swissmedic

Summary report on authorisation dated 13 January 2025

Padcev® (active substance: enfortumab vedotin)

Indication extension in Switzerland: 17 September 2024

Powder for concentrate for solution for infusion to treat inoperable or metastatic urothelial cancer (mUC) in combination with the active substance pembrolizumab in adults

About the medicinal product

Padcev contains the active substance enfortumab vedotin (enfortumab is genetically engineered using CHO [Chinese hamster ovary] cells) and is used in combination with the active substance pembrolizumab[1] for the first-line treatment of patients whose urothelial cancer (mUC)[2] cannot be surgically removed or has metastasised.

The indication extension for Padcev was authorised in connection with "Project Orbis". Project Orbis is a programme for promising cancer treatments coordinated by the FDA, the US regulatory authority. It provides a framework for the concurrent submission and review of cancer medicines by several international partner authorities in various countries. The ultimate aim is to give patients faster access to innovative cancer treatments. Currently, the authorisation authorities in Australia (TGA), Brazil (ANVISA), Israel (MOH), Canada (HC), Singapore (HSA), Switzerland (Swissmedic), and the United Kingdom (MHRA) are represented in Project Orbis.

Padcev was first authorised by Swissmedic on 9 November 2021 for monotherapy in adults with locally advanced or metastatic urothelial cancer (mUC) who have previously received platinum-containing therapy and treatment with PD inhibitors (PD-1/PD-L1[3]) but suffered a progression or relapse of the disease.

Mode of action

Enfortumab vedotin belongs to the class of antibody-drug conjugates (ADCs). The active substance consists of a monoclonal antibody (immunologically active protein) linked to

[1] Pembrolizumab: Pembrolizumab is contained in immunotherapy medication that blocks the protein PD-1 in order to help the immune system to better recognise and fight cancer cells.

[2] Urothelial cancer (UC): Urothelial cancer refers to bladder cancer and cancers of the urinary tract (renal pelvis, ureter or urethra).

[3] PD-1/ PD-L1: Cancer drugs that act as inhibitors of the programmed cell death receptor 1 (PD-1) or the programmed cell death ligand 1 (PD-L1).

the substance monomethyl auristatin E (MMAE). MMAE is a cytotoxin (cell poison) with the ability to kill cancer cells. The monoclonal antibody binds predominantly to a specific receptor (target site) on the surface of the urothelial cancer cells, causing MMAE to be released into the cells. The resulting initiated process leads to the death of the cancer cell.

Use

Padcev is a prescription-only medicine and is authorised as a powder for concentrate for solution for infusion. After preparation, it is administered as an infusion into a vein. The vials contain 20 mg or 30 mg of enfortumab vedotin.

The recommended dose of Padcev in combination with pembrolizumab is 1.25 mg/kg body weight (up to a maximum of 125 mg for patients ≥100 kg body weight) and is administered as an intravenous infusion over 30 minutes on days 1 and 8 of a 21-day cycle until progression of the disease or unacceptable side effects occur.

Efficacy

The efficacy of Padcev in combination with pembrolizumab was investigated in study EV-302, which involved 886 patients with untreated inoperable or metastatic urothelial cancer (mUC).

The participants received either Padcev together with pembrolizumab or a standard chemotherapy.

The study showed that the combination therapy significantly improved progression-free survival (PFS)[4], with a median[5] PFS of 12.5 months versus 6.3 months with the standard chemotherapy. In addition, the combination significantly improved the overall survival (OS)[6], with a median OS of 31.5 months versus 16.1 months.

Precautions, undesirable effects, & risks

Padcev must not be used in those who are hypersensitive to the active substance or any of the excipients.

The most frequent undesirable effects observed in all patients treated with Padcev were alopecia (excessive hair loss), fatigue, decreased appetite, peripheral sensory neuropathy (disorder of the nervous system), diarrhoea, nausea, pruritus (itching), dysgeusia (impaired taste), anaemia, weight loss, maculopapular (nodular and spotty) rash, dry skin, vomiting, increased AST/ALT[7], hyperglycaemia (excessively high blood sugar), dry eyes, and rash.

Compared to monotherapy with Padcev, an increase in skin reactions, pneumonitis/ILD, and peripheral neuropathies was observed with the combination therapy with pembrolizumab.

[4] Progression-free survival (PFS): Period between the start of a treatment or a clinical trial and the onset of disease progression or the death of the patient.

[5] Median: The value that lies exactly in the middle of a distribution of data is called the median or central value. Half of the data values are always less than the median, the other half are always greater.

[6] Overall survival (OS): Refers to the period between the start of treatment and the death of the patient.

[7] AST/ALT: Aspartate aminotransferase (AST) and alanine aminotransferase (ALT): are enzymes produced mainly in the liver. Elevated levels of activity of these enzymes in the blood may indicate liver-related diseases.

All precautions, risks, and other possible undesirable effects are listed in the Information for healthcare professionals.

Why the medicinal product has been authorised

The results of available treatment options are not satisfactory for patients with inoperable or metastatic urothelial cancer (mUC), particularly as regards overall survival.

In studies, Padcev in combination with pembrolizumab showed a significant improvement in overall survival and progression-free survival compared to standard chemotherapy.

Taking all the risks and precautions into account, and based on the available data, the benefits of the indication extension for Padcev outweigh the risks.

Swissmedic has therefore authorised the indication extension in Switzerland for the medicinal product Padcev in combination with pembrolizumab for the first-line treatment of adult patients with inoperable or metastatic urothelial cancer (mUC).

Further information on the medicinal product

Information for healthcare professionals: Information for healthcare professionals Padcev®.

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 Summary report on authorisation.

Swissmedic monitors medicinal products authorised in Switzerland. Swissmedic initiates the necessary action in the event of newly discovered adverse drug reactions or other safety-relevant signals. New findings that could impair the quality, efficacy, or safety of this medicinal product are recorded and published by Swissmedic. If necessary, the medicinal product information is adapted.