European Medicines Agency

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EUROPEAN PUBLIC ASSESSMENT REPORT (EPAR)

DULOXETINE BOEHRINGER INGELHEIM

EPAR summary for the public

This document is a summary of the European Public Assessment Report (EPAR). It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the studies performed, to reach their recommendations on how to use the medicine.
If you need more information about your medical condition or your treatment, read the Package Leaflet (also part of the EPAR) or contact your doctor or pharmacist. If you want more information on the basis of the CHMP recommendations, read the Scientific Discussion (also part of the EPAR).

What is Duloxetine Boehringer Ingelheim?

Duloxetine Boehringer Ingelheim is a medicine that contains the active substance duloxetine. It is available as gastroresistant capsules (blue: 20 mg; white and blue: 30 mg; orange: 40 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 being destroyed by the acid in the stomach.
This medicine is the same as Ariclaim, which is already authorised in the European Union (EU). The company that makes Ariclaim has agreed that its scientific data can be used for Duloxetine Boehringer Ingelheim.

What is Duloxetine Boehringer Ingelheim used for?

Duloxetine Boehringer Ingelheim is used to treat:

- moderate to severe stress urinary incontinence (SUI) in women. SUI is accidental leaks of urine during physical exertion or when coughing, laughing, sneezing, lifting or exercising;
- pain due to diabetic peripheral neuropathy (damage to the nerves in the extremities that can occur in patients with diabetes).

The medicine can only be obtained with a prescription.

How is Duloxetine Boehringer Ingelheim used?

For SUI, the recommended dose of Duloxetine Boehringer Ingelheim is 40 mg twice a day. Some patients may benefit from starting treatment at a dose of 20 mg twice a day for two weeks before increasing to 40 mg twice a day, to reduce nausea (feeling sick) and dizziness. Combining Duloxetine Boehringer Ingelheim with pelvic floor muscle training may provide additional benefit.
For diabetic neuropathic pain, the recommended dose is 60 mg once a day, but some patients may need a higher dose of 120 mg per day. The response to treatment should be assessed two months after starting treatment.
Duloxetine Boehringer Ingelheim can be taken with or without food. The benefit of treatment should be re-assessed at regular intervals. Duloxetine Boehringer Ingelheim should be used with caution in elderly patients. It should not be used in patients who have certain problems with their liver or severe kidney problems. The dose should be reduced gradually when stopping treatment.

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How does Duloxetine Boehringer Ingelheim work?
The active substance in Duloxetine Boehringer Ingelheim, duloxetine, is a serotonin-noradrenaline re-uptake inhibitor. It works by preventing the neurotransmitters 5-hydroxytrypamine (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.
How duloxetine works in SUI is not clear but it is thought that by increasing the levels of 5-hydroxytryptamine and noradrenaline at the level of the nerves that control the muscle of the urethra (the tube that leads from the bladder to outside), duloxetine causes a stronger closure of the urethra during urine storage. By closing the urethra more powerfully, Duloxetine Boehringer Ingelheim prevents the unwanted loss of urine during physical stress such as coughing or laughing.
Since these neurotransmitters are also involved in reducing the sensation of pain, blocking their re-uptake into nerve cells may also improve the symptoms of neuropathic pain.

How has Duloxetine Boehringer Ingelheim been studied?
For the treatment of SUI, Duloxetine Boehringer Ingelheim has been studied in a total of 2,850 women. The four main studies involved 1,913 women and lasted 12 weeks, comparing Duloxetine Boehringer Ingelheim (mostly as 40 mg twice a day) with placebo (a dummy treatment). The main measures of effectiveness were incontinence episode frequency (IEF, the number of episodes of incontinence per week) recorded in patient diaries and the patients' scores on an incontinence-specific quality-of-life (I-QOL) questionnaire.
For the treatment of diabetic neuropathic pain, Duloxetine Boehringer Ingelheim has been studied in two 12-week studies in 809 diabetic adults who had had pain every day for at least six months. The effectiveness of three different doses of Duloxetine Boehringer Ingelheim was compared with that of placebo. The main measure of effectiveness was the change in the severity of pain each week, as recorded by the patients on an 11-point scale in daily diaries.

What benefit has Duloxetine Boehringer Ingelheim shown during the studies?
In all four studies of SUI, the patients treated with Duloxetine Boehringer Ingelheim had fewer episodes of incontinence after 12 weeks, with about four or five fewer episodes of incontinence per week, in comparison with the number before the study. The IEF decreased by 52% in the Duloxetine Boehringer Ingelheim group, compared with a decrease of 33% in the placebo-treated group. The I-QOL questionnaire scores were also improved in the Duloxetine Boehringer Ingelheim group compared with the placebo group. Duloxetine Boehringer Ingelheim was more effective than placebo only in patients who had more than 14 incontinence episodes per week (moderate to severe SUI) at the start of the study.
For the treatment of diabetic neuropathic pain, Duloxetine Boehringer Ingelheim at doses of 60 mg once or twice a day 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, with patients taking Duloxetine Boehringer Ingelheim having pain scores between 1.17 and 1.45 points lower than those taking placebo.

What is the risk associated with Duloxetine Boehringer Ingelheim?
The most common side effects with Duloxetine Boehringer Ingelheim when used to treat SUI (seen in more than 1 patient in 10) are nausea, dry mouth, constipation and fatigue (tiredness). Most of these were mild or moderate, starting early in treatment and getting milder as treatment continued. The most common side effects when used to treat diabetic neuropathic pain (seen in more than 1 patient 10) are headache, somnolence (sleepiness), dizziness, nausea and dry mouth. For the full list of all side effects reported with Duloxetine Boehringer Ingelheim, see the Package Leaflet.
Duloxetine Boehringer Ingelheim should not be used in people who may be hypersensitive (allergic) to duloxetine or any of the other ingredients. Duloxetine Boehringer Ingelheim must not be used in patients with certain types of liver disease or with severe kidney disease. Duloxetine Boehringer Ingelheim must not be used together with monoamine oxidase inhibitors (a group of antidepressants), fluvoxamine (another antidepressant), or ciprofloxacin or enoxacin (types of antibiotic). Treatment must not be started in patients with uncontrolled high blood pressure, because of a risk of hypertensive crisis (sudden, dangerously high blood pressure).

Why has Duloxetine Boehringer Ingelheim been approved?
The Committee for Medicinal Products for Human Use (CHMP) decided that Duloxetine Boehringer Ingelheim's benefits are greater than its risks for the treatment of moderate to severe SUI and of diabetic peripheral neuropathic pain in adults. The Committee recommended that Duloxetine Boehringer Ingelheim be given marketing authorisation.

Other information about Duloxetine Boehringer Ingelheim:
The European Commission granted a marketing authorisation valid throughout the EU for Duloxetine Boehringer Ingelheim to Boehringer Ingelheim International GmbH on 8 October 2008.

The full EPAR for Duloxetine Boehringer Ingelheim is available here.

This summary was last updated in 03-2009.