

Acne, which is one of the most common disease affecting humans, can occur at any age and tends to inflict us during our vulnerable teenage years, causing irreversible scars, loss of confidence and even depression. Subsequently in the past decades, there have been many new treatments developed for fighting pimples. However, isotretinoin, which has been present in the market for more than half a century, is still the most effective of them all. It is easy to administer orally and if used properly, it can change lives.

The different retinoid compounds are effective in treating many diseases, including acne, psoriasis and T-cell lymphomas and are widely used for diseases of abnormal keratinisation. Isotretinoin is part of the retinoids group of medication, with functional and structural analogy to vitamin A. It is absorbed through the GIT and undergoes first pass metabolism in the liver and subsequent enterohepatic recycling. The oxidised metabolite migrates to target cells in the skin and effect its action by binding to certain nuclear receptors. Though there have been several retinoid receptors identified, the exact mechanism of action for isotretinoin is still unknown. Fortunately, there is no liver storage nor adipose storage for isotretinoin and its metabolites are completely eliminated by urine and faeces. After discontinuation, the natural concentrations of 13-cis-RA and its major metabolites are reached within 2 weeks, ranging from 2 days for at-RA to 10 days for 4-OXO-isotretinoin. Therefore, there is no long term effect on other organ system and one month post-therapy contraception is more than adequate.

Isotretinoin can be prescribed to most patients with acne depending on severity, relapses as well as the patient's needs. Patients can be very disturbed with what a clinician may qualify as mild acne and the constant recurrence of lesions may lead the person to social withdrawal. Thus the use of isotretinoin should be tailored according to individual needs. The capsules are available in 10mg and 20mg doses in South Africa and 40mg doses overseas, which makes it easier to administer. Generally a dose of 1mg/kg daily for 5-6 months will achieve a cumulative dose of 150-180mg/kg. However, lately, there have been several new studies where much higher doses have been used for severe cases, without an increase in adverse effects. Thus a dose of 2mg/kg daily for difficult to treat cases can be administered to certain patients.

This treatment can be used in almost all ages, however, it needs specialist guidance for paediatric patients. Factors, like severity of the disease, weight of the patient and the failure of other treatment modalities are taken into consideration when treating a child younger than 12 years of age. The adolescent patients need to be tested for pregnancy and started on contraception when required. Most times the teenage females hide their sexual activities during the interview and it may be safest to just initiate contraception when in doubt. In healthy individuals, a liver function test at month of treatment, tends to suffice. The lipid levels predictably, do rise in almost all patients and testing for that do not usually add any value to the treatment regime. Of course, patients at risk, need to be closely monitored and bloods tests need to be repeated regularly

Emphasis on compliance is very important for the success of this treatment. Administering high doses can be very tedious as the patient needs to take on average 4-6 capsules a day with fatty food. Thus they must be counselled properly and the common side-effects explained. Many of them may suffer from other unrelated diseases during their course on isotretinoin and should be managed accordingly with their general practitioners. They can take most other medications in moderation to treat other diseases, however, they should be careful not to consume excessive amounts of vitamin A and not to use tetracyclines. The latter can cause pseudotumour cerebri, leading to severe headaches.

Acne is becoming more and more resistant to treatment and several patients are needing 2-3 courses of isotretinoin and at times, long term maintenance. This is due to global warming, stress, pollution and the processed foods we consume. In the near future, more than half of the teenagers will end up taking isotretinoin to treat their acne. With the increasing use of this medication, there have been many attempts to discredit this drug, due to rare cases of depression. The media can sensationalise stories without revealing all the facts. Acne on its own, will depress most sufferers and not treating it aggressively, can result in permanent scars. No other medication or cosmetic product achieves the result one gets from this drug. Isotretinoin changes lives for the better.

Table I: Other uses of isotretinoin

Rosacea	It is very effective for all types of rosacea including phymatous type. Low dose isotretinoin can be used and once control is achieved, a maintenance dose of 10-20mg weekly may suffice
Seborrhoea	It is highly effective in the control of severe oiliness of the face. Low dose can be used.
Hidradenitis suppurativa	It can help with this disease, however, it does not offer full control. It is more effective when sinuses are absent and the anatomy is still intact.
Recurrent folliculitis of the scalp	Can be very effective in treating resistant folliculitis decalvans
Darier's disease	This rare disease has been controlled successfully with isotretinoin
Other diseases	Lichen planus (oral erosive, palmoplantar) lichen sclerosus, Lupus erythematosus, keratodermas, pityriasis rubra pilaris and sebaceous gland hyperplasia.

Table II: Contraindications

Absolute	Relative
Pregnancy and breast feeding	Moderate to severe cholesterol or triglyceride elevation
Non-compliance with contraceptives	Significant hepatic dysfunction
Hypersensitivity to parabens(in isotretinoin capsules)	Significant renal dysfunction

Table III Precautions in female patients of reproductive age

Guidelines:
<ol style="list-style-type: none"> 1. Female patients should not fall pregnant while taking isotretinoin and can try to conceive only one month after stopping the medication. This medication is completely eliminated from the body within 30 days. 2. Patients need to sign a disclaimer and must adhere to strict birth control. 3. It is safe to do a pregnancy test on sexually active patients and to ask them to start the medication after they have already started with their contraceptives. 4. Though 2 forms of contraceptives (e.g pills and condom) have been advocated by the FDA, it may not always be practical in our setting and compliance will be an issue. 5. The patient should undertake to inform the doctor immediately if the contraception fails and they end up falling pregnant. They will have to terminate the pregnancy. 6. This medication does not affect fertility.

Table IV: Side-effects of isotretinoin

Eyes	Reduced night vision, persistent dry eyes and repeated staph aureus infections. This is fairly common and is the reason why it is contraindicated in pilots
Bone	Diffuse skeletal hyperostosis, osteophyte formation and premature epiphyseal closure are fortunately uncommon
GIT	Can cause flare up of Inflammatory bowel disease and rarely cause pancreatitis. Rarely causes nausea, diarrhoea, abdominal pains, constipation and rarely rectal bleeding. Though mild elevation of transaminases is common, it rarely causes hepatitis
Endocrine effects	Hypothyroidism and diabetes mellitus are exceptionally rare with isotretinoin and may even be a co-incidence.
Neurologic	Pseudotumour cerebri: Transient headaches are relatively common early during the therapy, however, if it is accompanied by nausea, vomiting and visual changes, this should prompt further evaluation to exclude pseudotumour cerebri. The risk increases with the concomitant use of tetracycline, thus they should be avoided. Depression, suicidal ideation, mood changes: The exact link with the use of isotretinoin has not been fully elucidated. However, patients with a previous history of depression should be closely monitored

	and treatment should be stopped if their condition is aggravated. One should bear in mind that severe acne by itself can be the cause of depression and the use of isotretinoin can improve the mood of the patient. Very mild depression is common.
Cutaneous	Xerosis, palmoplantar and digital desquamation, photosensitivity (can lead to temporary darkening of skin colour), fine sensitive rash on sun-exposed areas, pyogenic granulomas as well as bacterial infections.
Hair	Telogen effluvium, abnormal hair texture and dryness
Nail	Fragility and nail softening, paronychia and onycholysis.
Mucous membranes	Cheilitis-esp lower lip, dry mouth, sore mouth and tongue. Dry nasal mucosa, decrease mucous secretion and epistaxis. Vaginal dryness is common.
Musculoskeletal	Arthralgias, neck and lower backaches, fatigue and muscle weakness. Rarely tendinitis

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