Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCTS

Iscador P 20 mg
Iscador P 10 mg
Iscador P 1 mg
Iscador P 0.1 mg
Iscador P 0.01 mg
Iscador P 0.001 mg
Iscador P 0.0001 mg

Solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ampoule of 1 ml contains:

Iscador P 20 mg:
Active substance: fermented aqueous extract from Viscum album ssp. austriacum (pine mistletoe), Herba rec. (plant to extract = 1:5) 100 mg

Iscador P 10 mg:
Active substance: fermented aqueous extract from Viscum album ssp. austriacum (pine mistletoe), Herba rec. (plant to extract = 1:5) 50 mg

Iscador P 1 mg:
Active substance: fermented aqueous extract from Viscum album ssp. austriacum (pine mistletoe), Herba rec. (plant to extract = 1:5) 5 mg

Iscador P 0.1 mg:
Active substance: fermented aqueous extract from Viscum album ssp. austriacum (pine mistletoe), Herba rec. (plant to extract = 1:5) 0.5 mg

Iscador P 0.01 mg:
Active substance: fermented aqueous extract from Viscum album ssp. austriacum (pine mistletoe), Herba rec. (plant to extract = 1:5) 0.05 mg

Iscador P 0.001 mg:
Active substance: fermented aqueous extract from Viscum album ssp. austriacum (pine mistletoe), Herba rec. (plant to extract = 1:5) 0.005 mg

Iscador P 0.0001 mg:
Active substance: fermented aqueous extract from Viscum album ssp. austriacum (pine mistletoe), Herba rec. (plant to extract = 1:5) 0.0005 mg

The strength in mg states the amount of fresh plant material used for the production of one ampoule of Iscador P. Example: “Iscador P 1 mg” contains the extract from 1 mg of fresh mistletoe plant.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

According to anthroposophical knowledge of man and nature.
This includes:
For adults:
Stimulation of formative and integrative forces to dissolve and re-integrate growth processes that have become disregulated, e.g.:

- in malignant tumours, also with concomitant diseases of the haematopoietic organs;
- in benign tumours;
- in defined precanceroses;
- for relapse prophylaxis following tumour surgery.

4.2 Posology and method of administration

Initiation phase:
Unless otherwise prescribed, a gradual dose increase of Iscador P Series 0 which contains the lowest dose levels in increasing strengths is recommended at the start of therapy with Iscador P to avoid overreactions. Even after previous treatment with a different mistletoe preparation, treatment with Iscador P must be restarted with the corresponding Series 0.

2 to 3 times a week, 1 ml of Iscador is injected subcutaneously in an increasing strength in accordance with the composition of the Series. If Series 0 is tolerated well, the treatment can be increased to Iscador P Series I to possibly Series II until the patient's individual reaction dose is reached.

The optimum strength or dose must be determined individually. For this, according to the current state of knowledge, the following reactions, which may occur individually or in combination, must be observed.

a) Change in subjective well-being
Exhaustion, shivering, general malaise, headaches and short-term dizziness which may occur on the day of the injection are not signs of intolerance, but indicate an effective dose which might already be too high. If these phenomena have not disappeared or still exceed a tolerable level on the next day, the strength or the dose should be reduced.
An improvement in well-being (increase in appetite and weight, normalisation of sleep, sensitivity to heat and performance capacity) and in the mental condition (brightening of moods, increase in vital energy and ability to take initiative) and an alleviation of pain indicate that an optimal dose range was administered.

b) Temperature reaction
Temperature reactions in the form of an above-average increase in body temperature a few hours after the injection, restoration of the physiological morning/evening difference of at least 0.5 °C or of an increase of the mean temperature level during treatment.
In cases of tumour fever, however, low strengths are administered with the aim of normalising and restoring a rhythmic core temperature.

c) Immunological reaction
For example, an increase in leukocytes (especially of absolute lymphocyte and eosinophil counts), an improvement in the cellular immune status in the recall antigen test and in the determination of the lymphocyte subpopulations.

d) Local inflammatory reaction
Local inflammatory reactions at the site of injection up to a maximum diameter of 5 cm.

Maintenance phase:
Unless otherwise prescribed:
The treatment is continued with the optimum individual strength or dose thus determined. The patient undergoes either continued therapy with the same Series for which the reaction dose represents the highest strength, or with the corresponding sort package (package with ampoules of one strength). In order to avoid habituation effects, a rhythmic administration is recommended:

- alternation with lower strengths and doses in the form of increasing and possibly also decreasing dosage series (only for rhythmically alternating doses with series)
- rhythmic injection intervals, e.g. injection on day 1, 2 and 5 of each week
- taking breaks, e.g. 1-2 weeks break after 2 x 7 ampoules; if the treatment lasts longer, the breaks can be extended as of the 3rd year of treatment.

If the therapy break lasts 4 weeks or longer, there may be a stronger initial reaction when the treatment is restarted. Therefore, restarting therapy with the next lower strength or Series is recommended, e.g. therapy before the break with Iscador P Series II, start after the break with 1 pack of Iscador P Series I, then continued treatment with Series II.
If the disease has progressed or if the patient feels worse on the days without Iscador, it may be expedient to inject 1 ml of Iscador P every day without a break.
The dosage should be checked at intervals of 3-6 months based on the patient's reaction and the tumour behaviour.

Administration frequency:
Unless otherwise prescribed: 2-3 weekly subcutaneous injections.

Dosage in patients with renal impairment:
Sufficient data do not exist for specific dosage recommendations in patients with impaired renal function. General experience has not yet indicated a necessity to adapt the dosage.

Method of administration:
Subcutaneous injection, if possible in the vicinity of the tumour or metastasis, otherwise in alternating parts of the body (e.g. abdominal skin, upper arm or thigh). Do not inject into inflamed parts of the skin or radiation fields. Pay attention to a strictly subcutaneous injection technique.

As a precaution it is recommended not to mix Iscador P and not to draw it into a syringe with other medicinal products (see also section 6.2 Incompatibilities).

Opened ampoules must not be kept for a later injection.

Duration of administration:
The treating doctor will decide on the duration of the treatment.

In principle, the duration of administration is not limited. It is determined by the doctor and is based on the risk of relapse and the individual well-being and findings of the patient in question. It ought to be a number of years and, as a rule, breaks of increasing length should be taken.

4.3 Contraindications

- Known allergy to mistletoe preparations
- Acute inflammatory or highly febrile diseases: the treatment should be interrupted until the signs of inflammation have subsided
- Chronic granulomatous diseases, florid autoimmune diseases and diseases undergoing immunesuppressive therapy
- Hyperthyroidism with tachycardia

4.4 Special warnings and precautions for use

Primary brain and bone marrow tumours or intracranial metastases with the risk of an increase in cerebral pressure: in this case, the preparations should be administered only following a strict indication and under close clinical monitoring.

The ampoule should be warmed briefly in the hand, as formation of cold agglutinins after IV injection of mistletoe solutions for injection which were not at body temperature has been described.

4.5 Interactions with other medicinal products and other forms of interaction

No studies are available on interactions with other immune-modulating substances (e.g. thymus extracts). If such preparations are used around the same time, careful dosage and monitoring of relevant immune parameters are advisable.

Interactions with other medicinal products have not been investigated, but are also not known.

4.6 Fertility, pregnancy and lactation

Animal studies are insufficient with respect to the effects on pregnancy, birth and postnatal development, especially regarding haematopoiesis and the immune system of the foetus/infant. The potential risk for man is not known. Caution is advisable if this medicine is used during pregnancy and lactation.

4.7 Effects on ability to drive and to use machines

No specific precautions are required.

4.8 Undesirable effects

A slight increase in body temperature and local inflammatory reactions at the subcutaneous injection site occur almost regularly at the start of therapy and are indications of the patient's reaction situation. Transient mild swelling of regional lymphatic nodes is also uncritical.

For increased temperatures above 38 °C (possibly accompanied by exhaustion, shivering, general malaise, headaches and short-term dizziness) or in cases of more extensive local reactions exceeding 5 cm in diameter, the next injection should only be given after these symptoms have subsided and in a lower strength or dose.

The fever caused by Iscador injections must not be suppressed by temperature-reducing drugs. If the fever lasts longer than 3 days, an infectious process or tumour fever should be considered.

Excessive local reactions can be avoided by administering a lower strength of the preparation or also of a smaller quantity of Iscador P. In this case, the administration of 0.1-0.5 ml of Iscador P with the help of a scaled 1 ml syringe is recommended.

Localised or systemic allergic or allergoid reactions may occur (normally in the form of generalised itching, urticaria or exanthema, sometimes also with Quincke's oedema, chills, shortness of breath and bronchospasms, in isolated cases with shock or as exudative erythema multiforme) and call for discontinuation of the preparation and initiation of medical therapy (see also section 4.9).

Activation of pre-existing inflammations and inflammatory irritation phenomena of superficial veins in the vicinity of the injection are possible. Here, too, a temporary treatment break until the inflammatory reactions abate is necessary.

The occurrence of chronic granulomatous inflammations (sarcoidosis, erythema nodosum) and of autoimmune diseases (dermatomyositis) during mistletoe therapy has been reported.

There have also been reports of symptoms of an increase in cerebral pressure in patients with brain tumours/metastases during mistletoe therapy.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Federal Institute for Drugs and Medical Devices, Dept. of Pharmacovigilance, Kurt-Georg-Kiesinger-Allee 3, D-53175 Bonn, website: http://www.bfarm.de.

4.9 Overdose / overreaction: symptoms, emergency measures, antidotes

If the individually tolerated dose is exceeded, the following symptoms may occur:
Local inflammation reaction exceeding 5 cm in diameter, fever or flu-like symptoms. In such cases, the next injection should only be given after these symptoms have subsided and in a lower strength or dose.

Occurrence of anaphylactic reactions
Signs suggesting onset of an anaphylactic reaction include, among others, itching or burning of the palms of the hands or soles of the feet, of the tongue and palate; also itching, erythema and urticaria of the skin and mucous membranes. During the further course, patients may develop nausea, cramps, vomiting, rhinorrhoea, hoarseness, dyspnoea, tachycardia and a drop in blood pressure culminating in shock and circulatory arrest.
In the event of an anaphylactic reaction, emergency treatment follows the current guidelines. Adequate emergency equipment must be at hand.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Cancerostatic properties have been described for Iscador solutions for injection, both *in vitro* and in animal experiments; immune-modulating properties have been described *in vitro* in animal experiments and human pharmacology testing. *In vitro*, a protective effect against DNA damage and stimulation of DNA repair has been shown for various cell suspensions for Iscador, host tree P. In an animal experiment in healthy mice, the number of leukocytes in the group treated with Iscador, host tree P increased 7-10 days following radiation or chemotherapy, as compared to the control group.

5.2 Pharmacokinetic properties

Studies on the pharmacokinetics and bioavailability have not been conducted for methodical reasons.

5.3 Preclinical safety data

Animal tests with respect to acute toxicity (animal species: rat) show a good therapeutic index.
Animal studies with respect to immunotoxicity in the mouse model, conducted representatively with the Iscador preparation with the highest quantity of lectin (Iscador Qu 20 mg), showed no immunotoxicologically relevant influence on general and specific immune parameters or on the humoral and cellular immune response up to four times higher than the maximum daily therapeutic dose. In further animal experiments, indications of a weakening of the resistance against mouse melanoma cells were observed at four times the maximum daily therapeutic dose of Iscador Qu 20 mg.
In vitro examinations (Ames test) and *in vivo* examinations (microcore testing in rats) showed no signs of mutagenicity.
Studies with respect to chronic toxicity and cancerogenicity are not available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride, water for injection

6.2 Incompatibilities

None known. As a precaution it is recommended not to mix Iscador P and not to draw it into a syringe with other medicinal products.

6.3 Shelf life

30 months

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).

6.5 Nature and contents of container

Ampoules with 1 ml solution for injection

Pack sizes

Series packs
Iscador P Series 0: 7 ampoules und 14 (2 x 7) ampoules
Iscador P Series I: 14 (2 x 7) ampoules
Iscador P Series II: 14 (2 x 7) ampoules

The Series are composed as follows:

Iscador P Series 0	
Strength	Number of ampoules
0.01 mg	2
0.1 mg	2
1 mg	3

Iscador P Series I	
Strength	Number of ampoules
0.1 mg	2
1 mg	2
10 mg	3

Iscador P Series II	
Strength	Number of ampoules
1 mg	2
10 mg	2
20 mg	3

For administration in increasing strengths, the ampoules in a Series pack must be used in the order from left to right (numbering 1-7 in the folding boxes).

Sort packs each with 7 ampoules of the same strength:
Iscador P 0.0001 mg

Iscador P 0.001 mg
Iscador P 1 mg
Iscador P 10 mg
Iscador P 20 mg

6.6 Special precautions for disposal

No special requirements.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

Iscador P 20 mg	6647405.08.00
Iscador P 10 mg	6647405.01.00
Iscador P 1 mg	6647405.02.00
Iscador P 0.1 mg	6647405.03.00
Iscador P 0.01 mg	6647405.04.00
Iscador P 0.001 mg	6647405.05.00
Iscador P 0.0001 mg	6647405.06.00

9. DATE OF RENEWAL OF THE AUTHORISATION

Iscador P 20 mg	10.05.2010
Iscador P 10 mg	10.05.2010
Iscador P 1 mg	10.05.2010
Iscador P 0.1 mg	10.05.2010
Iscador P 0.01 mg	10.05.2010
Iscador P 0.001 mg	10.05.2010
Iscador P 0.0001 mg	10.05.2010

10. DATE OF REVISION OF THE TEXT

July 2018

11. GENERAL CLASSIFICATION FOR SUPPLY

Available in pharmacies only