Latruvo®

(olaratumab)

10 mg/ml concentrate for solution for infusion

Summary of Risk Management Plan (RMP)

Summary of the risk management plan (RMP) for Lartruvo (olaratumab)

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimize them.

The RMP summary of Lartruvo is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the „Arzneimittelinformation / Information sur le médicament“ approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization. Please note that the reference document which is valid and relevant for the effective and safe use of Lartruvo in Switzerland is the „Arzneimittelinformation/ Information sur le médicament“ (see www.swissmedicinfo.ch) approved and authorized by Swissmedic.

Eli Lilly is fully responsible for the accuracy and correctness of the content of this published summary RMP of Lartruvo

Overview of disease epidemiology

Soft tissue sarcomas (STS) are a rare and diverse group of solid tumours that develop from soft tissues like fat, muscle, nerves, fibrous tissues, blood vessels, or deep skin tissues. There are more than 50 different subtypes of STS. Furthermore, many of these subtypes can occur at any age and are not restricted to a specific location of the body. The rarity of the disease combined with the diverse number of subtypes can make STS very difficult to study. Soft tissue sarcomas account for approximately 1% of all new cancers in adults, and approximately 2% of total cancer-related death. In the EU, an estimated 23,574 new cases are expected per year. There has been relatively little improvement in patient outcomes from chemotherapy, with the overall 5-year survival rates of about 50% for the cancer that reappears in the same place after treatment (local tumour recurrence) and in the range of 15% for those that has spread (metastasised) to other organs.

Summary of treatment benefits

Depending on the type and stage of STS, chemotherapy may be given as the main treatment or as an addition (adjuvant) to surgery. Chemotherapy for STS generally uses a combination of several anti-cancer drugs. Anthracyclines (a class of drugs used in cancer chemotherapy) are considered standard of care for STS. As of 2014, there is no formal demonstration that combination of several anti-cancer drugs is superior to single-agent chemotherapy with anthracyclines (such as doxorubicin) alone in terms of survival. The addition of other chemotherapy agents, such as ifosfamide or gemcitabine, to doxorubicin has increased toxicity without a survival benefit. Some chemotherapy side effects can last a long time or even be permanent. For example, doxorubicin can weaken the heart if too much is given.

Targeted therapy is a newer type of cancer treatment that uses drugs or other substances to identify and attack cancer cells while doing little damage to normal cells. These therapies attack the cancer cells' inner workings (the programming) that makes them different from normal, healthy cells. Each type of targeted therapy works differently, but all alter the way a cancer cell grows and divides (proliferation), changes (differentiation), repairs itself, or interacts with other cells.

Members of the platelet-derived growth factor (PDGF) family stimulate the growth, survival, and movement of components within cells and cell mobility. Olaratumab is a fully human monoclonal antibody that specifically binds to PDGF receptor alpha (PDGFRα) and blocks PDGFRα activation that is important for cell growth and survival.

A Phase 2 study in 133 patients with advanced STS compared 2 drugs, doxorubicin plus olaratumab, against doxorubicin alone. This study showed that patients who received the 2 drugs together lived longer (11.8 months) over doxorubicin alone. Tumour growth slowed down in patients treated with the 2 drugs compared with patients on doxorubicin alone.

Unknowns relating to treatment benefits

In the main and supporting United States clinical study of advanced STS, nearly all patients were white Caucasian (aged between 22 and 85 with most patients younger than 65). There is no information about olaratumab use in children (<18 years) and women who are pregnant or breast feeding.

Summary of safety concerns

Table VI.4. Important Identified Risks

Risk	What is Known	Preventability
Allergic type reaction (Infusion-related reaction)	In patients given olaratumab for advanced STS, about 14.7% developed allergic-type reactions. These reactions were mild or moderate in most cases. Symptoms of infusion-related reaction may include: increased muscle tension, back pain, chest pain and/or tightness, chills, flushing, difficulty in breathing, wheezing, and feeling of tingling or numbness in hands or feet. In severe cases, symptoms may include difficulty breathing caused by narrowing of the airways, faster heartbeat, and feeling faint.	Patients allergic to olaratumab or any of the other ingredients it contains must not be given olaratumab. Olaratumab is given as an intravenous infusion via a drip. A doctor or nurse will check for side effects during the infusion. Patients will be watched closely and treatment for allergic reaction will be given right away if any symptoms are seen. To reduce the likelihood of an allergic-type reaction, all patients should receive medications called H1 antagonist before every olaratumab infusion. Before the first 2 olaratumab infusions, patients will also receive a corticosteroid to further reduce this risk. If a patient has a mild or moderate infusion-related reaction to olaratumab, she/he will be given medication to prevent another reaction before all future olaratumab infusions. Olaratumab will be immediately and permanently stopped if a patient experiences a severe infusion-related reaction.

Important Potential Risks

Risk	What is known (including Reason Why it is Considered a Potential Risk)
Risks to the embryo/foetus when pregnant (Embryo-foetal toxicity)	No animal studies have been done to test olaratumab for the potential to effect foetal development. Based on olaratumab's mechanism of action, it is likely that olaratumab may cause foetal harm and potentially result in harmful effects on embryo-foetal development. There are no data on olaratumab use in pregnant women to help assess any risks during pregnancy. Olaratumab use is not recommended during pregnancy or in women of child-bearing potential not using contraception. Olaratumab should only be used in pregnant women if the treating physician considers the benefit to the patient outweighs the potential risk to the foetus.
Malformations (Teratogenicity)	No animal studies have been done to see if olaratumab has the potential to cause malformations in the foetus during pregnancy. Olaratumab should be used during pregnancy only if the benefit to the mother justifies the potential risk to the foetus.

Important missing Information

Risk	What is Known
Developing another kind of cancer (Carcinogenicity) Damaging DNA within cells (Genotoxicity)	No animal studies have been done to test olaratumab for the potential to develop another kind of cancer and/or damage genetic (DNA) within cells.
Problems getting pregnant (Long-term fertility impairment)	No animal studies have been done to evaluate whether olaratumab can cause harmful effects on fertility (ovulation), placental development, the developing foetus, and postnatal development. There are no available data on olaratumab use in pregnant women to inform any drug-associated risks. Avoid the use of olaratumab in pregnant women and only use if the potential benefit to the mother justifies the potential risk to the foetus. Inform women of child bearing potential or women who become pregnant during treatment of the potential risks of olaratumab to the foetus and for maintaining pregnancy.
Effect on breast feeding	There have been no studies using olaratumab on breastfed infants. Because of the potential risk for serious adverse reactions in nursing infants from olaratumab, breastfeeding is not recommended during treatment with olaratumab and for at least 3 months following the last dose.
Effect on rare STS subtypes	No studies investigating the benefit of olaratumab on rare types of STS have been completed.

Abbreviations: DNA = deoxyribonucleic acid; STS = soft tissue sarcoma.

Planned Post-authorisation development plan

Table VI.9. List of Studies in Post-authorisation Development Plan

Study/Activity (including Study Number)	Objectives	Safety Concerns /Efficacy Issue Addressed	Status	Planned Date for Submission of Final Results
I5B-MC-JGDJ (JGDJ):	To compare the safety and efficacy in patients with advanced or metastatic STS after treatment with doxorubicin plus olaratumab versus doxorubicin plus placebo	To confirm the efficacy and safety results of the randomised Phase 2 study	Ongoing	Estimated CSR at end of 2020
An observational study	To assess the effectiveness and safety of olaratumab in very rare STS subtypes in the real-world setting	Lack of understanding of how well olaratumab works in patients with very rare types of STS	Planned (will start within 6 to 12 months of olaratumab being in the EU market)	Exact date will be driven by the number of patients receiving olaratumab in each of the rare subtypes of interest.

Abbreviations: CSR = clinical study report; EU = European Union; STS = soft tissue sarcoma.

Studies which are a condition of the marketing authorization

Clinical study I5B-MC-JGDJ will be performed as a condition of the marketing authorisation.

Summary of changes to the risk management plan over time

This summary was last updated in 21-03-2017