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EPAR summary for the public

Dukoral

cholera vaccine (inactivated, oral)

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

What is Dukoral?

Dukoral is a vaccine that is given by mouth. It is available as a suspension in a bottle together with effervescent granules in a sachet. The granules are dissolved in water and mixed with the vaccine before intake.

The vaccine contains four different inactivated strains (types) of the bacterium *Vibrio cholerae* (*V. cholerae*) serotype O1, and part of a toxin from one of these strains as active substances.

What is Dukoral used for?

Dukoral is used to protect against cholera (a very serious disease caused by *V. cholerae*, which is caught from contaminated food or water and causes severe diarrhoea). Dukoral is used in adults, adolescents and children from two years of age who will be visiting high-risk areas. Dukoral should be given according to official recommendations, taking into account where cholera is found and the risk of contracting the disease. Dukoral should not replace standard protective measures against cholera, including advice on diet and hygiene.

The vaccine can only be obtained with a prescription.

How is Dukoral used?

In adults and children from six years of age, Dukoral is given as two doses, one to six weeks apart. Children aged between two and six years should receive three doses, with an interval of one to six weeks between each dose. The course should be completed at least one week before potential exposure to cholera. For continuous protection against cholera, a single booster dose is recommended



within two years for people from six years of age, and within six months for children aged between two and six years. The course should be repeated in adults who have not been given a booster within two years and in children not given a booster within six months.

The vaccine is made up by dissolving the granules in a glass of water to prepare an effervescent (sparkling) solution, and adding the contents of the bottle. Once prepared, the suspension should be drunk within two hours. Food, drink and other medicines taken by mouth should be avoided for one hour before and one hour after each dose of Dukoral.

How does Dukoral work?

Dukoral is a vaccine. Vaccines work by 'teaching' the immune system (the body's natural defences) how to protect itself against a disease. Dukoral contains small amounts of inactivated (killed) cholera bacteria and a part of the cholera toxin called the 'B subunit'. This subunit is not toxic by itself. When a person is given the vaccine, the immune system recognises the bacteria and the toxin, and makes antibodies against them. In the future, the immune system will be able to produce antibodies more quickly when it is exposed to cholera bacteria. These antibodies will help to protect against cholera by preventing the bacteria and the toxins from attaching to the walls of the gut and entering the body's cells.

How has Dukoral been studied?

Because Dukoral has been in use in Sweden since 1991, the company presented the results of three main studies that had already been carried out in order to support the use of Dukoral. The company also presented data from the published literature.

The three main studies involved a total of almost 113,000 people. In all three studies, Dukoral, given as either two or three doses, was compared with placebo (a dummy vaccine). The studies took place in areas where cholera is found. The first study involved over 89,000 people in Bangladesh and compared Dukoral with the same vaccine without the toxin and with placebo. In this study, Dukoral was made using cholera toxin extracted from cholera bacteria in place of the newer recombinant toxin. The other two studies compared Dukoral (containing recombinant cholera toxin) with placebo in over 22,000 people in Peru. The people in the final study also received a booster dose 10 to 12 months later.

In all three studies, the main measure of effectiveness was the 'protective effectiveness' of the vaccine, calculated by comparing the number of people in the studies who developed cholera after receiving Dukoral and after receiving placebo.

A further study was carried out to show that Dukoral could produce antibodies in people who do not come from areas where cholera is found. The company also presented information on the use of Dukoral for the prevention of a severe type of traveller's diarrhoea caused by a bacterium called 'enterotoxigenic *Escherichia coli*'.

What benefit has Dukoral shown during the studies?

In the study in Bangladesh, the protective effectiveness of Dukoral was 85% over the first six months of follow-up. The length of protection was different for adults and children, lasting for six months in children and for two years in adults. In adults, two vaccine doses were shown to be as effective as three. In the first of the two studies in Peru, the protective effectiveness of Dukoral was 85% for the first five months of follow-up. The other study in Peru showed that after a booster dose, the protective effectiveness of Dukoral during the second year of follow-up was 61%.

The information presented was not sufficient to support the use of Dukoral in traveller's diarrhoea.

What is the risk associated with Dukoral?

Side effects with Dukoral are not common. However, the following side effects are seen in between 1 and 10 patients in 1,000: headache, diarrhoea, and abdominal (tummy) pain, cramps, gurgling (gas) or discomfort. For the full list of side effects reported with Dukoral, see the package leaflet.

Dukoral must not be used in people who may be hypersensitive (allergic) to any of the active substances, to any of the other ingredients or to formaldehyde. Its use should be postponed in patients with a short-lived illness affecting the stomach or gut, or with a fever.

Why has Dukoral been approved?

The CHMP noted that the risk of cholera for regular tourists is minor, but that Dukoral could be important for certain groups, such as healthcare workers in cholera epidemics. The Committee decided that Dukoral's benefits are greater than its risks and recommended that it be given marketing authorisation.

Other information about Dukoral:

The European Commission granted a marketing authorisation valid throughout the European Union for Dukoral on 28 April 2004.

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

This summary was last updated in 10-2014.