



## *Patient Resource: Mistletoe*



### What is mistletoe?

Mistletoe is a parasitic plant that is commonly prescribed within European out-patient cancer clinics. There are three main types: European Mistletoe (*Viscum album*), Korean Mistletoe (*Viscum album* var. *coloratum*) and American Mistletoe (*Phoradendron leucarpum*).

### Why do people use mistletoe?

Mistletoe is most commonly used in cancer care to:

- Stimulate the immune system
- Improve quality of life
- Improve cancer- and treatment-related symptoms
- Reduce tumour size
- Slow disease progression

### How does mistletoe work?

Mistletoe's effectiveness in cancer care is attributed to its ability to kill cancer cells, and enhance the immune system. Several active compounds within mistletoe are thought to be responsible for killing cancer cells, including lectins, viscotoxins and alkaloids. These compounds are thought to inhibit protein synthesis, trigger cell death, and increase natural killer cell and macrophage activity. Lectins and polysaccharides are believed to enhance immune function by increasing the number and activity of white blood cells, including natural killer cells, and also help these cells more effectively recognize cancer cells.

### Does mistletoe work?

Several clinical studies, including randomized controlled trials (RCTs) and systematic reviews, have been conducted to assess the safety and effectiveness of mistletoe as a treatment in cancer care. Overall, mistletoe therapy appears to be effective in particular for improving immune response, quality of life and symptom management. Results are mixed in terms of tumour response and survival. There is a range of mistletoe preparations used across studies which might attribute to inconsistent results. Effects of the therapy might vary depending on the extract and dose used, way of administration, type of subspecies, manufacturing process, and the time of harvest.

#### *Immune Response*

In several studies mistletoe has been found to effectively stimulate the immune system in people diagnosed with stomach, brain, head and neck cancers. Mistletoe treatment seems to also decrease the immunosuppressive effects of surgery. Longer term therapy might be more effective than shorter term therapy.

#### *Quality of Life*

Several systematic reviews of RCTs have consistently shown a benefit of mistletoe treatment on quality of life across a range of cancer types.

#### *Symptom Management*

Mistletoe treatment likely leads to improvements in quality of life in part due to its ability to decrease cancer and treatment related symptoms, in particular related to chemotherapy. Studies of several designs have documented a benefit for people treated with mistletoe therapy in terms of symptom management.

#### *Tumour Response*

Studies that document the effect of mistletoe treatment on tumour response, including recurrence and remission, are inconclusive. Some studies document a benefit, some no effect and some show mixed results.

#### *Survival*

A small number of studies have shown the potential for a survival benefit for people treated with mistletoe therapy, but overall studies have documented mixed results. Additional clinical research is needed to study any potential survival benefit.



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### Is mistletoe safe?

Several studies have explored the use of mistletoe in combination with a range of chemotherapies where no adverse events attributable to the combination were documented. Instead, the combination of chemotherapy plus mistletoe seems to contribute to reduced chemotherapy-related reactions.

Because mistletoe has been shown to stimulate the immune system, it should not be used in combination with immunosuppressants.

Mistletoe should not be used by anyone with a known allergy or hypersensitivity to mistletoe and used with caution in pregnancy and breast feeding. Raw European and American Mistletoe leaves and berries are toxic.

### What are the side effects of mistletoe?

Mistletoe is generally well tolerated. Most side effects are mild and depend on the dose use, and may only last a few days after treatment. The most common side effects include fatigue, mild flu-like symptoms, anemia, fever, diarrhea and reactions at the injection site, including redness, swelling, itchiness and rash. Severe localized reactions at the injection site occur in less than 1% of people, with less severe localized reactions occurring in approximately 25% of people.

Serious adverse events are rare. Reported serious adverse events include urticaria and angioedema, hypotension and loss of consciousness, anaphylaxis, and liver reversible toxicity.

The risk of chemotherapy associated adverse events might be reduced if people are treated with mistletoe alongside chemotherapy.

### What is the recommended dose of mistletoe?

At the OICC, mistletoe is prescribed through subcutaneous injections. Prescriptions are based on cancer type, stage, metastasis, other concurrent treatments and gender. Treatment typically begins with an induction phase at a lower dose to assess tolerability. If injections are well tolerated during the induction phase are, people move on to a maintenance dose, involving increasing dosages. Studies have shown the maximum tolerated dose to be between 5-6mg/kg body weight.

Some people continue treatment for many years, if well-tolerated and they are finding a positive impact on their well-being.