swissmedic

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Zeposia® (active substance: ozanimod as ozanimod hydrochloride)

Indication extension in Switzerland: 19 August 2022

Medicinal product (hard capsules) for the treatment of moderate to severe ulcerative colitis (UC) in adults

About the medicine

The medicinal product Zeposia, containing the active substance ozanimod, is supplied as a hard gelatin capsule. It is used to treat adults with moderate to severe active ulcerative colitis (UC) who have not responded adequately or are no longer responding to conventional therapies or treatment with a biological agent[1] or who do not tolerate the therapy.

UC is a chronic, usually episodic inflammation of the mucous membrane lining the large intestine. Zeposia helps to reduce the inflammation associated with UC by preventing certain white blood cells from reaching the intestinal mucosa.

Zeposia has already been authorised by Swissmedic, on 11 August 2020, for the treatment of adult patients with relapsing-remitting multiple sclerosis.

Mode of action

Ozanimod, the active substance in Zeposia, is a sphingosine 1-phosphate (S1P) receptor modulator.

S1P plays an important role in signal transmission in a large number of immunological functions. The exact mechanism of action by which ozanimod exerts a therapeutic effect in UC is not known. It is assumed that ozanimod retains white blood cells (lymphocytes) in lymphoid tissue such as lymph nodes and the spleen and in this way prevents the lymphocytes from migrating to sites of inflammation (e.g. the intestinal mucosa). This suppresses the local inflammatory reaction and supports the recovery of the mucous membrane.

[1] Biological agent: A medicinal product manufactured from biological substances.

Indication

Zeposia, containing the active substance ozanimod, is a prescription-only medicine.

The recommended dosage of Zeposia is 0.92 mg once daily. In order to keep the risk of side effects affecting the heart (see below) at the start of treatment as low as possible, the daily dose is increased slowly over a period of 7 days until the target dose of 0.92 mg is reached.

Changes in the rate at which the heart beats may occur when treatment is started even at the low initial dosage. In particular, the heart rate may become slower (bradycardia). It is recommended that patients with a known history of cardiac problems, in particular, are monitored for 6 hours after the first dose. Zeposia cannot be used at all in patients with a history of some cardiac problems because of these risks (see below).

Efficacy

The efficacy and safety of Zeposia were investigated in two trials (TRUENORTH-I and TRUENORTH-M) involving adult patients with moderate to severe active UC who had previously not responded adequately, had stopped responding or had developed an intolerance to a conventional therapy or treatment with a biological agent.

The first trial, TRUENORTH-I, consisted of a 10-week initial phase. The second trial, TRUENORTH-M, investigated the subsequent maintenance therapy for 42 weeks.
In the TRUENORTH-I trial, 429 trial subjects treated with Zeposia were compared with 216 subjects who were given a placebo (dummy drug).
Clinical efficacy was evaluated on the basis of the occurrence of rectal bleeding, stool frequency and endoscopic examination of the intestinal mucosa. A significantly larger proportion of the trial subjects treated with Zeposia were in clinical remission[2] after 10 weeks of treatment compared with the placebo-treated subjects.
The trial subjects first had to have responded clinically to Zeposia in TRUENORTH-I in order to take part in the TRUENORTH-M maintenance trial. During TRUENORTH-M, these trial subjects were treated for 42 weeks with either Zeposia (230 subjects) or placebo (227 subjects). After 52 weeks of therapy (10 weeks of initial and 42 weeks of maintenance therapy), 37% of the trial subjects treated with Zeposia had achieved a clinical remission compared with 19% of the trial subjects treated with placebo. This group difference was significant ($p < 0.0001$). The proportion of patients with a clinical response and an improvement in their endoscopic findings was also significantly higher in the group treated with Zeposia.

Precautions, undesirable effects & risks

Zeposia must not be used if the patient has a hypersensitivity to the active substance ozanimod or any other ingredient in the medicine.

Treatment must not be given to patients who, in the previous 6 months, have had a heart attack, unstable angina pectoris (sensation of constriction in the chest), a stroke,

[2] Remission: During clinical remission the symptoms of the disease subside temporarily or permanently without the disease being cured.

a transient ischaemic attack (temporary impairment of circulation in the brain with remission of the neurological symptoms within 24 hours) or heart failure (requiring hospitalisation or class III/IV). Furthermore, treatment must not be instigated in patients with severe untreated sleep apnoea or certain cardiac arrhythmias unless the patient has a functioning cardiac pacemaker.

Treatment must also not be instigated in patients with an impaired immune system, an increased risk of opportunistic infections[3], severe active or active chronic infections (hepatitis or tuberculosis), active cancer, severe liver failure, macular oedema (accumulation of fluid in the central region of the retina) or during pregnancy.

Treatment with Zeposia may cause a decreased heart rate. Before treatment with Zeposia is started, certain previously unknown heart conditions should be ruled out in all patients by means of an electrocardiogram (ECG) and the opinion of a cardiologist should be sought if necessary.

The side effects recorded most frequently in clinical trials in patients with UC comprised a reduction in certain white blood cells (lymphopenia), elevated liver enzymes in the blood, inflammation of the nose and throat (nasopharyngitis), headaches and infections caused by viruses from the herpes group (herpes zoster (shingles) and herpes simplex).

All precautions, risks and other possible side effects are listed in the Information for patients (package leaflet) and the Information for healthcare professionals.

Why the medicinal product has been authorised

It was demonstrated in clinical trials that a significantly larger number of patients with moderate to severe active ulcerative colitis who were treated with Zeposia achieved clinical remission than trial subjects treated with placebo. All patients had previously not responded adequately to conventional therapies or treatment with a biological agent, or had not responded at all, or did not tolerate the therapy.

During treatment with Zeposia there is a potential risk of, among other things, a reduction in heart rate, liver damage and infections caused by pathogens including viruses from the herpes group.

Taking all the precautions into account, and based on the available data, the benefits outweigh the risks of Zeposia. Swissmedic has therefore authorised the extension of the indication for Zeposia with the active substance ozanimod in Switzerland.

[3] Opportunistic infections: An opportunistic infection occurs when the immune defences are impaired. The body is consequently weakened and opportunistic pathogens such as bacteria, fungi, viruses and parasites can cause an infection.

Further information on the medicinal product

Information for healthcare professionals: Information for healthcare professionals Zeposia®

Information for patients (package leaflet): Information for patients Zeposia®

Healthcare professionals can answer any further questions.

The date of revision of this text corresponds to that of the SwissPAR. New information concerning the authorised medicinal product in question will not be incorporated into the Public Summary SwissPAR.

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