoms of depression, anxiety and neuropathic pain.

How has Xeristar been studied?

For major depression, Xeristar has been compared with placebo (a dummy treatment) in eight main studies involving a total of 2,544 patients. Six of the studies looked at the treatment of depression and measured the change in symptoms over up to six months. The other two studies looked at how long it took for symptoms to return in patients who had initially responded to Xeristar, including 288 patients with a history of repeated episodes of depression for up to five years.

For neuropathic pain, Xeristar has been compared with placebo in two 12-week studies in 809 diabetic adults. The main measure of effectiveness was the change in the severity of pain each week.

For generalised anxiety disorder, Xeristar has been compared with placebo in five studies involving a total of 2,337 patients. Four studies looked at the treatment of the disorder by measuring the reduction in symptoms after nine to 10 weeks. The fifth study looked at how long it took for symptoms to return in 429 patients who had initially responded to Xeristar.

What benefit has Xeristar shown during the studies?

Although the results of the depression studies varied, Xeristar was more effective than placebo in four of the studies. In the two studies where the approved dose of Xeristar was compared with placebo, Xeristar was more effective. It also took longer for symptoms to return in patients taking Xeristar than in those taking placebo.

For the treatment of diabetic neuropathic pain, Xeristar was more effective at reducing pain than placebo. In both studies, pain reduction was seen from the first week of treatment for up to 12 weeks.

For generalised anxiety disorder, Xeristar was also more effective than placebo at treating the disorder and preventing symptoms returning.

What is the risk associated with Xeristar?

The most common side effects with Xeristar (seen in more than 1 patient in 10) are nausea (feeling sick), headache, dry mouth, somnolence (sleepiness) and dizziness. Most of these were mild or moderate, starting early in treatment and getting milder as treatment continued. For the full list of all side effects reported with Xeristar, see the Package Leaflet.

Xeristar should not be used in people who may be hypersensitive (allergic) to duloxetine or any of the other ingredients. Xeristar must not be used together with monoamine oxidase inhibitors (another group of antidepressants), fluvoxamine (another antidepressant), or ciprofloxacin or enoxacin (types of antibiotic). Xeristar must also not be used in patients with certain types of liver disease or patients with severe kidney disease. Treatment must not be started in patients with uncontrolled hypertension (high blood pressure), because of a risk of hypertensive crisis (sudden, dangerously high blood pressure). As with other antidepressants, isolated cases of suicidal thoughts and behaviour have been seen in patients taking Xeristar, particularly in the first few weeks of treatment for depression. Any patients taking Xeristar who have distressing thoughts or experiences at any time should tell their doctor immediately.

Why has Xeristar been approved?

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

Other information about Xeristar:

The European Commission granted a marketing authorisation valid throughout the European Union for Xeristar on 17 December 2004. The marketing authorisation holder is Eli Lilly Netherlands B.V. The marketing authorisation is valid for an unlimited period.

The full EPAR for Xeristar can be found here. For more information about treatment with Xeristar, read the Package Leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 05-2010.