# A Review of the Misuse of Isotretinoin in South Africa

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**Abstract**

Isotretinoin is a potent retinoid drug that is primarily used for the treatment of severe acne. Because of this, the drug has attracted attention and has the potential for abuse and misuse, including use without a prescription and overdose. This manuscript aims to explore the dimensions of isotretinoin misuse or abuse in South Africa. The epidemiological trends, underlying motivations, and associated health risks of Isotretinoin are discussed herein. Despite the strict regulatory control for access without a prescription and severe side effects, there is evidence of abuse of the drug for the effects it produces. The sociocultural and economic factors that contribute to this abuse are explored. Furthermore, Isotretinoin is rather perceived as a cosmetic enhancement tool, while it is indicated to treat severe cases of acne. Hence, the regulatory framework governing access to controlled scheduled substances such as isotretinoin in South Africa was analyzed and the gaps and enforcement challenges that allow for the misuse are described.

Isotretinoin remains a valuable drug in the management of severe acne. However, its potential for misuse and abuse in South Africa requires a comprehensive approach involving healthcare professionals, policymakers, and the public to ensure safe and appropriate use through innovative rational medicine use (RMU) interventions to protect the public while providing access for those with sincere needs.

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**Keywords:** Isotretinoin; Abuse; South Africa; Misuse; Controlled Substances

## Introduction to Isotretinoin

Isotretinoin is a retinoid and is related to vitamin A (1). It is the cis form of the naturally occurring tretinoin, a molecule consisting of a cyclohexenyl structure substituted by an isoprenoid structure (2). It is indicated for severe resistant cystic acne and severe acne which has failed to respond to the appropriate doses of systemic antibiotics and the conventional oral acne treatments (3, 4). In some cases, it may also be indicated for preventing extensive sebaceous follicle damage during the early teenage years. The patient needs to be well-informed about the drug before receiving isotretinoin. Patients should also be aware of the abuse of the medicine by some healthcare providers who suggest it for very mild acne.

Isotretinoin is one of the only drugs with a higher potential to cure acne and is therefore considered the "gold standard" for treating this condition (5, 6). However, many factors should be taken into account when considering isotretinoin therapy. It is a very potent drug with known harmful side effects, and it is also, frequently misused in that it is often given to patients with mild acne who do not have the severe scarring type of acne for which it is best indicated (7, 8). It is marketed under various trade names. It is considered the most effective treatment available for acne and has been used by millions of people (9). Isotretinoin is unique due to its potential effect on stable long-term reduction in the number of sebaceous follicles and a decrease in the ratio of Propionibacterium acnes bacteria colonizing these follicles (10, 11). Furthermore, it normalizes keratinization and is a potent anti-inflammatory agent. It also has clinically important effects on wound healing and pigmentation. Since most acne lesions have a minor inflammatory component, isotretinoin significantly reduces the overall inflammatory load.

Misuse and abuse of isotretinoin, refer to its use without a prescription, in greater amounts than recommended by the manufacturer, or longer than what is prescribed (12).

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The misuse and abuse have also occurred, paradoxically, with lower dosage regimens and less severe types of acne (13). The high dose use involves regular, sometimes daily, increases in dosage more than the recommended doses, often interrupted by brief periods of discontinuing the drug and then resuming with a high dosage. The primary motivation for such abuse is the hope of clearing acne more rapidly, even at the risk of local or systemic adverse effects of varying severity. It is, therefore, important that dermatologists and general practitioners who prescribe isotretinoin are aware of its abuse and can identify such patients as early as possible (14, 15).

Over the past three decades, significant progress has been made in understanding the isotretinoin mechanism of action and its adverse effects (5). This knowledge has been used to guide the development of regulations such as the implementation of risk management programs, which have helped to minimize the number of isotretinoin-exposed pregnancies. However, isotretinoin-exposed pregnancies and the consequences still occur, hence isotretinoin misuse and abuse remains a global challenge (16, 17).

### *Factors Contributing to Isotretinoin Misuse and Abuse*

Various factors drive the misuse and abuse of Isotretinoin in South Africa, ranging from the root causes of acne to the availability of the drug (see Figure 1). Isotretinoin misuse and abuse is related to the perceived desirability of its symptomatic effects, namely its ability to induce mood changes, low-dose stimulation, anxiolysis, and feelings of well-being (18, 19, 20). Several abnormalities have been identified in the cholinergic, serotoninergic, and opioid neurotransmitter systems in acne, to which Isotretinoin offers a plausible remedy (21). It is also believed to enhance the psychological effects brought on by acne, effectively erasing the visibility of the problem and the associated negative self-image. In South Africa, Isotretinoin is classified as a Schedule 5 medicine, which limits its accessibility from both private and public health facilities. The pharmaceutical industry thrives on the demand for medicines. However, while the marketing of such drugs is controlled there is still a high demand for them. Therefore abuse is inevitable when isotretinoin can be effective for both physical and psychological aspects of acne and is easily accessible.

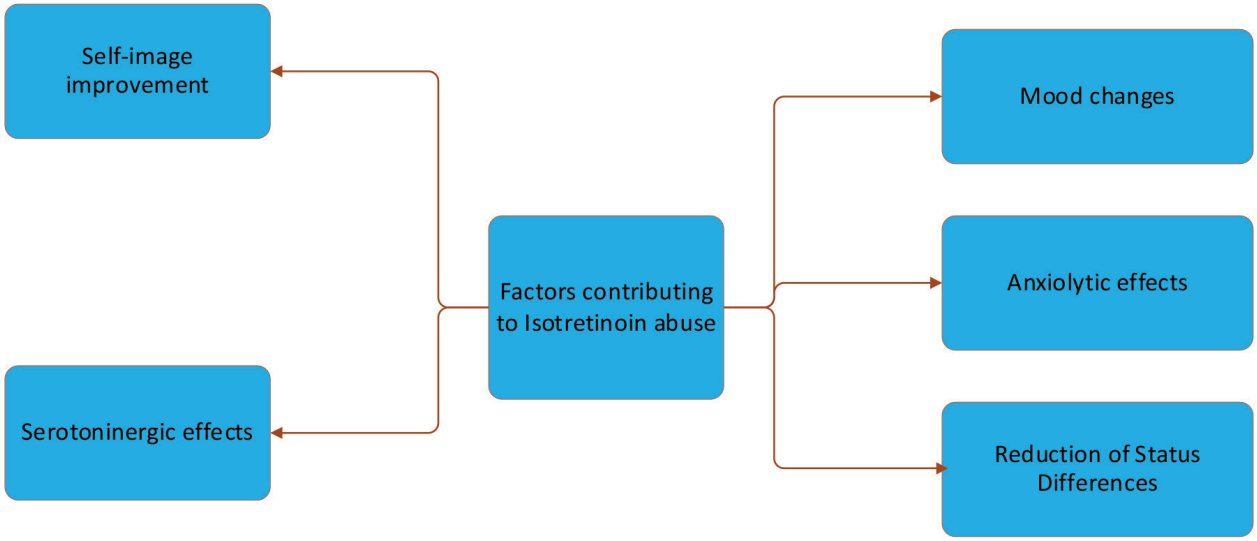


**Figure 1. Factors Contributing to Isotretinoin Abuse**

### *Social and Cultural Influences*

Several studies have shown that violent behavior in males is linked to hormonal patterns, which is one of the reasons why healthcare professionals may be concerned about the use of isotretinoin (22, 23). Although it may be argued that prescribers are applying a double standard to the use of isotretinoin, with limited concern being expressed about the misuse of the drug in the treatment of acne, it is important to acknowledge that South Africa is a unique country with a specific set of social circumstances (19). These circumstances have an influence not only on the prescriber's management of acne but also on their approach to the patient,

the patient's acceptance of treatment, and the potential adverse effects on the patient of both the isotretinoin and the prevailing social environment.

The unique social structure of South Africa is characterized by high levels of violence and crime. The high levels of unemployment and poverty have resulted in a relatively conservative society. It has been suggested that this form of society encourages conformity at an individual level and that low self-esteem is part of the national psyche. Physical appearance is heavily scrutinized, and deviations from societal norms can lead to significant psychological distress (2, 24).

### *Health and Societal Impacts of Isotretinoin Misuse and Abuse*

The abuse of isotretinoin is not only limited to teratogen-exposed pregnancies but also presents serious consequences for Rational Medicine Use (RMU). First, isotretinoin is frequently prescribed as a single therapeutic agent, although it is not indicated for the treatment of mild acne (5, 26). Secondly, the duration of isotretinoin therapy is extended for more than six months, which is a prerequisite for the selection and emergence of resistant Propionibacterium acnes strains (27, 28). The abuse of isotretinoin, as well as its disease-modifying effects, poses a serious threat to the control of medicines.

Skin lightening is common in South Africa and retinoids have been found in most skin-lightening products that are freely available in regular retail shops and not pharmacies (29). Despite the risk of isotretinoin misuse and abuse, a disproportionate focus has been placed on the abuse during pregnancy or only after it has occurred, with limited focus on the problem in non-pregnant patients. Pregnancy prevention is not a legal responsibility of the prescriber according to the South African isotretinoin guidelines; however, reports have provided evidence that prescribers are morally obligated to prevent pregnancy and that the prevention of pregnancy is feasible (30). A further overlooked aspect in both national and international isotretinoin guidelines is the failure to acknowledge that pregnancy exposure occurs in women who do not disclose their pregnancy status, as well as the inherent risk of exposing a fetus to teratogenic doses of isotretinoin at any given moment in time (31).

Isotretinoin has a wide range of health effects, both wanted and unwanted, which result from its systemic action. The positive effect is that isotretinoin decreases androgen activity and the production of sebum (32). In moderate doses, it is beneficial for the treatment of severe acne. However, its negative effects include teratogenicity, effects on the lipid profile, and damage to the mucous membranes (33). It also has the potential to increase the risk of developing pseudo-tumor cerebri, a condition that mimics a brain tumor and is associated with high intracranial pressure, resulting in severe headaches and vision disturbances. The misuse and abuse of isotretinoin is neither novel nor recommended, but it is growing as a trend to use it as a treatment to enhance features in individuals with low self-esteem and believe that isotretinoin will improve their appearance.

Some of the side effects of isotretinoin misuse and abuse include headache, dizziness, vomiting, abdominal pain, seizures, vision problems, swelling of the brain, hallucinations or other severe psychiatric symptoms, tinitus, hearing loss, and heart problems (10, 15). Chronic overdose of isotretinoin will also result in bone and joint damage, calcification of soft tissues, such as tendons, ligaments, and cartilage, and problems with metabolism, resulting in hyperlipidemia (35). It must be mentioned that many parameters need to be set before starting isotretinoin, as it has severe adverse effects. Thus, attention must be drawn to the fact that isotretinoin should not be used without medical supervision because of these serious health effects, as well as its potential for misuse and abuse.

South Africa has not only been overwhelmed by the widespread misuse and abuse of sunless tanning agents and unregistered skin-lightening products, but also by the abuse of isotretinoin for non-therapeutic reasons (36).

### *Regulatory Measures to Address Isotretinoin Misuse and Abuse*

Isotretinoin is a controlled medicine (Schedule 5) in South Africa, which should only be used under the care and supervision of a healthcare professional, under the Medicine and Related Substances Act 101 of 1965, as displayed in Figure 2. This classification signifies the need for strict regulatory measures to prevent misuse and ensure patient safety according to the Act. A key element of the Act is the monitoring of the controlled dispensing of isotretinoin by pharmacists. The Act does not allow for telephonic sales and requirements include that the patient must sign an information pamphlet received from the hospital or consulting room that all relevant information was given to the patient. In addition, the pharmacist must provide the patient with a medicine guide and reinforce the iPLEDGE requirements (37).

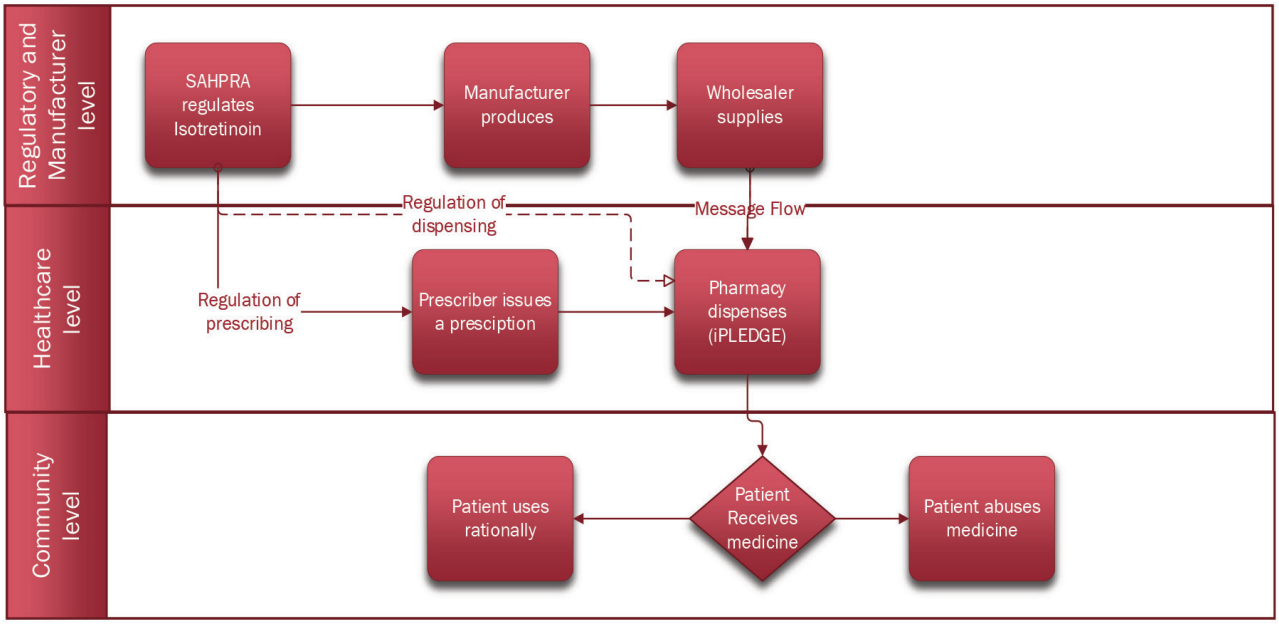


**Figure 2. Process flow for the lifecycle of isotretinoin**

The Act mandates that isotretinoin can only be dispensed by or under the direct supervision of a registered pharmacist (see Figure 2). This ensures the controlled distribution of drugs, thereby reducing the risk of inappropriate or excessive use. Pharmacists play an important role in monitoring prescriptions, verifying patient information, and ensuring that all guidelines for isotretinoin use are strictly followed.

Before initiating isotretinoin treatment, healthcare providers must provide comprehensive information to patients about the potential side effects, the importance of adherence to prescribed dosages, and the risks associated with misuse. Patients are required to sign an informed consent form acknowledging that they have received and understood this information. This step ensures that patients are fully aware of the implications of isotretinoin use and the necessity of following medical advice. Patients on isotretinoin must undergo regular follow-up appointments with their healthcare providers. These appointments are essential for monitoring the patient's response to the treatment, adjusting dosages as necessary, and detecting any early signs of adverse effects. Continuous monitoring helps ensure the safe and effective use of isotretinoin. Regular inspections of pharmacies are conducted to ensure compliance with regulatory requirements. Inspections also serve as a deterrent against non-compliance (38). They are there to reinforce compliance with regulatory requirements as required by the South African Health Products Regulatory Authority (SAHPRA), the National Regulatory Agency in South Africa.

Isotretinoin is sought after for its secondary effects, such as improvement in skin texture and decreased sebum production (39). The abuse of isotretinoin is especially prevalent among the youth, and it is well-recognized in South Africa as a public health issue (40). The concern is with both the high dosages used by the abusers, as well as the risk profile of isotretinoin, which is unique from other pharmaceuticals. The pharmaceutical industry and drug regulatory authorities need to recognize this risk of abuse and undertake suitable regulatory and policy measures to prevent and manage it.

## Conclusion

A comprehensive examination of the misuse and abuse of isotretinoin in South Africa has been studied, considering multiple studies and expert viewpoints. Further investigation is needed to fully understand the consequences and potential solutions for this issue. Therefore, the findings outlined in this manuscript enhance the existing body of knowledge and emphasize the importance of addressing this matter in future discussions and initiatives. It is hoped that this manuscript has provided valuable perspectives and facilitates an interest in further investigation around the use of isotretinoin. It is essential to continue the dialogue and collaborate with all stakeholders in the healthcare community to develop effective strategies for preventing and managing the misuse of isotretinoin. The widespread misuse and abuse of isotretinoin in South Africa poses a significant public health concern and requires urgent intervention. By working together, healthcare workers, especially prescribers and dispensers (i.e. prescribers and pharmacists) can create a safer and more responsible

environment for administering isotretinoin, ultimately improving patient outcomes and public health.

**Conflicts of interest**

The author declares no Conflicts of interest, financial or otherwise.

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