Mistletoe therapy

Patient information

Patient information on
mistletoe therapy compiled
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Almond blossom, almond tree, host tree to almond mistletoe (Viscum album, Amygdali)

Dear reader

With many forms of cancer it is nowadays possible to achieve a lasting cure. Nevertheless, however positive this statement may be, the diagnosis of "cancer" is justifiably always associated with many questions and anxieties for the patient, his family and circle of friends. This brochure is intended to help encourage discussions between doctor, patient, family and friends, to answer unresolved questions, and to stimulate an informed approach to the disease. We would be happy if reading this brochure encourages you to adopt an active approach to your cancer, for this is a definite step towards successful therapy.

The staff at
ABNOBA GmbH

Contents

Apple tree, host to apple mistletoe (Viscum album, Mali)

What is cancer?

Historically, cancer has been detectable from the earliest times. However, the frequency and nature of the disease have changed with the different civilisations. Today, for example, tumour diseases of the bowel are increasing because of changes in dietary habits.

The question "What is cancer?" used to be answered on the basis of externally visible symptoms, but today molecular biological and genetic explanations have taken precedence.

The terms "tumour", "cancer", "leukaemia" and many other names cover more than a hundred different diseases which have in common the uncontrolled and malignant growth of body cells.

All healthy cells follow an ordered life course. The life cycle of **malignant** cells and their proliferation by cell division, however, no longer fits in with the body as a whole and develops an independent "life of its own". Scientifically, the cause of this lies in the presence, in the diseased cells, of "disrupted" genes which are responsible for cell growth and function. In healthy subjects, this genetically ordained programming is also controlled by the neighbouring cells and by messenger substances in the human blood so that human organs or tissues assume an appropriate size and form. Each organ grows or regenerates itself to its natural individual size and shape. The diseased cell, however, lacks "information" about its function and its intended location. It therefore invades foreign tissue as well and migrates,

establishing itself (metastasising) in other regions of the body. Generally, the cellular changes occur years before the disease is ever apparent.

However, not only has the individual cell and the enclosing organ- or tissue-forming architecture lost its capacity for control to the tumour, but so has the whole body as well. Cancer is therefore always also a disease of the human **immune system**. In the human body, new cells are constantly being formed and old ones dying. This natural process that occurs daily in millions of different ways is "monitored" by the immune system. In cancer, the immune system has, among other things, lost the ability to intercept messenger substances that stimulate the unbridled growth of cells and to destroy malformed cells.

There are therefore three disorders regularly associated with cancer disease:
the degenerated genetic information in the cell,
the lack of communication between cells which determines the shape and size of tissues or organs
and the disorientation or weakness of the immune system.

Tumours present as solid and sometimes palpable growths or systemically in the whole body, for example as a lymphoma or leukaemia. In solid tumours, the removal of tumour tissue **(biopsy)** determines how malignant the tumour is. The more similar the tumour is to the tissue out of which it is growing, the more likely it will be "graded" as **benign (harmless)** because at that stage it has only to a limited extent developed its own dynamic processes distinct from the rest of the body. In addition to grading, tumours are also classified in terms of the TNM system which describes the size of the tumour, the involvement of the lymphatic system and the spread of metastases. (For "Grading" and "TNM system" see also the detailed index in the appendix.)

What causes cancer?

An unambiguous and conclusive causal relationship can at present only be established for certain **carcinogenic**, i.e. cancer-producing, substances and radiation. The essential factor here is the quantity of harmful substances absorbed in relation to the "strength" of the individual defences or the immune system. In this context, it should be noted that nowadays more than half of all cancers are related to smoking and alcohol consumption or to unbalanced dietary habits.

In certain forms of cancer, a hereditary incidence can be observed (e.g. breast cancer). In this case, it is possible to talk of a latent predisposition and with it an associated increased risk of disease. What however ultimately results in the loss of control of genetic information in the cell and the associated malignant growth cannot yet be answered scientifically.

The attempted explanation so often given previously, that underlying the disease was a weakened immune system, is no longer tenable in the current state of knowledge. It is, however, certain that once the disease has appeared, the **immune system** no longer recognises the cancer as a foreign process and therefore fails to fight it, or at least to fight it adequately. It is therefore important therapeutically to boost the immune system and to influence it in such a way that it recognises the cancer specifically.

Apart from the mainly psychological addictive habits, such as tobacco misuse, which frequently precede an illness, no psychological causes have been demonstrated. Yet it appears that stress, worry or irregular life styles are sometimes closely related to the disease, or result in the manifestation of a previously 'dormant' disease. To date, however, no scientifically conclusive evidence has been found for this. This is due not only to the complicated nature of the facts, but also to the still young scientific

disciplines which study the interaction between psychological and physical processes, psychosomatics or psycho-oncology. Also, the simple explanation often advanced that there is a specific **cancer type**, in other words a personal predisposition to cancer, has not proved correct in any respect. These comments, however, should not conceal the fact that there is undoubtedly a relationship between psychological constitution and physical process which current scientific methodology are unable to describe adequately.

Self-reproach or the gnawing question of **"why me?"** are therefore only beneficial if they do not result in excessive fatalism, but instead in a change of previous habits. **Artistic activities** or art therapy can here provide a very meaningful and successful supplement to medical therapy. Taking up new interests should also be mentioned in this context.

As a rule, it is the interaction of several factors which is used today to explain the disease. Each therapy is therefore only rarely limited to one particular aspect, and should instead take account of and include a wide range of social, individual, environmental, physical and psychological factors. An exact description of your condition and your situation will be extremely useful to your doctor in establishing your individual therapeutic plan.

Psychological reactions to the diagnosis

Just the suspicion of cancer unleashes many **fears**. This applies to the patient and also, in terms of the uncertainty, to the doctor who, although he knows what the disease is when it is first detected, does not know its severity. In spite of this he is expected to provide definite responses from the outset.

Many patients describe their experience of waiting for the test results, of the associated uncertainty, of the hopes and fears relating to a life t reatening disease, as often being more unbearable than the knowledge of being ill.

To ensure that wild speculation is not given free rein at a time when so many different suspicions are circulating, discuss the nature and scope of the information that is available to you, your family and friends with your doctor. This can form the basis for intimate and honest discussions for everyone involved.

The patient often has the feeling "as if the floor had been taken away from under his feet" if he suspects and then finally knows that he is suffering from cancer. This experience is described as diagnosis shock and is an entirely normal reaction to a so extraordinary event. A "healthy" **self-confidence** and the active deployment of all one’s usual resources will not always be possible in this situation and are only rediscovered with time. It is only natural that patients under huge psychological stress should experience rapid changes of mood and a greater debility than they previously have done. This requires a considerable amount of consideration and objectivity on the part of family and friends. Objectivity, however, also includes expressing hopes and wishes clearly and basing them on truth as far as successful therapy is concerned.

The patient can, however, also tell himself that people close to him would be happy to help and are also faced with an entirely new situation. A clear discussion of what is and is not good for him constitutes a good basis for agreeable help and support.

Many patients want to approach the disease intellectually in order to make a definite assessment and to provide a healthy corrective to fluctuating moods. Obtaining information and, through first hand experience, supporting medical measures on the basis of one's own judgement can then be a major help for all those involved. It is sometimes necessary here to seek advice from another doctor or pharmacist. However, you as a patient can enhance the confidential relationship with your doctor from the start if you discuss any questions and opinions with him openly, including "well-meaning" advice from family and friends. If treatment is to be successful, it is important to back one's own decisions as well as those made jointly.

Everything that the patient can do to achieve psychological balance and mental alertness represents the basis for "healthy" control of the disease.

Pine, host tree to pine mistletoe (Viscum album, Pini)

Cancer treatments

In the treatment of cancer the following types of therapy are distinguished from one another :

Curative therapies, such as surgery and radiotherapy, are intended to cure the disease.

Adjuvant therapies, i.e. supporting therapies, are intended to support the success of curative therapy, for example when chemotherapy is started after surgery to suppress the growth of, or kill, any cells that have spread.

Palliative therapies result for instance in the relief of tumour pain and are intended in particular to produce a higher quality of life, such as improved appetite and deeper sleep in patients. These therapies are often used in severely ill patients.

Supportive therapies serve to relieve or suppress severe side-effects that regularly occur with chemotherapy and radiotherapy. For instance, disorders of the blood-forming function of the bone marrow, nausea and pain are treated, but also psychosocial disorders in the course of the disease with the aim of achieving a more effective therapy.

A further distinction is made between **local therapies**, which combat a tumour directly by surgery, radiotherapy or the targeted administration of drugs, and systemic therapies. **Systemic therapies** have a cytostatic or hormonal effect and suppress the growth of diseased cells and tissue in the whole body or, as mistletoe therapy does, stimulate the immune system in its role against the cancer.

Surgery and radiotherapy

If a tumour can be removed surgically, particularly in the early stages of disease, this is the most effective treatment of all. To ensure that no affected tissue remains in the body, a small part of the healthy tissue surrounding the tumour is always removed at the same time. The surgeon thus often removes neighbouring lymph nodes because metastatic cells use the lymphatic system in particular (see Index page 54) to spread through the body. With cancer that has already spread, it may be useful to remove the primary tumour before beginning systemic treatment, i.e. involving the whole body, in order to then administer effective therapy with drugs or radiation. Only in the case of rare, slow-growing tumours are distant metastases also included in surgical therapy.

Surgery is frequently followed by chemotherapy, radiotherapy and/or hormonal therapy. **Radiotherapy** is administered either by means of radiation from the outside (percutaneous therapy) or by implanting radiation-emitting substances into the body (brachytherapy). Different types of ionising radiation, e.g. X-rays or gamma rays, are used to destroy the genetic information (DNA) of cells found in the cell nucleus in such a way as to cause them to die or to inhibit their growth. Depending on the nature and size of the tumour, radiation must be given for several treatments in order to achieve a therapeutically effective total dose. The techniques used today enable the tumour to be targeted very specifically and consequently reduce the damage to irradiated, healthy tissue. Side-effects of this therapy appear after months and even years if healthy cells are also damaged by the radiation. The symptoms of the side-effects during and shortly after therapy are very similar to those of chemotherapy.

Mistletoe therapy in support of surgery and radiotherapy

With radiotherapy and surgery, mistletoe preparations can supplement and promote treatment both **neoadjuvantly**, in other words before the beginning of local therapy, and **adjuvantly**, i.e. accompanying or supporting it. Surgery, particularly when associated with anaesthesia, and radiotherapy expose the whole body to considerable stress. A previous improvement in the general state of health and immune status with mistletoe therapy therefore regularly results in improved tolerability of these therapies, which are intended to work locally only, but have an undermining effect on the body as a whole.

The granulocytes and macrophages stimulated by mistletoe therapy and thus occurring to an increased extent in the blood help to produce a more rapid recovery after radiotherapy or surgery. Granulocytes and macrophages are white blood cells which remove diseased or dead cells.

The aim of adjuvant Viscum therapy (Viscum is the Latin term for mistletoe) is to stimulate the body's own defensive system and thus prevent a recurrence of the tumour, or relapse. This is because an altered or stimulated immune system can counteract the recurrence of the disease.

In addition, the genetic information (DNA) of healthy cells can be protected by Viscum during radiotherapy.

Viscum therapy can be started up to two weeks before surgery or earlier and is then discontinued two days before surgery. Treatment is then continued if there are no longer any after-effects of the drugs necessary for surgery and if inflammation-free wound healing is observed. Depending on the duration of the treatment-free interval, a lower dose of the mistletoe preparation may need to be used initially.

It is not recommended to begin mistletoe therapy only one week before surgery as the whole body experiences too great a stress as a result.

Medical therapies

All cancer therapy is supplemented by drugs or administered solely by drugs. In Germany, chemotherapy, mistletoe therapy and hormonal therapy are the options most commonly used.

Chemotherapy

Acute leukaemia in children, certain types of testicular cancer, Hodgkin's disease and many other tumour diseases can today be treated successfully with the use of chemotherapeutic agents (also known as cytostatics).

Although not as successful as in the examples mentioned above, chemotherapeutic agents have been developed for almost all cancer diseases. Most of them exploit the reproductive and metabolic mechanisms known for cancer cells and healthy cells and their chronological sequence to produce a growth-inhibiting effect on the formation of new cells. Tumour cells frequently proliferate by a more rapid cell division than most healthy cells. The genetic information which is the cause of the rapid and uninhibited cell division is attacked by chemotherapeutic agents and thus further tumour growth or the survival of already existing malignant cells is prevented. A reduction in the size of the tumour or its complete disappearance can also occur. This is referred to as a partial or complete remission.

During chemotherapy, in most cases several substances are used to proceed effectively against the cancer. This "polychemo" combats cell division with a variety of substances in order to interfere with a wide variety of mechanisms of cell division, but also to avoid , for example, a one-sided resistance on the part of the tumour. One typical side-effect of chemotherapy also derives from the mechanism described above. Mucous membranes and hair-forming cells are regularly severely affected because their growth or reproduction is also based on rapid cell division.

Slow-growing tumours (e.g. epithelial tumours) therefore, in some cases, offer chemotherapy fewer points of attack.

The vomiting (Latin: emesis) that is frequently associated with some drugs used in chemotherapy is treated by anti-emetic medications. The exact cause of this vomiting is still not sufficiently explained.

The success of a chemotherapy is based not only on the reduction in size of the tumour but also on the relapse-free period after the end of therapy. This requires the chemotherapy where possible to reach all the diseased cells in the body.

The optimal dose is established individually in chemotherapy - as also in therapy with mistletoe - and is dependent in particular on blood values which show the functional capacity of the bone marrow. This relates in particular to leucocytes. The number of leucocytes in the blood is a measure of the functional capacity of the human immune system.

Chemotherapy is generally administered over several sessions lasting about a week, known as "cycles" or "courses". All cycles and the treatment-free intervals introduced after each cycle generally cover a period of about six months. Detailed information on chemotherapy and hormonal therapy in cancer which correctly describes the effects and side-effects can be obtained from the addresses given on page 40.

Hormonal therapy

The growth of sex-specific organs is controlled in healthy human beings by hormones. In the 1940s, it was recognised that specifically those tumours which form on or in such organs can be regulated in their growth by withdrawing hormones. The withdrawal of hormones prevents thediseased cells from dividing because of the elimination of growth-promoting signals. It does not act like chemotherapy or radiotherapy by damaging the genetic material.

The withdrawal of hormones can be done surgically, e.g. by removing adrenal glands, ovaries or testes, or by medically suppressing female or male hormone formation. Thus, by administering female hormones, ostrogens, a successful outcome can be achieved in prostate carcinoma, and vice versa with gestagens, the artificially manufactured male hormone, in breast cancer in women. Other methods again suppress the signals for hormone formation in the pituitary gland and thus the subsequent formation of hormones in the reproductive glands. Finally, the "communication pathway" between hormones and cells can be interrupted by administration of drugs which block or change the cell receptors necessary for growth signals. Receptors are cell organs for receiving food and information, e.g. on cell division or cell growth.

Typical side-effects of hormonal therapy are menopausal symptoms in women and a loss of desire in men and also of potency with some medicines.

Hormonal therapy can last from a few weeks to several years. In unfavourable cases, however, resistance to hormones can develop in tumour cells after long-term therapy, so that hormonal therapy is often supplemented by chemotherapy.

Immunotherapies / Monoclonal antibodies

To understand the mode of action of immunotherapies, a distinction must first be drawn between two spheres of the immune system: the innate or non-specific immune system and the specific immune system. The cells of the innate immune system rapidly recognise and combat pathogens, because the characteristics of these diseases are known to the immune system. Thus, the body reacts rapidly to a flu virus, a cold or inflammations, for example. The reaction of specific immune system cells is delayed, because they first have to "learn" to react to a previously unknown disease. This learning is usually triggered by mediating cells (e.g. T or B cells and dendritic cells). In the case of a tumour, the interaction of the two spheres of the immune system – specific and non-specific – and the learning process itself are impaired in a variety of different ways.

The essential function of therapeutically administered monoclonal antibodies is to act on these disorders. The antibodies alter the information that is exchanged between the cells of the immune system or between the immune system and diseased cells or during the learning process of the specific immune system.

Information is also found on the surface of cancer cells that allows the immune system to recognise these cells as foreign or malignant. However, it is a particular property of tumours that over the course of time they are no longer recognised as 'foreign' by the innate immune system and, as a result, also evade an immune reaction by giving the specific immune system false information with regard to recognising the tumour cell and learning the immune response.

Tumour cells therefore prevent both the recognition of the tumour and the learning process necessary to combat it.

One example of the deception perpetrated by the tumour cells is the provision of particular information on their surface at what are known as immune checkpoints. The information conveys to the immune system‘s

cytotoxic T cells that the cancer cell is a harmless, endogenous cell and therefore does not need to be combatted. Monoclonal antibodies can intervene therapeutically at this level to suppress the false information provided by the immune checkpoint and thus allow the cytotoxic T cells to once again proceed actively against the tumour.

A further therapeutic mechanism of action exploits a particular property of cytotoxic T cells. In order to prevent healthy tissue from also being attacked by such T cells, these cells must not proliferate excessively. They therefore possess a healthy self-reduction mechanism, which is activated by surface information on the cell, known as a PD-1 receptor, if too many T cells are present. Monoclonal antibodies can interfere with the actually healthy 'selfrestriction' information of this receptor. Cytotoxic T cells are then present in very large numbers. The increased number of these T cells thereupon generates a more effective control of cancer cells.

Both mechanisms of action, the prevention of deception (the cancer cell pretends to be a healthy cell) and the proliferation of cytotoxic T cells, are also often used simultaneously for treatment with monoclonal antibodies.

The simultaneous use of mistletoe therapy and antibody therapies has been studied and can be undertaken without any restriction on the antibody therapy. There was also evidence to show benefits in terms of adverse reactions for patients receiving both treatments.

Mistletoe therapy to support chemotherapy and hormonal therapy

Chemotherapeutic agents damage the body's own formation of leucocytes, as a result of which the patient is highly susceptible to infection. Infections, including a harmless cold, can further weaken the body to a considerably greater extent during chemotherapy and may even result in the cycle being stopped or in a non-optimal dosage of chemotherapy.

Treatment with mistletoe activates **natural killer cells** (NK cells), among others, which belong to the leucocytes, and stimulates their proliferation. **Granulocytes** and **macrophages**, which are also leucocytes and which remove dead or diseased cells and thus reduce the susceptibility to infections, are likewise increased. Furthermore the adjuvant (supportive) administration of mistletoe enables the dose of those drugs intended to prevent vomiting during chemotherapy to be reduced.

All these effects contribute to a better general state of health. This is also supported by the release of interleukins. Interleukins increase, among other things, the production of the body's natural morphines (socalled endorphins) and lighten the depressed mood often produced by chemotherapy, therefore increasing acceptance of the therapy. The appetite-enhancing and mood-lightening effect of mistletoe therapy can in this way be used to support chemotherapy.

Hormonal therapy effectively suppresses, albeit ‘only’ one-sided, the hormonally controlled growth of tumour cells. Therapy with mistletoe can be viewed here as a holistic, supplementary treatment of the ill patient. The serious attack on the patient’s hormone balance requires the accompanying immunomodulation described in the beginning of the next section.

Mistletoe plant in winter, birch, host tree to birch mistletoe (Viscum album, Betulae)

Mistletoe therapy

Therapy with mistletoe products is used in a number of different ways and for a broad spectrum of tumour diseases. Within a treatment plan, it can have a supportive (adjuvant), alleviating (palliative) or, most commonly, a general strengthening and preventive character.

In oncology, attention is devoted principally to the aspects of quality of life, prolonging survival and relapse prophylaxis. Mistletoe therapy can be used in a variety of ways for these purposes:

The body's own defences are strengthened by mistletoe therapy in such a way that granulocytes, lymphocytes and natural killer cells appear in the blood to an increased extent. Any degenerated cells still found in the body can therefore be combated and the risk of metastatic spread reduced.

Mistletoe therapy can therefore improve the immune system weakened by surgery, anaesthesia, radiotherapy and chemotherapy in its role against cancer.

A healthy immune system, i.e. one which reacts in a variety of ways, makes relapses less likely. To this extent, mistletoe therapy is also a preventive measure in terms of **relapse prophylaxis**.
Mistletoe therapy can reduce or make more bearable the pain which can occur in advanced stages of tumours by stimulating **the release of endorphins**. Endorphins are natural morphines produced by the body which have a pain-relieving action.

The loss of appetite and the disturbed sleep pattern that frequently occur in association with a cancer disease can be eliminated or alleviated. **Healthy eating and sleeping behaviour** should not be underestimated as a precondition for long-term recovery. This also applies to the reduced susceptibility to infectious diseases that can be observed during mistletoe therapy.

It has been shown in several studies that mistletoe injections have a protective effect on the genetic material (DNA) of human cells. This also explains the improved tolerance of chemotherapy or radiotherapy during mistletoe therapy.

As well as these effects which are based primarily on immunomodulation, a cytotoxic effect of Viscum album on tumour cells has also been demonstrated. Cytotoxic effects, i.e. which destroy cells, are exerted in particular by the lectins and viscotoxins contained in mistletoe.

Therapeutic effects of the ingredients of mistletoe

Mistletoe preparations are plant-based medicines, and use the whole plant or the composition of active substances in the plant as the basis for their therapeutic effect. However, some manufacturers concentrate their efforts solely on one ingredient, the lectin content of mistletoe.

In this respect, the widespread belief that plant medicines are harmless is incorrect, for although the side-effects of therapy with mistletoe preparations are comparatively minor, some of the individual ingredients are among the most poisonous substances known. Mistletoe preparations for this reason can only be obtained on prescription and are not to be used without medical supervision. The fact that, despite this, the side-effects that occur are only minor is due to the interaction of the various ingredients in mistletoe. This effect, known as synergy, is however also shown in a totally different way when laboratory tests on different tumour cells have shown that individual ingredients of mistletoe, such as lectins, have a markedly lower therapeutic effect than the extract of the mistletoe plant as a whole.

Two important groups of substances in mistletoe are viscotoxins and lectins.
Viscotoxins produce necrosis, in other words they cause cell death by poisoning the cell, accompanied by inflammation. Lectins, however, act on the cell nucleus where they cause an apoptotic reaction of the cell. Apoptosis means the stimulation of an ordered degradation of all the cell components, comparable to natural cell death. At present, four groups of mistletoe lectins are known.

In addition to the function described, directed specifically against the diseased cell, mistletoe possesses the property, as already mentioned, of having a modulating effect on the immune system. In this way, the immune system can be stimulated as a whole, non-specifically or specifically, in its capacity to deal with diseased cells or foreign substances. The nonspecific reactions, which are inherent in the immune system, include a marked increase in leucocytes in the blood. Specific reactions, i.e. the immune system learns this reaction as a result of administration of the drug, are for example the increased formation of T-cells and B-cells (see Index pages 53). Mistletoe therapy therefore stimulates the immune system to "remember" its tidying and cleaning function. This is confirmed by clinical studies.

Mistletoe therapy may therefore be seen as a meaningful supplement to conventional therapies.

The normal method of giving the subcutaneous injection is described

below and reference is made to the typical side-effects and the readily observed therapeutic effects.

Practical use and effect

Mistletoe preparations are administered by **subcutaneous injection**, i.e. the contents of the ampoules are injected under the skin. As a rule, this is done two or three times weekly. Only freshly opened ampoules should be used. The administered dose is increased during the first few weeks, depending on the state of health and the therapeutic aims. The **increase in dose** is intended to achieve the most effective individual dose. It can however happen that an optimum level is achieved with the very first dose used. An effective and tolerated dose is readily recognised by the patient on the basis of the reactions described below. It should be mentioned first of all however that these reactions or **side-effects** are normally a sign that the body is responding to treatment. Side-effects are therefore to a certain extent therapeutically desirable.

With an adequate dose, redness and/or swelling of up to five centimetres in diameter will form at the injection site after about six to eight hours. This **local reaction** is associated with itching and will persist for not more than three days. If the local reaction occurs to a lesser extent after about 2.5 weeks of treatment, a further increase in dose can be undertaken. This can often result in the local reaction once again having a diameter of up to five centimetres. The dose is increased once or twice at the beginning of therapy. After about nine weeks of uninterrupted use of the same dose, the local reaction will decline and finally disappear altogether.

The following side-effects may also occur at the beginning of treatment and be experienced as unpleasant: **fatigue, flu-like sensation** or **dizziness**. These reactions appear a few hours after the injection for a maximum of 24 hours and can be accompanied by a slight **fever**. Fever is unpleasant, but is also always a sign of increased positive activity of the immune system. The **daily timetable** should always allow for the occurrence of a slight fever at the beginning of therapy. However, even these sideeffects have disappeared after the first nine weeks or are only very slightly apparent.

The doctor will adjust the number of weekly injections and the dose used according to the severity of these effects. If there are no symptoms at all, a change in the type of mistletoe, i.e. the host tree on which the mistletoe has grown, may be considered (e.g. changing from Viscum album Mali (apple tree mistletoe) to Viscum album Abietis (fir mistletoe).

In the first two weeks of therapy the tendency to slight "chills" that frequently occurs in cancer patients will decrease and they will experience a greater feeling of warmth throughout their whole body. In general, a deeper, more recuperative night's sleep is also obtained and the appetite will increase. In addition, in many patients a lightening of mood and an associated feeling of greater well-being and hence increased quality of life will be observed.

Some doctors place particular emphasis on the fact that the patient’s body temperature should be measured and recorded in the morning and evening because the temperature difference can show an **immunomodulatory** effect of mistletoe therapy. In patients there is almost always only a minor difference in temperature, whereas healthy subjects show a marked difference between morning and evening temperature. This **"circadian"** temperature rhythm will in most cases adjust to the natural rhythm after a few weeks and is also the sign of a response to therapy.

Maple, host tree to maple mistletoe (Viscum album, Aceris)

Duration of therapy, treatment-free intervals

Mistletoe products are used for a period of two to seven years depending on the aim of treatment. This period, also known as **"maintenance therapy"**, is intended for immunomodulation and thus indirectly for the effective prevention of relapses. Relapses are tumours which recur after a successful curative treatment (e.g. after surgery). Often there is an interval of several years between the successful treatment and the occurrence of a relapse. Preventive (prophylactic) therapies against relapses are therefore long-term and should be directed at the whole body. Mistletoe preparations are suitable for effective relapse prophylaxis because any medication directed solely at the diseased cell would fail to achieve a long-term improvement in the health of the whole body.

Treatment-free intervals can be introduced during this long-term maintenance therapy. This is frequently done to restimulate the immune system to a greater extent by means of different stimuli or because, for example, additional stress must be avoided during flu. However external circumstances can also justify a break.

In this context, it should be pointed out **that after a break of more than two months a low dose must again be used to begin with** because the immune system has a learning capacity and once it has "learnt the poisons of mistletoe" it can respond very violently to a large quantity of these substances.

Maintenance therapy is programmed according to the individual treatment plan. In most cases an unchanged dosage is prescribed during this period. However, different dosages are also used to act rhythmically on the immune system. In modulating the immune system, it can also be helpful for the doctor to change the species (see here also the section "Mistletoe host trees," page 36).

If the body has become accustomed to the medication in the course of

long-term therapy, a further increase in dose can be undertaken, as at the beginning of therapy. Towards the end of maintenance therapy injections are carried out normally only once a week, interspersed by longer treatment-free intervals.

Manufacture of the medicine

Mistletoe products are manufactured as an extract of mistletoe from the relevant host trees. Many manufacturers use the mistletoe collected in both summer and winter, while others only use the plants harvested in winter. Different extraction procedures and solvents are also used. The spectra of ingredients and active substances therefore differs in each product that is on the market.

The Abnoba company uses both summer and winter mistletoe for the manufacture of the medicinal product in order to ensure a wide spectrum of ingredients. The mistletoe is then extracted without exposure to air according to a patented procedure so that as a result more than 75% of the plant material used is available in the drug. All essential ingredients such as lectins, viscotoxins, polysaccharides and triterpenoids (including oleanolic acid, betulinic acid) are then contained in the extract in very high quantities.
This procedure also allows the formation of mistletoe liposomes (vesicles) which are formed from the cell membranes occurring naturally in the plant cell. These structures may be imagined as very small spheres, invisible to the naked eye, which bind or incorporate the active substances and other ingredients of mistletoe. Pure mistletoe liposomes have an effect in their own right: they are immunologically active. This should also be taken into account in the direct effect of the product on tumour growth. The good tolerability of these products is also probably due to this.

Using special procedures, manufacturers who use two collection times mix the extracts with one another and then dilute them appropriately to the required dose. All the products obtained are then filled in ampoules following sterile filtration.

Mistletoe products from the Abnoba company are processed under careful protection from oxidation from the time of collection until sealing of the ampoules. As a concentrated extract, they have a light yellowishgreen colour which shows that the liposome-forming and fat-related membrane substances have been transferred to the aqueous extract. The high extract yield and the presence of liposomes distinguish these mistletoe products from other mistletoe products. Greenish or clear preparations also show that no degradation products resulting from oxidation have been formed.

The constant quality of the extract is ensured by the specified collection time, the formula for the plant parts used and the precise organisation of the manufacturing process as far as this is possible for plant products at present. Numerous "in-process controls" test the contents of the extract qualitatively and quantitatively and exclude prohibited impurities. Manufacture and quality control is performed in accordance with international standards and the rules of "Good Manufacturing Practice" (GMP rules) which relate to the current state of knowledge and technology and are constantly revised in the interests of patient safety.

Mistletoe host trees

Depending on the tree on which a mistletoe plant has grown - the host tree - the composition of its ingredients can differ. This fact is used therapeutically. Thus, for example, the high concentration of viscotoxins and lectins in Viscum album Fraxini can be recommended for the treatment of metastatic tumour diseases. The Latin word "Fraxini" means "ash" and designates the tree on which the mistletoe has grown. For Mali (apple tree) there is good experience, acquired over decades and confirmed by studies, in the treatment of breast cancer. This applies in the same way to the oak mistletoe (Quercus), which is used in particular in tumours of the gastro-intestinal tract, i.e. the digestive tract, and the male sex organs.

The selection of the host tree by your doctor, however, also depends very substantially on the treatment plan and above all on the individual disease. In individual cases it may occur that in the treatment of breast cancer that mistletoe from the pine tree (Pini) or Viscum album Abietis (fir tree) is used instead of the frequently employed "Mali" species (apple tree). This is done in order to make the body react in a different way to the different compositions of the ingredients.

Oak, host tree to oak mistletoe (Viscum album, Quercus)

Where to obtain support and counselling

You will always find practical social and nursing care and counselling in your neighbourhood from the welfare institutions. In the telephone book you will find the addresses of

The Samaritans www.samaritans.org.uk
Department for Work & Pensions www.gov.uk/dwp
British Red Cross www.redcross.org.uk

These institutions can help you with home nursing, housekeeping and medical care. Your medical insurance or nursing insurance company is responsible first and foremost for financing of this assistance.

For more specific questions, such as:
Which aftercare or rehabilitation clinic is recommended?
Where can I find a pain clinic in my neighbourhood?
What financial assistance can a cancer patient claim?
Who finances domestic help during a period in hospital?
Who bears the costs for care at home and who for care in a nursing home and whom should I contact in this respect?
and for practical questions about coping with the disease or about the situation of relatives, you will find the appropriate contacts mentioned below.

Useful addresses

Cancer Research UK
www.cancerhelp.org.uk
Helpline: 0808 800 404 (free, only UK)

Macmillan Cancer Support
www.macmillan.org.uk
Helpline: 0808 808 0000 (free, only UK)

Camphill Wellbeing Trust
http://www.mistletoetherapy.org.uk/

NHSinform. Cancer Information Online at your fingerTIPS
(Tailored information for the People of Scotland)
www.nhsinform.co.uk/cancer/TIPS

For specific questions about
Mistletoe therapy please contact
ABNOBA GmbH
eMail: info@abnoba.de

Notes

Ash, host tree to ash mistletoe (Viscum album, Fraxini)

Frequently asked questions

When should mistletoe therapy be started?

Therapy can be started before the beginning of what are known as standard therapies (surgery, chemotherapy and radiotherapy) and is then intended particularly to improve the tolerability of the standard therapies. Mistletoe therapy may also possibly be started in the intervals between cycles of chemotherapy.

In most cases, mistletoe is prescribed after the end of the standard therapies to prevent recurrences (relapses) and to improve the immune status and the quality of life.

Mistletoe therapy should always be taken on medical advice and under medical supervision.

Is there a special diet?

Certain dietary habits make a substantial contribution to health. You should therefore ensure that wholemeal products, fruit and vegetables are on the daily menu. The excessive consumption of meat, sugar and fat should be avoided. Changing your eating habits overnight however should not cause you to lose your pleasure in eating! Brochures from medical insurance companies and bookshops offer a rich selection of recommended diets.

What is the right way to give an injection?

To begin with, your doctor or her/his assistant will show you how to use the ampoule and the syringe. During the therapy, you yourself or a member of your family can give the injection. Please note the following: At the beginning of treatment (for about 8 weeks) when stronger reactions are possible, the injections should be followed by half an hour's rest. Change the injection sites. As a rule, injections are given under the

abdominal skin and possibly also under the skin on the upper leg. See also page 60/61.

The area of redness at the injection site, the "local reaction", is much too large. What does this mean and what can I do differently?

Initially, the local reaction also depends on the angle and the depth beneath the skin at which you have given the injection. If the injection has been given at a very shallow angle, a correspondingly large local reaction may be expected; on the other hand, if the angle of the injection is very steep, a weaker reaction will be apparent. The diameter of this redness should be about five centimetres. The local reaction is basically a sign of a healthy reaction to the medicine. For this reason, an excessive local reaction is not harmful in terms of an overdose. Obviously, the burning and itching at the injection site is unpleasant. For this reason, if you have an excessive reaction, discuss with your doctor whether only half the contents of the ampoule should be used for the next injection or whether the dose should be reduced still further.

Storing the ampoules

Active plant substances react sensitively to frequent and excessive temperature fluctuations. It is therefore recommended that the ampoules should be stored in a cool, dark place, for instance in the refrigerator. Before use, however, the ampoules should be brought to room temperature by warming them briefly in your hands.

Can the contents remaining in the ampoule be used later for other injections?

No, the contents of an opened ampoule can be contaminated with bacteria and become unsterile, even when handled carefully. In addition, the drug can oxidise on contact with the oxygen in the air.

I was not able to inject myself on one day. What effects can this have?

As this is a long-term therapy, it is not of major importance. You should however realise that the stimulus for the immune system to be modulated is less pronounced as a result.

When should a mistletoe injection not be given?

In general, if the patient has a high fever or if they react allergically to the injections. The "local reaction" sometimes associated with slight swelling and itching is not an allergy! If however the itching at the injection site develops into a generalised itching over the whole body, there may be an allergy. This very rare reaction should only be described as allergic if the itching or burning does not disappear with a reduced dose.

Is mistletoe therapy also possible with a malignant disease of the lymphatic system or the blood?

There have been laboratory tests which suggested that growth of diseased lymphoma cells would be stimulated by therapy with mistletoe extracts. This suspicion has not been confirmed either in further cell studies or in retrospective (i.e. looking back) studies of disease processes. A repeated laboratory test also contradicts this suspicion. Nevertheless, this rumour has persisted and has led to uncertainty among patients and doctors, which is the reason why we are discussing this question here.

No treatment processes are known in which mistletoe has stimulated the growth of malignant cells. In fact, there are a large number of well-documented cases that prove the opposite. The question has also been studied by a wide range of scientists who also came to the conclusion that this suspicion is not tenable.

Research by the University of Tübingen commissioned by the Abnoba company confirms this result.

Can the medicine also be drunk?

No, because mistletoe products lose the effect necessary for cancer therapy when they come into contact with the mucous membranes of the mouth and with gastric acid.

What sort of a plant is mistletoe? How is it collected?

There are a variety of species of mistletoe. The mistletoe used for cancer therapy is the white-berried mistletoe (Viscum album L.), whose main habitat extends from Europe via Central Asia to Korea and Japan. In Europe, three subspecies are distinguished within the species of Viscum

album: pine, fir and deciduous mistletoe.

Birds like to eat white mistletoe berries in winter and thus ensure the dispersal of the seeds and thus the plant. The mistletoe seedling attaches itself to the bark of the host tree and germinates in the spring. It first of all seeks access to the water-conducting vessels in the tree and instead of a root drives a so-called sinker through the bark. Over a period of about 4 years, the mistletoe grows - like any normal plant - against gravity, upwards towards the light. At this stage, the mistletoe is not yet collected. Only from the 5th year onwards does the typical spherical bush shape appear. The plant achieves this through oscillating growth movements which it performs annually in the early summer. Some manufacturers see this as being the appropriate time for the summer collection. The mistletoe thus does not just direct its shoots in one direction, but grows actively in all directions. In winter, the evergreen mistletoe is particularly apparent as a spherical bush in the middle of the bare trees. When other plants are resting, mistletoe does not. There is no seed dormancy. The nutrient tissue of the mistletoe berry which first ripens in winter contains a green, already germinating embryo with cotyledons (seed leaves) and a root pole which is attracted to the light shining through the mistletoe berry. The ripening of the flowering organs is already complete in October. Flowering in most plants follows rapidly on from this cell division. The mistletoe takes its time and does not flower until January/February. Some manufacturers carry out the winter collection at the beginning of January - at this point the mistletoe berries are ripe and the male and female flowers not yet open.

Thus, compared to other plants, mistletoe is distinguished by a series of characteristics which can be described by biological development processes that are both time-lagged and also spatially independent. These specific features of mistletoe can also be observed in its spectrum of substances, which is subject to seasonal variations. For this reason, it is suggested that a single collection time is not appropriate for the medicinal product, which involves the whole plant, but that two collection times are necessary for the production of medicines. For this reason, collection is performed in summer and winter at predefined collection times identifiable by specific characteristics of biological development.

The mistletoe used for manufacture by the Abnoba company does not come from crops, but from naturally growing stocks. At each collection time both the plant and the site are examined, assessed and documented by experienced biologists. The collected material is processed on the spot within the first 4 hours of collection. Even in these very early stages of production, care is taken to ensure that environmental oxygen is excluded in the processing of the mistletoe. At this stage also measures are taken to prevent the product later on from containing plant or bacterial degradation products. Mistletoe leaves, shoots and berries are weighed in accordance with the predefined formula, divided into portions and stored in transport containers which prevent any oxidative change in the collected material until the beginning of drug production. Before use in production, the collected material is tested for impurities from pesticides and heavy metals or infestation with micro-organisms.

Is mistletoe therapy reimbursed by the medical insurance companies?

The use of mistletoe therapy in cancer diseases is permitted by the National Health Service (NHS) as well as by private insurance companies (available on prescription on a named patient only).

There are other forms of therapy. What does this mean?

Forms of treatment other than the subcutaneous injection of Viscum album are mentioned and discussed on the internet and in self-help groups. These include the following forms of therapy in particular: intravenous (into the blood circulation), intratumoural (into the tumour or a metastasis), intrapleural (into the gap in the chest lining) and intravesical (into the urinary bladder) therapy.
The forms of therapy mentioned are predominantly still in the process of scientific development and therefore should always only be given by a doctor and under clinical supervision.

Can mistletoe products be injected together with other medicines?

Mistletoe products should only be injected on their own.

Are there any incompatibilities when taking other medicines at the same time?

A slight increase in temperature after the injection is desirable at the beginning of therapy with mistletoe products used in holistic therapy. These mistletoe preparations should therefore not be taken together with medicines that lower temperature.

It is essential to seek medical advice if you are taking thymus preparations during mistletoe therapy.

No incompatibility or interactions with medicines other than those mentioned is known.

How long does mistletoe therapy last? Can breaks be introduced into long-term therapy?

Depending on the risk of relapse of the tumour concerned and/or the required stimulus for immunomodulation, mistletoe therapy will continue for a period of a few months to several years. Injections are given more often at the beginning of therapy and subsequently often only once or twice a week and breaks can be introduced into the treatment.

Following a break of more than two months, the treatment should be started again at a low dose (as at the beginning of therapy), and at all events under medical supervision.

Mistletoe branch in winter

Medical and pharmaceutical terms

Adenokarzinom = a cancer arising from the glandular parts of the mucous membrane.
Adjuvant = accompanying, in the sense of accompanying and supportive therapy
Allergy = hereditary or acquired, hypersensitive reaction of the body's immune system to foreign substances.
Apoptosis = describes the process programmed naturally into all healthy cells, resulting in the death of diseased or "obsolete" cells. This process is also induced in diseased cells by lectins.
Axillary = belonging to or situated in the armpit (axilla)
B-cells = see lymphocytes
Biopsy = removal of tissue samples. In the context of a tumour disease, tissue is removed to determine the nature of the tumour.
Carcinoma = a cancer
Carcinoma in situ = initial tumour stage in which the tumour has not yet invaded the surrounding tissue and has no connection to the blood circulation.
Circadian = daily 24-hour rhythm
Colon = belonging to the large bowel
Colon carcinoma = cancer in the large bowel
Complementary = supplementing
Cytokines = proteins which are released, among others, by cells of the immune system and serve as "information" between cells, tissues and

organs.

Cytostatic = a medicine which is intended to stop uncontrolled cell growth.

Cytotoxic = a poison which damages a cell so much that it dies (see also apoptosis and necrosis).

Dysplasia = pathological change in a tissue

Endocrine therapy = pain-blocking substances within the body

Endorphins = pain-blocking substances within the body

Epithelium = uppermost or outermost tissue of an organ or internal and external body surface, e.g. of the skin or the inner wall of the bladder.

Gliomas = tumours of the supporting tissue of the nervous system known as glia.

Grading = assessment of tumour tissue according to the degree of malignancy. G1 means: well differentiated, the tumour tissue is still largely the same as the tissue from which it is growing; G2: moderately differentiated; G3: poorly differentiated; and Gx: an exact classification is not possible. A tumour defined as G1 may be considered less malignant than one defined as G2 (see also keyword: TNM; Page 56)

Granulocytes = various subgroups of these cells belonging to the white blood corpuscles digest bacteria, fungi and in particular the "waste" from tissue destroyed by inflammation, as a result of which the susceptibility to infections is reduced.

Haematology = field of internal medicine which deals with the causes and therapy of blood diseases.

Histology = istudy of the body's tissues

Hodgkin's disease = is a specific group of diseases of the lymphatic system which usually initially develop locally in a lymph node (see also lymph nodes and lymphatic system).

Hormonal therapy = see page 22

Host tree = tree on which a mistletoe grows. The Latin names are for example: Abietis (fir), Aceris (maple), Amygdali (almond), Betulae (birch), Crataegi (whitethorn), Fraxini (ash), Mali (apple), Pini (pine), Quercus (oak).

Immune system = individual system for fighting off foreign substances and destroying abnormal cells. A distinction is made between inherited and acquired, e.g. learnt by taking drugs, immune defence.

Infiltration = Infiltration is the process by which a tumour invades surrounding tissue.

Infiltrate = to invade surrounding tissue

Inject = to administer a substance using a needle

Instillation = Instillation describes the introduction of medicines into the body cavities of the human body (e.g. bladder).

Invasive = see infiltration above

Lectins = lectins are medicinal substances contained in mistletoe which cause apoptosis in particular.

Leukaemia = tumour disease of the blood-forming organs or of the blood.

Leucocytes = so-called "white blood corpuscles", see also granulocytes and lymphocytes.

Liposomes = see page 34/35

Local reaction = at the injection site, the skin often reacts in the form of redness and swelling. This reaction to an injection, which is also accompanied by itching, appears about seven hours after the injection and lasts for up to three days.

Lymph nodes = organ of the lymphatic system (see below) which in particular purifies lymph fluids and, stimulated by messenger substances from the bone marrow, releases lymphocytes among others.

Lymphomas = are, if described as malignant, a cancer disease of the lymphatic system. The unbalanced overproduction of malignant cells results in disease.

Lymphocytes = belonging to the group of "white blood corpuscles", lymphocytes are cells in the blood which are "produced" by the spleen and the lymph nodes. These organs in turn are stimulated by cells from the bone marrow to form lymphocytes. The lymphocytes comprise:

B-lymphocytes = these perform "recognition and memory functions" for fighting foreign substances.

T-lymphocytes = "fight" these substances or foreign cells directly.

Natural killer cells = these cells also "fight" foreign substances and cells. They perform this activity by virtue of their naturally assigned function (non-specific immunity).

Lymphatic system = the lymphatic system consists in particular of lymph tracts, lymph nodes, the spleen, the bone marrow and sections of the intestine; in children it also includes the thymus, but this regresses during puberty. Lymph tracts and nodes are distributed throughout the whole body and collect the lymph fluid produced from the tissue, which is returned to the blood in the neighbourhood of the heart. The lymphocytes (see there), which are important for the immune system and the production of which is stimulated in the bone marrow or thymus, are also transported with the lymph. However, dietary fat also reaches the blood from the intestine via the lymphatic system.

Macrophages = ("scavenger cells"), mobile and locally based cells in the immune system which have predominantly cleaning functions but which also stimulate other cells to perform their respective functions (e.g. by releasing interleukins).

Maintenance therapy = is the treatment that follows on from the initial therapy. This therapy is usually followed at an unchanged dosage over several years.

Mammary carcinoma = breast cancer

Malignoma = malignant, independent tumours with uncontrolled growth, in contrast to benign tumours, such as warts or polyps.

Malignant dysplasia = pathological change of the tissue; preliminary stage of cancer

Metastasis = secondary growth of a tumour which is found elsewhere in the body from the original tumour.

Natural killer cells = see lymphocytes

Side-effects of mistletoe injection = see pages 30/31

Necrosis = in contrast to apoptosis (see there), natural cell death, necrosis describes the death of the cell caused by an external influence, often accompanied by inflammation. The viscotoxins contained in mistletoe can cause this form of cell death. Mistletoe harvested in summer in particular contains viscotoxins.

Neoadjuvant = the term used for a therapy used before another therapy, e.g. before surgery.

NK cells = see lymphocytes

Oncogenes = tumour-producing genes

Oncology = field of internal medicine dealing with the origin and therapy of cancer diseases.

Oxidation = chemical change/production of a substance by oxygen among others, e.g. rust formation on iron

Palliative = Latin for “cloaking”, palliative therapy = alleviating therapy

Pancreas = a gland that secretes a gastric juice

Phytopharmaca = medicinal products obtained from plants.

Pleura = (Latin for chest lining) two-layered tissue closely enveloping the lung. During a cancer disease, fluid can accumulate between these layers.This accumulation is known as pleural effusion.

Prophylaxis = preventive measure

Process standardisation = term used in pharmaceutical production which describes a system of quality assurance measures that result ultimately in a defined and constant drug quality.

Psychosomatic = interaction between mental and physical health.

Reconvalescence = recovery phase after a disease or severe stress

Relapse/Local relapse = recurrence of a tumour at the place in the body from which it was previously removed.

Relapse prophylaxis = preventive therapy to avoid relapses

Sarcoma = malignant tumour affecting the connective and supporting tissue.

Spontaneous cure = spontaneous remission = rare but constantly recurring, complete cure of the cancer disease without any explanation.

Radiotherapy = see page 18

Subcutaneous, abbreviated sc. = Latin for "under the skin", meaning the injection of a medicine under the skin.

T-cells = see lymphocytes

Therapeutic eurhythmy = a movement therapy which stimulates in particular the ordering immune and life forces.

TNM system, TNM classification = this internationally used classification is used to describe a tumour:

- **T**X: The tumour (=**T**) cannot be assessed.
- **T**is: Carcinoma in situ = initial tumour stage without invasive formation in surrounding tissue.
- **T**0: No evidence of primary tumour
- **T**1, 2, 3, 4: size and spread of the tumour (1 = small, 4 = large)
- **N**X: The involvement of regional lymph nodes (i.e. in the area of the tumour) cannot be assessed.
- **N**0: No evidence of regional lymph node involvement.
- **N**1, 2, 3, 4: Weak (= 1) or marked (= 4) lymph node involvement.
- **M**X: Distant metastases cannot be assessed.
- **M**0: Distant metastases are not detectable.
- **M**1: Distant metastases are detectable.
  A"**T**1,**N**0,**M**0"-classification is thus associated with a good therapeutic prognosis.

Tumour markers = Blood constituents which can reveal the presence of a cancer disease.

Viscotoxins = group of substances of cytotoxic ingredients of the mistletoe extract which can in particular cause necrosis (see there) of tumour cells.

Viscum = Latin name for “mistletoe“.

Dear reader

Obviously, this brochure does not claim to be a scientific publication. What it intends to do instead is to provide an informative, factual overview of the purpose and practice of mistletoe therapy in cancer disease and, at the same time, to show its relationship with standard therapies.

Thank you for your interest, please send your criticisms and suggestions for improvement to us! And naturally we would also be happy to receive any positive feedback.

With best wishes and kind regards

The staff at
ABNOBA GmbH

Instructions for injection of mistletoe preparations

Mistletoe preparations are injected subcutaneously beneath the skin in cases of cancer. Please note the following points:

You will need: A 2 ml disposable syringe and a short disposable needle, size 0.4 x 20 mm

Injection site:: Abdomen, possibly thigh or site indicated by your doctor

Instructions:

1. Attach the needle to the syringe.
2. Break the ampoule below the red dot: hold the ampoule with the red dot facing upwards and snap off the top of the ampoule with a downwards movement (fig. 1).
3. Draw up the contents of the ampoule into the syringe (fig. 2). Remove any air remaining in the syringe by holding the syringe with the needle uppermost and depressing the plunger carefully until all the air has been expelled and a drop of liquid appears at the tip of the needle (fig. 3).
4. Pinch up a fold of skin between the index finger and thumb of one hand; using the other hand, insert the entire needle into the skin fold at an angle of about 45° (fig. 4).
5. Check that the needle is in the right place by pulling back briefly on the plunger. If blood appears in the syringe, take the needle out and insert it again at a flatter angle.
6. Inject the entire contents of the syringe slowly into the fold of skin while continuing to hold it.

fig. 1

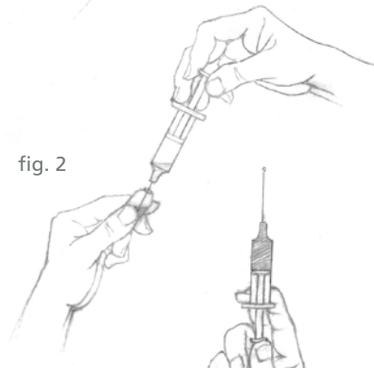

fig. 2

fig. 3

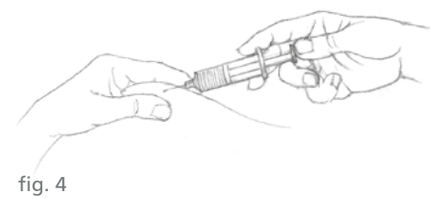

fig. 4

Notes:

Do not inject

- into areas of inflamed skin
- around recent surgical scars
- near areas that have been irradiated during radiotherapy
- into the arm or breast on the side operated on for breast cancer

Use different injection sites (e.g. alternate the right and left sides of the abdominal skin).

Dispose of syringe and needle carefully after use.

Reddening, hardness and itching at the injection site may occur briefly at the start of therapy. These are desirable reactions. However, the redness should not exceed 5 cm in diameter.
If the area of red skin is clearly more than 5 cm across, or you have a temperature of more than 38.5°C, you should wait until these symptoms have abated before you give yourself the next injection. If this should happen, please tell your doctor, who may reduce the dose you are using.

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