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Public Summary SwissPAR dated 29 December 2022

Koselugo® (active substance: selumetinib)

Temporary authorisation in Switzerland: 29 July 2022

Medicinal product (hard capsules) for the treatment of neurofibromatosis type 1 in children and adolescents from 3 years of age

About the medicine

The medicinal product Koselugo, containing the active substance selumetinib, is used to treat children and adolescents from 3 years of age with neurofibromatosis type 1 (NF1) and symptomatic inoperable plexiform neurofibromas (PN).

Neurofibromatosis type 1 (NF1) is a rare genetic disorder. It is caused by mutations in the so-called NF1 tumour suppressor gene, which codes for the tumour suppressor protein neurofibromin 1.

Early signs of NF1 include café au lait spots[1] and general hyperpigmentation[2] of the skin that develop in the first two years of life. Plexiform (having the form of a network) neurofibromas (PN) occur in one third of patients with NF1.

Superficial neurofibromas are benign and do not need to be removed unless they are causing problems. Surgical removal is the standard therapy for patients with PN. However, it is often not an option because of nerve involvement and the associated risk of nerve damage or severe bleeding.

Since this is a rare, life-threatening disease, Koselugo has been authorised as an orphan drug. The term "orphan drug" is used to refer to important medicines for rare diseases.

Koselugo was authorised under Article 13 of the Therapeutic Products Act (TPA). This means that the medicinal product is already authorised in another country with comparable medicinal product control. In this case, Swissmedic takes into consideration the results of checks carried out by the foreign regulatory agency, provided certain requirements are fulfilled. These involve checks on the quality, efficacy and safety of the medicinal product, and the extent to which the results can be accepted for Switzerland.

The consideration of the results of foreign authorisation procedures is intended to help ensure that medicines that are already authorised abroad can be made available to patients in Switzerland as quickly as possible.

In deciding whether to authorise Koselugo in Switzerland, Swissmedic has accepted

[1] Café au lait spots: light brown, evenly pigmented spots on the skin that can occur in different sizes anywhere on the body.

[2] Hyperpigmentation: darkening of the skin caused by an abnormally increased amount of the skin pigment melanin.

parts of the assessment and approval decision of the U.S. Food and Drug Administration (FDA).

Accordingly, in the SwissPAR (Swiss Public Assessment Report) and the resulting Public Summary SwissPAR, Swissmedic refers to the Assessment Report and the short report issued by the reference authority: (www.fda.gov)

Mode of action

The active substance selumetinib is what is known as an MEK inhibitor. It acts by blocking certain proteins which are known to play a role in the growth of tumour cells.

Indication

Koselugo, containing the active substance selumetinib, is a prescription-only medicine and is available as hard capsules in the dosage strengths 10 mg and 25 mg.

The dose taken by the patient depends on their body surface area. This is measured in square metres (m^2) and calculated by the doctor on the basis of the patient's height and weight.

The capsules must be swallowed whole with a little water and must not be chewed, dissolved or opened.

Efficacy

The efficacy of Koselugo was investigated in the SPRINT trial involving 50 patients between 3.5 and 17.4 years of age with inoperable PN caused by NF1.

The patients were given Koselugo twice a day for periods of 28 days (1 treatment cycle) until the disease progressed (became more severe) or unacceptable toxicity occurred.

The primary analysis[3] was the overall response rate (ORR), defined as the percentage of patients who responded fully (defined as the disappearance of the target PN) or had a confirmed partial response (defined as reduction of the PN volume by ≥20%, confirmed by a tumour assessment within 3-6 months). The primary efficacy endpoint ORR was 66%. Of the 66% of patients who responded to the therapy, all had a partial response, corresponding to a reduction of the PN volume by at least 20%. The median[4] time to onset of the response was 7.2 months.

[3] Primary analysis: The primary analysis takes place when the primary endpoint of a clinical trial is reached. The primary endpoint is the main objective of the study determined before the trial starts. If the primary endpoint is reached or exceeded, the study proves that a treatment is effective. Secondary endpoints, on the other hand, refer to other effects that do not clearly prove efficacy or that do not allow any clear conclusions to be drawn about the actual target criterion (primary endpoint).

[4] 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 smaller than the median, the other half are always greater.

Precautions, undesirable effects & risks

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

The most common undesirable effects are vomiting, skin rash, abdominal pain, diarrhoea, nausea, dry skin, musculoskeletal pain, fatigue, fever, inflammation of the mucous membrane lining the mouth, headache, pain on swallowing, inflammation of the nail bed, pruritus, cough, dermatitis (inflammatory reaction of the skin), constipation, nasal congestion, hair loss and hair colour change.

The safety-relevant adverse effects of Koselugo include visual impairment, change in bowel habits, skin damage and heart disorders.

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

No systemic therapies[5] are currently approved in Switzerland for patients with NF1. There is accordingly a high level of unmet medical need, particularly in view of the considerable burden imposed by the disease.

The SPRINT trial showed significant ORR rates. However, the data for progression-free survival (PFS[6]) are not yet informative and it is therefore not possible to assess whether the ORR rates will lead to longer PFS. As yet there are no long-term safety data. In addition, a different delivery form (granules) more suitable for younger children is currently being investigated. The current capsule formulation can be problematic for children under 6 years of age, in particular, who are unable to swallow the capsule whole.

The medicinal product Koselugo was therefore authorised temporarily in Switzerland (in accordance with Art. 9a TPA) since not all clinical trials were available or had been concluded at the time of authorisation. The temporary authorisation is contingent on the timely submission of the data requested by Swissmedic. Once these authorisation conditions have been met, the temporary authorisation can be converted into an ordinary authorisation in the event of a positive benefit-risk assessment of the results.

Further information on the medicinal product

Information for healthcare professionals: Information for healthcare professionals Koselugo®

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

Healthcare professionals can answer any further questions.

5 Systemic therapy: In contrast to local therapy (treatment at the site of the disorder), systemic therapy involves treatment of the entire body to eliminate a disorder.

6 PFS: progression-free survival. Period between the start of a treatment or a clinical trial and the onset of disease progression or the death of the patient.

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.

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.