Isotretinoin or 13-cis retinoic acid is a very effective medication for the treatment of acne. It is a retinoid; this means it is derived from vitamin-A (retinoic acid). The liver naturally makes small quantities of isotretinoin from vitamin-A, but the drug we prescribe is made synthetically.

Isotretinoin has been available in New Zealand since 1982 but receives Drug Tariff funding only on the prescription of a Vocationally Registered (Specialist) Dermatologist. In New Zealand, isotretinoin is available as 10 mg and 20 mg capsules, trade name Isotane®. In other countries, there are other brands of isotretinoin including Accutane®/Roaccutane® and Oratane®.

Most people receive a course of isotretinoin for 16 to 30 weeks (4 to 7 months), but some require it for longer. If necessary, it can be prescribed for children as well as adults.

If you are prescribed isotretinoin it is very important you read and understand about the medication. Ask your dermatologist to explain anything you do not understand.

Do not give your medication to anyone else. Do not start the medication if you are pregnant, and do not become pregnant during treatment as this medication may cause major birth defects.

Do attend all booked appointments with your dermatologist. Do not hesitate to phone your doctor or dermatologist if you have any concerns about your treatment.

**Properties of isotretinoin**

- Isotretinoin markedly reduces sebum production and shrinks the sebaceous glands.
- It gets rid of comedones and prevents new ones forming.
- Treated skin is dry, inhibiting the growth of acne bacteria.
- It has anti-inflammatory properties.

**Indications for treatment**

Dermatologists prescribe isotretinoin for patients with acne in the following circumstances:

- Nodular or nodulocystic acne (i.e. where there are large deep lumps)
- Acne conglobata or acne fulminans
- Severe disfiguring inflammatory acne vulgaris
- Acne which is resulting in scarring
- Moderate acne which has failed to respond to topical agents combined with oral antibiotics, or in women, hormonal treatment
- Acne which relapses rapidly on discontinuing treatment
- Acne which has persisted for several years, or arises in an individual over 25 years old
- Dyssmophophobic acne
- When the acne has a significant adverse occupational, social or psychological effect on the patient's life
Isotretinoin is also useful for patients severely affected by other follicular conditions. These include:

- Acne keloidalis nuchae
- Chloracne
- Gram negative folliculitis
- Hidradenitis suppurativa
- Oil folliculitis
- Pityrosporum folliculitis
- Pseudofolliculitis barbae
- Pyoderma faciale
- Rosacea & rhinophyma
- Scalp folliculitis & acne necrotica
- Sebaceous hyperplasia
- Seborrhoea
- Steatocystoma multiplex

Isotretinoin has proved helpful as a second-line treatment for scaly skin conditions and other inflammatory skin diseases such as:

- Darier disease
- Discoid lupus erythematosus
- Epidermal naevi
- Folliculitis decalvans
- Granuloma annulare
- Grover's disease
- Hidradenitis suppurativa
- Ichthyosis
- Sarcoidosis
- Skin cancers especially when they arise in those with organ transplants or xeroderma pigmentosa

**Dosage**

The individual dose prescribed by the dermatologist depends on:

- The patient's body weight
- The specific condition being treated
- The severity of skin condition
- The response to treatment
- Other treatment used at the same time
- The severity of side effects

For severe acne, the total dose over a course of treatment is ideally between 120 and 150–mg/kg–body weight. The range of doses used each day for acne is 0.1 to over 1mg/kg body weight. Generally the side effects are easier to cope with if one starts with a reasonably small dose, perhaps 0.5mg/kg/day. The dose can be gradually increased over the next few weeks depending on tolerance and its effect on the skin condition. Sometimes it needs to be reduced or even temporarily stopped. Your dermatologist will advise you.

The medication requires fat to help its absorption into the bloodstream so it is taken after food. This can be as a single daily dose after the main meal of the day, swallowed with water or another non-alcoholic drink.

If you forget your daily dose, do not double up the next day. The occasional missed dose will not make much difference to the outcome of the treatment.

http://www.dermnetnz.org/treatments/isotretinoin.html
Drug interactions

Isotretinoin should not be taken with the following medications:

- Vitamin-A (retinoic acid) – side effects could be severe. Beta-carotene (provitamin-A) is permitted.
- Tetracyclines (including doxycycline, minocycline, and tetracycline) – these could increase the risk of headaches and blurred vision due to raised intracranial pressure.

Side effects

Unfortunately isotretinoin can make acne worse at first. Usually the flare-up lasts only a couple of weeks, but in some people the flare-up can be very severe and occur for several months. If you have a severe flare-up of your skin condition, let your dermatologist know straight away. Additional medication such as oral steroids, antibiotics or acne surgery (cauterity of comedones) may be required, and the dose of isotretinoin may need to be adjusted.

All treated patients suffer from some side effects. The range and severity of the side effects depends on the disease being treated, the dose of isotretinoin and personal factors. Contact lens wearers have more problem with dry eyes; those with a history of eczema may find isotretinoin aggravates it; fair skinned people burn more easily; sportsmen may have more problems with muscles and joints aching.

If the side effects are troublesome, they will be easier to cope with on a lower dose of isotretinoin. They clear up completely within a few days to a month after the medication has been discontinued. Discuss your side effects with your dermatologist.

The majority of side effects are mucocutaneous i.e. they affect the skin and mucous membranes:

- Dry and cracked lips (cheilitis) affect all treated patients. Apply a lip balm frequently and liberally. Petroleum jelly can be applied indoors or at night. A lip preparation with a sunscreen is preferred during the day. Topical antibiotic such as mupirocin or fucidic acid may be required.
- Dry skin: especially on exposed skin (face, neck, arms, and hands). Apply an emollient cream frequently and liberally to dry skin, especially after bathing.
- Dry nostrils: use petroleum jelly. Do not pick the dry scabs. Nosebleeds may occur in those disposed to them. If this occurs put your head forward and pinch the fleshy part of your nose firmly. Do not swallow the blood (this could make you feel sick). The bleeding usually stops within a few minutes. Topical antibiotic may reduce nosebleeds.
- Dry eyes: severely dry eyes are sore and red. There is a risk of conjunctivitis and/or keratitis, an inflammatory condition of the cornea. Rarely, this scars. Stop your isotretinoin and contact your dermatologist if you have sore red eyes that fail to improve with "artificial tears" (eye drops). Sometimes, paradoxically, patients complain of watery eyes. Do not start wearing contact lenses for the first time while you are taking isotretinoin.
- Dry genitals and anal mucosa: bleeding at the time of a bowel motion may occur from a split anus. Sexual intercourse may be uncomfortable: use plenty of suitable lubrication such as K-Y Jelly or Silk.
- Fragile skin: minor injuries such as grazes occur more readily and heal more slowly. Shave rather than wax: the top layer of your skin may strip off as well the hairs!
- Increased sweating: keep cool.
- Facial erythema (redness) &/or flushing: most noticeable in fair skinned people.
- Sunburn: a particular problem for fair skinned people. Careful sun protection is most important. All the year round, make sure you apply a cream-based sunscreen before going outdoors. Apply it frequently and liberally if you are skiing in the spring at high altitude, or if outside during the summer months between 11 am and 5 pm. Do not expose your skin to a sun bed or sun lamp.
- Eczema: red itchy patches may appear on the dry skin. A topical steroid may be required for a few days to clear the rash: obtain a prescription from your doctor or dermatologist. Apply emollients liberally and frequently.
• **Impetigo**: a secondary infection with *Staphylococcus aureus* and/or *Streptococcus pyogenes* bacteria. Impetigo is also known as "school sores"; there are yellowish crusted patches, most often around the lips and nostrils or affecting the acne spots. See your doctor for a course of topical and/or oral antibiotics.

• **Pyogenic granuloma**: red juicy lumps may rarely appear around acne nodules or elsewhere. See your dermatologist for treatment (topical steroids & cautery).

• **Paronychia**: an infection of one or more nail folds, usually with *Staphylococcus aureus*. It is especially common in ingrowing toenails or nails that are chewed or picked. Paronychia can be particularly stubborn and resistant to treatment but settles once the isotretinoin has been discontinued.

• **Hair loss**: some hair may fall out temporarily, and the hair may lose condition. It grows normally once the isotretinoin has been stopped. Normal shampoo and conditioners may be used but won't influence the hair fall. If the scalp is scaly, an anti-dandruff shampoo twice a week may help.

• **Nail changes**: the nails may become brittle and slow growing. They recover when treatment has been discontinued, but it will take several months for the new healthy nail to grow out.

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### Adverse effects of isotretinoin

- **Acne flare early in the course of isotretinoin**
- **Dry lips on isotretinoin**
- **Sunburn aggravated by isotretinoin**
- **Dermatitis due to isotretinoin**
- **Granulomas provoked by isotretinoin in a patient with acne conglobata**
- **Staphylococcal impetigo complicating a course of isotretinoin**
- **Infected nailfold (paronychia) due to isotretinoin**

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### Other side effects:

- **Headache**: generally mild and responding to paracetamol. Severe headache associated with blurred vision could indicate raised intracranial pressure, a rare but severe side effect. Contact your dermatologist or general practitioner if this occurs to you.

- **Muscle aches (myalgia) especially after exercise. Low backache is not uncommon. Joint aches (arthralgia) especially after exercise can sometimes be debilitating. These symptoms respond to nonsteroidal anti-inflammator**

- **Tiredness (lethargy and drowsiness)** is common; it responds to a good night's sleep.

- **Mood changes and depression (rarely). If this occurs, seek help immediately from your dermatologist or general practitioner. Severe depression is rare but may require the isotretinoin to be discontinued. Antidepressant medications may be helpful.**

- **Eye problems**: night blindness and slow adaptation to the dark. This arises because isotretinoin replaces retinoic acid on receptors on the rods, the cells in the retina that enable us to see in poor light. Drivers may experience increased glare from car headlights at night. If you have eye problems, do not drive or pilot a plane after dark. Discuss your visual problems with your dermatologist; a lower dose of isotretinoin
may be advised or you may need to consult an ophthalmologist. Cataracts have rarely been reported.

- Hypertriglyceridaemia (high blood fats) can result in pancreatitis, a painful and dangerous condition. Make sure you follow a low-fat diet while you are on isotretinoin and avoid simple carbohydrates (sugar, sweet drinks, lollies etc). Have blood tests as advised by your dermatologist and make sure you have found out whether the results are normal or not. If your blood fats rise significantly on isotretinoin you may have to reduce the dose or discontinue the treatment.

- Diarrhoea or bleeding from the bowel may rarely occur, especially in those with colitis.

- Irregular or heavier menstrual periods may sometimes occur. This is not harmful. If you miss a period, make sure you are not pregnant by having a blood or urine test.

- Allergy to isotretinoin. This is rare but may include liver disease and a febrile illness. High-tone deafness, vasculitis and urticaria have rarely been reported.

### Monitoring

Most patients are advised to have blood tests before and on one or more occasions during isotretinoin treatment. Patients with certain serious health problems may be advised against taking isotretinoin, or may be treated with a lower dose than usual. Such health problems include severe liver or kidney disease, high blood fats, diabetes and depression.

The tests may include:

- Pregnancy test (beta–HCG) for women and girls of child–bearing potential (you will probably be asked to have this performed even if you tell your dermatologist you are not sexually active, still a teenager, or your partner has been sterilised). Please do not be offended.

- Blood fats (cholesterol and triglyceride levels). These are most reliable if measured on a fasting sample, i.e. no food for some hours (perhaps first thing in the morning, eating your breakfast after the test has been completed).

- Liver function tests. Occasionally, isotretinoin may disturb liver function; this requires monitoring but if the reaction is mild the drug can usually be continued. Rarely, it causes a symptomatic hepatitis: the drug must then be discontinued. Drink minimal alcohol while taking isotretinoin, as alcohol also affects the liver.

- Blood count: this is to check for anaemia and to monitor white cell count and platelets (clotting cells).

### Contraception and pregnancy

Isotretinoin must not be taken in pregnancy because of a very high risk of serious growth abnormalities in the baby.

It should not be taken during breast–feeding as it enters the breast milk and might affect the baby.

You must tell your dermatologist if you think you may be pregnant before you start on isotretinoin. If you intend getting pregnant within the next six months or so, you should not take isotretinoin.

All females who could biologically have a child should take the following precautions during treatment with isotretinoin and for four weeks after the medication has been discontinued:

- Abstinence. The most reliable method of avoiding pregnancy is not to have sex. No method of contraception is completely reliable. "Natural" family planning is particularly risky.

- If sexually active, two reliable methods of contraception should be used. Discuss contraception with your doctor (general practitioner, family planning specialist, gynaecologist or dermatologist). The combined oral contraceptive, IUD (intrauterine device) combined with condoms or "the injection" (medroxyprogesterone or Depo–Provera) may be suitable. Isotretinoin may reduce the efficacy of these medicines in some women, and they are not 100% reliable. Subcutaneous hormone implants or Mirena® may also be considered.

- A prescription for emergency contraception (a high dose of progesterone, trade name Postinor®) can be obtained from a medical practitioner (GP or family planning clinic) or accredited pharmacy. It prevents 85% of pregnancies if taken within 72 hours of unprotected sexual intercourse.
If your contraception fails, termination of pregnancy (an abortion) may be advised if pregnancy arises during treatment with isotretinoin or within a month of discontinuing it. Do not put yourself in this situation!

Isotretinoin has a very high chance of resulting in a spontaneous miscarriage or a severe birth deformity if a fetus is exposed to it during the first half of pregnancy. The deformities affect the growth of tissues developing at the time of exposure to the drug:

- Cranium (skull and brain)
- Cardiac (heart)
- Eye, ear
- Limbs

Males and females. Do not give blood while you are on isotretinoin or for a further four weeks after you have discontinued it, in case your blood is used for a pregnant woman.

Males. Isotretinoin has no effect on sperm or male fertility and has not been shown to cause birth defects in children fathered by men taking it. No specific contraceptive precautions are necessary for men.

Children. Children can take isotretinoin if necessary to control severe skin disease.

**Slow responders**

Some patients with acne respond unexpectedly slowly and incompletely to isotretinoin. The reasons are thought to be:

- Large comedones ("macrocomedones")
- Nodules
- Secondary infection with *Staphylococcus aureus*
- Unknown factors

Options available to slow responders include:

- Cautery or diathermy of comedones
- Prolonged course of isotretinoin
- Additional treatment with oral antibiotics

**Treatment of relapses**

At least fifty per cent of patients with acne are lucky enough to have a permanent cure after a single course of isotretinoin. Unfortunately, in some patients, acne recurs few months to a few years after the medication has been discontinued.

If indicated, these patients may receive one or more further courses of isotretinoin. This may be at a similar dose and duration as before, or it may differ from previously.

A small number of people with particularly troublesome skin conditions require long term treatment with isotretinoin. With the exception of patients with skin cancers due to immunosuppressive medications eg organ transplant patients (who required 0.5 to 1mg/kg/day), generally only a small dose is required, such as 20 mg twice weekly. Another regime is to take 0.5 –1 mg/kg/day for one week out of every four weeks for a minimum of six monthly cycles. These regimes may be used for patients with:

- Persistent acne (all types)
- Severe seborrhoea
- Rosacea
- Scalp folliculitis
Besides the worry about pregnancy in treated women, the main concern with long term treatment is that isotretinoin may have effects on the bones. Diffuse interstitial skeletal hyperostosis ("DISH"), a normal and common ageing process may be accelerated in those taking excessive doses of isotretinoin for long periods. The result can be seen on X-rays of the affected bones and includes spurs on the heel, knee, and spine. DISH may result in aching discomfort, which does not necessarily resolve when isotretinoin is discontinued.

Related information

On DermNet NZ:
- Acne

Other websites:
- Medsafe consumer information on Roaccutane
- Medsafe consumer information on Isotane
- Family Planning (FPA) New Zealand for contraceptive advice

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DermNet does not provide an on-line consultation service. If you have any concerns with your skin or its treatment, see a dermatologist for advice.