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EPAR summary for the public

Constella

linaclotide

This is a summary of the European public assessment report (EPAR) for Constella. 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 Constella.

What is Constella?

Constella is a medicine that contains the active substance linaclotide. It is available as capsules (290 micrograms).

What is Constella used for?

Constella is used to treat the symptoms of moderate to severe irritable bowel syndrome (IBS) with constipation in adults. IBS is a long-term disorder of the gut characterised by pain or discomfort in the abdomen and bloating together with altered bowel habit.

The medicine can only be obtained with a prescription.

How is Constella used?

The recommended dose of Constella is one capsule once a day, taken at least 30 minutes before a meal.

The doctor should periodically assess the need of continued treatment. If the patient has not experienced an improvement in symptoms after four weeks of treatment, the benefits and risks of continuing treatment should be reconsidered.

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How does Constella work?

The active substance in Constella, linaclotide, attaches to some receptors in the gut called guanylate cyclase C. By attaching to these receptors, it reduces pain and increases the secretion of fluid into the gut, thereby loosening the stools and increasing bowel movements.

How has Constella been studied?

The effects of Constella were first tested in experimental models before being studied in humans.

Constella was investigated in two main studies involving a total of 1,608 patients with IBS with constipation, where it was compared with placebo (a dummy treatment). The main measures of effectiveness were the number of patients who experienced at least a 30% improvement in their pain and discomfort and the number of patients who were considerably or completely relieved from all IBS symptoms for at least 6 out of the 12 weeks of treatment. One of the studies also looked at the effects of Constella following 26 weeks of treatment.

What benefit has Constella shown during the studies?

Constella was shown to be more effective than placebo at improving the symptoms of IBS. In the first study, 55% of patients who received Constella experienced a 30% or higher improvement in their pain and discomfort for at least 6 out of the 12 weeks of treatment, compared with 42% of patients who received placebo. In addition, 37% of patients who received Constella were considerably or completely relieved from symptoms for at least 6 out of the 12 weeks of treatment, compared with 19% of patients who received placebo.

Similar results were obtained in the second study, with 54% of Constella patients experiencing an improvement in their pain and discomfort and 39% of them feeling considerably or completely relieved from symptoms for at least 6 out of the 12 weeks of treatment, compared with 39% and 17% of patients in the placebo group, respectively.

The results after 26 weeks of treatment showed an improvement in pain (for at least 13 weeks out of the 26 weeks) in 54% of patients taking Constella compared with 36% of patients taking placebo, as well as relief from symptoms for at least 13 weeks in 37% of Constella patients, compared with 17% of patients in the placebo group.

What is the risk associated with Constella?

The most common side effect with Constella is diarrhoea, mainly mild to moderate, occurring in between 10 and 20 patients in 100. In rare and more severe cases, diarrhoea may lead to dehydration, hypokalaemia (low blood potassium levels), decrease in blood bicarbonate, dizziness and orthostatic hypotension (low blood pressure on standing up).

Constella must not be used in people who are hypersensitive (allergic) to linaclotide or any of the other ingredients. It must also not be used in patients with a known or suspected blockage in their stomach or gut.

Why has Constella been approved?

The CHMP noted that Constella has been shown to have clinically relevant, beneficial effects in patients with IBS with constipation in the long term (for up to six months). It has also been shown to have a beneficial impact on the quality of life of patients. However, the Committee also noted that about half of the patients did not adequately benefit from treatment, and therefore recommended that the need

for continued treatment should be reconsidered after four weeks. Regarding safety, the CHMP concluded that the side effects with Constella, mainly diarrhoea, are manageable. The CHMP therefore decided that Constella's benefits are greater than its risks and recommended that it be given marketing authorisation.

Other information about Constella

The European Commission granted a marketing authorisation valid throughout the European Union for Constella on 26 November 2012.

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

This summary was last updated in November 2012.