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EMA recommends that Symbioflor 2 can continue to be used for irritable bowel syndrome

Medicine should no longer be used for other disorders of the gut

On 22 June 2017 a review by European Medicines Agency (EMA) concluded that Symbioflor 2 and associated names can continue to be used for treatment of irritable bowel syndrome (IBS) in adults. However, the medicine should no longer be used more widely to treat so-called functional gastrointestinal disorders, a group of disorders with a variety of causes that may require different treatment approaches.

Symbioflor 2, which contains *Escherichia coli* bacteria, has been described as a probiotic, which means that it encourages the growth of beneficial organisms ('flora') in the gut. It was first made available in Germany in the 1950s and subsequently in Austria and Hungary.

In reaching its conclusions, EMA's Committee for Medicinal Products for Human Use (CHMP) reviewed all available evidence on the effectiveness and safety of Symbioflor 2. The data included clinical studies, scientific publications, post-marketing experience, as well as information provided by the company and the views of an expert group formed for evaluating Symbioflor 2. The review did not find any new evidence on the effectiveness of Symbioflor 2 since the product was last approved. Available evidence suggests that the risk of harm from Symbioflor 2 is low.

A randomised study involving around 300 adults suggested that Symbioflor 2 was effective for treating IBS. However, the study had weaknesses. Benefit has not yet been established in children with IBS.

Since the available data were not sufficiently robust for the CHMP to draw conclusions on how well Symbioflor 2 works and whether it is effective for any particular type of IBS, the CHMP has asked the company to carry out a well-designed study on effectiveness and safety among patients with different features of IBS (e.g. those with diarrhoea or with constipation as an important feature). Submission of the study report to national authorities will be a condition for maintaining Symbioflor 2's marketing authorisation.

The company that markets Symbioflor 2 did not submit data to support its use in 'functional gastrointestinal disorders' and agreed to remove this use from the medicine's authorisation.

The CHMP recommendation was sent to the European Commission which issued a legally binding decision valid throughout the EU.

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Information for patients

- You can continue to take Symbioflor 2 for treating symptoms of irritable bowel syndrome by following the information in the medicine's revised package leaflet.
- Speak with a pharmacist or your doctor if you have any problems affecting your stomach or gut. You should not use Symbioflor 2 for conditions affecting the gut other than irritable bowel syndrome.
- Speak with a pharmacist or your doctor if your symptoms of irritable bowel syndrome do not improve with Symbioflor 2 or if they get worse.
- If you have any questions or concerns, speak with a pharmacist or your doctor.

Information for healthcare professionals

- Symbioflor 2 should be used for the treatment of irritable bowel syndrome (IBS) only, and it should no longer be used for treating 'functional gastrointestinal disorders' or other conditions of the gastrointestinal tract.
- A study comparing Symbioflor 2 with placebo suggested that it was effective at treating IBS in adults. However, the study had some weaknesses and it did not provide evidence on how well Symbioflor 2 works in different types of IBS.
- The company will need to carry out a well-designed study to demonstrate the efficacy and safety of Symbioflor 2 for treating different variants of IBS, as a condition for continuing to market it.
- An observational study involving adolescents and children aged over 4 years did not provide sufficient evidence of efficacy and safety in children and adolescents.
- The safety profile of Symbioflor 2 is acceptable.
- The product information will be updated in line with this review of Symbioflor 2.

More about the medicine

Symbioflor 2 and associated names contains *Escherichia coli* bacteria some of which have been broken down (autolysed) while others are living. It is marketed in some European Union countries for treating irritable bowel syndrome, functional gastrointestinal diseases and some other gastrointestinal disorders and for regulating the immune system.

Medicines containing *Escherichia coli* are available as oral drops in Austria, Germany and Hungary under the following invented names: Symbioflor 2, Symbioflor E. Coli and Symbioflor Escherichia.

The medicine has been described as probiotic, which means that it encourages the growth of beneficial organisms ('flora') in the gut. *Escherichia coli* bacteria form part of the normal gut flora. The way it works in irritable bowel syndrome is not fully understood.

More about the procedure

The review of Symbioflor 2 (and associated names) was initiated on 30 March 2016 at the request of Germany, under Article 31 of Directive 2001/83/EC.

The review was carried out by the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which adopted the Agency's opinion. The CHMP opinion was forwarded to the European Commission, which issued a final legally binding decision applicable in all EU Member States on 28/08/2017.