Liderma®
Isotretinoin

Acne
Important information

for Liderma® patients

This brochure contains important information about treatment with Liderma®.

Liderma® is a very powerful medicine.

Read this brochure carefully. You are sure to have questions, which you should note down in the space provided. Your doctor will be able to give you clear answers to these questions.

Keep this brochure safely during the entire period of treatment with Liderma®.

Please read the package insert carefully before taking this medication. It contains updated and important information about Liderma®.

Treatment with Liderma® must be under medical supervision.

Doctor (Stamp)

Family name of patient _____

Given name of patient _____

This brochure is also available in other languages. Ask your doctor who will be pleased to provide the right one for you.

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General rules for Liderma®

Liderma® is a very powerful medicine. Close medical supervision is necessary and justified.

The effects of Liderma® first appear after a few days to a few weeks. So be patient and keep taking the treatment regularly, according to your doctor's instructions.

Please note the following

- Take the medicine exactly as your doctor has instructed. Never change the prescribed dose yourself without discussing it with your doctor.
- Read the package insert carefully before you take the medicine.
- Tell your doctor if you are allergic to any foods or medicines. This could be very important.
- Any questions? Is anything not clear? Your doctor will explain.
- Are you experiencing any side effects? Has anything troublesome, unexpected or unusual happened? Call your doctor.
- Tell your doctor if you are taking any other prescription or over-the-counter medicines, either regularly or even only on occasion.
- Liderma® has been linked with depressive moods and mental health problems. Talk to your doctor immediately if you notice that you have feelings of sadness, loss of interest in your normal activities or sleep disturbances, changes in your appetite or weight, trouble concentrating or other unusual symptoms.

Keep the package insert; you may want to read it again later.

Make absolutely sure that you

- Never share your Liderma® with anyone else; it has been prescribed for you personally. Even if someone else has the same symptoms as you, this medicine could cause them considerable damage.
- Never give Liderma® capsules to a pregnant woman or a woman of childbearing age who might become pregnant, since this may cause severe damage to her unborn child.
- Don't give blood! During the entire period of treatment with Liderma® and for one month afterwards, you must not give blood. If a pregnant woman were to be transfused with your donated blood, the active ingredient of Liderma® could lead to severe birth defects of her baby.

General rules for LIDERMA®

How must you take Liderma® capsules?

- **Your doctor will decide how many capsules** you must take each day. Follow these instructions exactly and do not change the prescribed dose without consulting him/her first.
  Have you forgotten to take a dose? Don't take twice as many capsules next time, but continue with the treatment as if nothing had happened.
- Swallow the capsules whole with liquid **during a meal.**
  Do not chew the capsules.
- Liderma® must **be stored safely.** Store the capsules in the original packaging and protect them from heat, light and moisture to prevent loss of strength.
- **Keep Liderma® out of reach of children** and away from others for whom they are not intended.
- Do not use the capsules after the **expiry date** printed.
- Bring any open packs of Liderma® that you do not need for your treatment back to the pharmacist or your doctor so that they can be disposed of correctly.
  On no account must you keep an opened package in your medicine cupboard, or give it to anyone else.

Call your doctor if you have any questions.

Liderma capsules look like this:

Liderma® 10mg

Liderma® 20mg (original sizes)

Acne is a skin disease

Acne is a skin disease, more specifically a disease of the sebaceous glands, which can affect both men and women in adolescence but also as adults. On average, men suffer from more severe forms of acne than women.

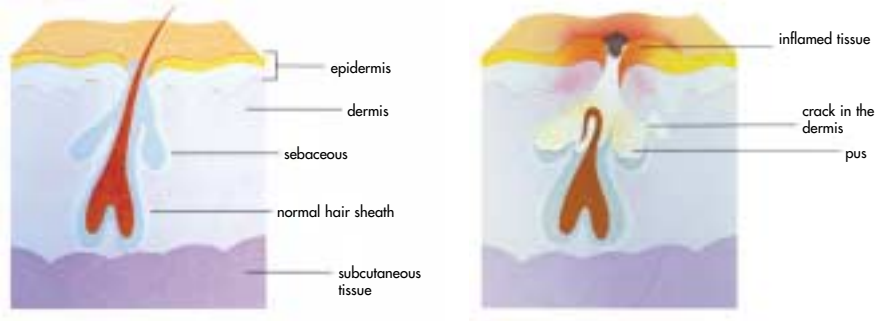
Severe acne usually spreads over the face and often over the trunk (chest and back). It is characterised by severely infected sometimes pus-filled changes in the skin. On healing, these leave behind large irregular scars.

What are the changes in acne?

Acne arises in the oil-secreting structures of the skin, the sebaceous glands. Every hair follicle has one or more of these sebaceous glands which secrete an oily substance called sebum. The sebum passes along the hair follicle to reach the surface of the skin.

In acne, the sebaceous glands are enlarged – particularly on the face, chest and back – and produce more sebum than is necessary.

In severe acne, the sebum collects in the gland. In addition, the hair/sebaceous follicle becomes over-keratinised and the sebum mixes with skin cells which die (keratinise) there. The mixture of sebum and dead cells can no longer flow freely, so it collects and forms a plug (blackhead). This plug finally breaks through the wall of the hair follicle and forms a painful, inflamed, pimple (papule, pustule) in the skin.



Acne is not caused by a poor diet, dirt or greasy skin.

Factors which may make acne worse:
- Mental and physical stress
- Tiredness
- Cosmetics
- Medicines (iodine and bromide preparations)

How does Liderma® work?

The active ingredient in Liderma® is a substance related to vitamin A, and has similar effects to this vitamin. Vitamin A itself is part of a normal diet and plays a significant part in important biological processes such as growth, reproduction and vision. Vitamin A is essential for the formation of the skin and its normal functions. It is known that Vitamin A-related substances are successfully used in the topical treatment of acne.

Liderma® in capsule form is taken long-term only in cases of severe acne. After a few weeks to months, Liderma® overcomes the papules, pustules and pimples. The skin regains its normal appearance. In addition, Liderma® reduces the oily deposits on the skin and hair associated with severe acne.

Liderma®

- Reduces sebum production
- Slows down the over-keratinisation of the hair/sebaceous follicle
- Makes the sebaceous glands smaller
- Stops the inflammation
- Reduces bacterial colonisation (Propionibacterium acnes)

When should you use Liderma®?

Liderma® is used only for **severe acne** and **forms of acne that lead to scar formation.** These severe skin diseases often do not respond to other treatments.

Liderma® is not indicated for treatment of the less severe forms of acne that occur in young people during puberty.

Since this condition is a severe skin disease, treatment is prescribed by dermatology specialists. The precautions necessary with Liderma® require **close medical supervision of therapy.**

Are you of childbearing age? Then, together with your doctor, you must decide whether you should take Liderma®.

WARNING: Don't get pregnant

Birth control (contraception) absolutely essential for women

Liderma® is teratogenic, that is to say, it damages the developing baby. If you are pregnant, Liderma® may cause **severe defects in your unborn child.** Likewise, there is an increased risk of miscarriage.

The size of the dose and the length of time for which you take Liderma® do not make any difference – even low doses and very short courses of treatment can cause severe birth defects in the unborn child.

You must therefore obey the following instructions very carefully

- You must not take Liderma® if you are pregnant or wish to become pregnant during treatment.
- Before you start treatment with Liderma® you must have a pregnancy test (blood or urine sample) which shows that you are not pregnant. This must be done not more than 11 days before you take the first dose of Liderma®. Your doctor may require further pregnancy tests during the course of Liderma® treatment.
- You must wait until the 2nd or 3rd day of your period before starting to take Liderma®.
- You must use effective birth control (contraception) the whole time:
  - for at least 1 month before the start of treatment
  - during treatment and
  - 1 month after the end of treatment.

WARNING: Don't get pregnant

Birth control (contraception) absolutely essential for women

All women must

- Ask your doctor about the contraceptive methods most suitable for you. Read carefully the brochure **«Contraception»** which has been given to you along with this information booklet.
- Start effective birth control at least 1 month in advance of treatment with Liderma. Continue with this without a break for 1 month after you have stopped taking Liderma®.
- For this purpose, you should use two reliable methods of contraception together. Discuss this with your doctor.
- **Always use effective birth control.** Even when you think there is no chance of you getting pregnant (except if you have had an operation to remove the womb).
- Even reliable **methods of contraception can fail.** So you should always use two methods.
  Stop taking Liderma® immediately if you discover that you are pregnant or your period is unexpectedly late.
  Call your doctor immediately to determine whether you should have an abortion.
- **Don't get pregnant on Liderma®!**

Progesterone-only pills, minipills

The contraceptive effect of low dose progestagen preparations (so-called minipills) may be affected by Liderma®. You should therefore not rely on pure progestagen preparations (contraceptives without oestrogen components) for birth control while of treatment with Liderma®.

Before starting treatment

Blood tests are necessary before the start of and during treatment with Liderma®. These are to find out how your body is reacting to Liderma®.

You must not use Liderma® if you have any of the following **illnesses:**

- Severe liver disease
- Raised blood lipids (fats)
- Hypersensitivity to any of the components of Liderma®
- Diabetes (high blood sugar)

Inform your doctor if **you or any member of your family** suffers or has suffered from any of the following **illnesses:**

- Diabetes (high blood sugar)
- Liver disease
- Heart disease
- Depression

Liderma® is closely related to vitamin A. **Do not take any vitamin preparations or tonics that contain vitamin A.** Vitamin A may increase some of the possible side effects of Liderma.
If you want to take vitamins or tonics, discuss this with your doctor.

Are you taking any other medicines?

Tell your doctor if you are taking any prescription or over-the-counter medicines, either regularly or even only on occasion.

Warning: Don't get pregnant

Before starting treatment with Liderma®, you must discuss everything carefully with your doctor. You must also sign an **informed consent for patients** (see appendix).

When can you start treatment with Liderma®?

- When you are absolutely sure that you **are not pregnant**
- When you have been practising effective **birth control** for **one month before the start of treatment**
- When you have had a **pregnancy test** within the last **11 days** that shows that you are definitely not pregnant before you start treatment with Liderma®
- When you have waited for the **2nd or 3rd day of your next menstrual cycle**

You must not start treatment with Liderma® if you cannot be absolutely sure that you are not pregnant. Mothers who are breast-feeding may not take Liderma®.

During treatment

- Liderma® is **prescribed for you personally.** The reasons for prescribing Liderma® may vary greatly from one patient to another. You must therefore never share your Liderma® with anyone else.
- **Individual dosage**
  The number of capsules that you have to take has been determined for you personally. Take exactly the dose prescribed by your doctor.
- Your doctor may change the prescribed dose during the course of treatment. Follow the new instructions exactly.
- **If you have any questions, please call your doctor.**

How to take Liderma®

- Take Liderma® capsules with liquid **during a meal.**
  Do not chew the capsules.
- Have you **forgotten to take a dose?** Don't take twice as many capsules next time but continue with the treatment as if nothing has happened.

Storing Liderma®

- **Store Liderma®** carefully. Keep the capsules in the **original packaging. Protect from heat, light and moisture** so that they do not lose strength.
  Do not leave Liderma® in direct sunlight or on the shelf above a radiator.
- **Keep Liderma® out of reach of children** and away from others for whom they are not intended.
- Do not use the capsules after the **expiry date** printed.

Warning: Don't get pregnant

During treatment with Liderma® you must continue to use effective **birth control.** It is recommended that you **have regular check-ups** and carry out **pregnancy tests** as required by your doctor.

If your **period is unexpectedly late,** stop taking Liderma® **at once** and tell your doctor **immediately.**

Side effects

What **side effects** can Liderma® have?

Especially at the start of treatment there is frequently marked dryness of the lips, mouth and nose, as well as reddening of the face and eyes. The feeling of «dry eye» may remain for some months after stopping treatment with Liderma®. In rare cases, you may react more sensitively to sunlight. In addition, itching and sweating may occur. Your doctor will advise you how to relieve these undesirable effects; they are not dangerous and will disappear again if you follow your doctor's instructions.

Worsening of the acne is sometimes seen at the start of treatment. This is, however, normal and does not mean that you should change the prescribed dose on your own initiative.

During the course of treatment, a varying degree of hair loss may occur. You should not be too disturbed by this side effect, as in most cases the hair grows again within a few months of stopping Liderma®. In rare cases, the hair does not grow again even after some time.

In a few cases reduced night vision is noticed during Liderma® therapy. You should therefore take special care if you drive at night or have to operate machines.

Inform your doctor as soon as possible if you have any of the following symptoms:
- unusually severe or persistent headaches
- visual disturbances
- muscle or joint pains
- nausea
- severe stomach ache
- bleeding from the back passage
- diarrhoea or
- yellowish discoloration of the skin or eyes and/or
- dark urine

All of the above require adjustment in your treatment. In isolated cases, asthma-like symptoms (difficulties breathing) have been reported.

Liderma® has been associated with depressive moods and the risk of suicidal thoughts, suicide attempts and suicide. A mechanism of action which would explain these side effects is not known. Contact your doctor immediately if you notice that you have feelings of sadness or disturbances of your normal sleep pattern.

After treatment

Like most patients, you will notice that **the appearance of your skin continues to improve** even after stopping Liderma® therapy.

Most **side effects disappear completely** a few days (to weeks) after stopping treatment with Liderma®. Please contact your doctor if you still have side effects after this time.

A few patients who have been treated with Liderma® may need a **second treatment cycle** in order to obtain the desired results. If this is necessary for you, the second course of treatment will start 8 weeks after the end of the first cycle.

You have finished your course of Liderma® as instructed by your doctor. If you have any **left-over capsules,** please take these back to the pharmacist or your doctor so that they can be disposed of correctly.

You must never keep an opened pack in your medicine cupboard or give these capsules to anyone else.

Do not give blood: You may not donate blood for at least one month after the end of treatment.

Don't get pregnant

You must continue to practise effective birth control without a break for at least 1 month after the end of Liderma® therapy.

Notes

Declaration of informed consent

(Copy for the patient)

The treatment with LIDERMA® proposed for me has been fully explained to me personally by my doctor. Along with other information, I have taken particular note of the following points:

1. I know that I may not take LIDERMA® if I am pregnant or wish to get pregnant during treatment. Also, I may not take LIDERMA® if I am breast feeding.
2. I am not pregnant or breast-feeding at the present time.
   I also agree not to become pregnant during treatment with LIDERMA® and not to get pregnant for one month after LIDERMA® treatment.
3. I understand that the children born to mothers who have taken isotretinoin (the active ingredient in LIDERMA®) during pregnancy have had severe birth defects.
   My doctor has warned me that there is a very high risk of severe damage to my unborn child if I am pregnant or if I get pregnant during treatment with LIDERMA®.
4. My doctor has explained to me that I must always use effective birth control (contraception) without a break
   – for at least 1 month before starting treatment,
   – during the entire period of treatment as well as
   – for 1 month after the end of treatment with LIDERMA®
   As an extra precaution I should use two reliable methods of contraception together.
5. I know that I must have a pregnancy test from a blood or urine sample, within 11 days before starting treatment with LIDERMA®, to prove that I am not pregnant. I am also aware that I must wait until the 2nd or 3rd day of my next menstrual period before taking the first dose of LIDERMA®.
6. I fully understand the risks which are associated with the failure of birth control; my doctor has informed me of these.
7. I know that I must stop taking LIDERMA® and contact my doctor immediately if
   – my menstrual period is unexpectedly late
   – I get pregnant during treatment with LIDERMA®
   – I get pregnant during the month following the end of treatment with LIDERMA®.
8. If I do get pregnant, I know that I have to discuss with my doctor whether an abortion would be advisable.
9. I know that I must read very carefully the Patient Information brochure about LIDERMA® which my doctor has given me. I have done this and discussed all my questions with my doctor.
10. I hereby confirm that all the above-mentioned points have been explained by my doctor and expressly drawn to my attention. I am aware of the risks of pregnancy during treatment with LIDERMA® and for one month after the end of treatment.

Place _____ Family name _____ Given name _____

Date of birth _____ Signature _____
(Minors: signature of parent/legal guardian)

Declaration of informed consent

(Copy for the doctor)

The treatment with LIDERMA® proposed for me has been fully explained to me personally by my doctor. Along with other information, I have taken particular note of the following points:

1. I know that I may not take LIDERMA® if I am pregnant or wish to get pregnant during treatment. Also, I may not take LIDERMA® if I am breast feeding.
2. I am not pregnant or breast-feeding at the present time.
   I also agree not to become pregnant during treatment with LIDERMA® and not to get pregnant for one month after LIDERMA® treatment.
3. I understand that the children born to mothers who have taken isotretinoin (the active ingredient in LIDERMA®) during pregnancy have had severe birth defects.
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   – for 1 month after the end of treatment with LIDERMA®
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6. I fully understand the risks which are associated with the failure of birth control; my doctor has informed me of these.
7. I know that I must stop taking LIDERMA® and contact my doctor immediately if
   – my menstrual period is unexpectedly late
   – I get pregnant during treatment with LIDERMA®
   – I get pregnant during the month following the end of treatment with LIDERMA®.
8. If I do get pregnant, I know that I have to discuss with my doctor whether an abortion would be advisable.
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10. I hereby confirm that all the above-mentioned points have been explained by my doctor and expressly drawn to my attention. I am aware of the risks of pregnancy during treatment with LIDERMA® and for one month after the end of treatment.

Place _____ Family name _____ Given name _____

Date of birth _____ Signature _____
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