THIS MEDICINE MAY CAUSE SEVERE BIRTH DEFECTS. YOU MUST NOT TAKE THIS MEDICINE IF YOU ARE PREGNANT OR MAY LIKELY BECOME PREGNANT DURING TREATMENT. YOU SHOULD ALSO AVOID PREGNANCY FOR 6 MONTHS AFTER STOPPING THE TREATMENT.

For the use of a Dermatologist only

1. GENERIC NAME AND BRAND NAME

Isotretinoin Capsules I.P. 10mg
Tufacne® 10
Isotretinoin Capsules I.P. 20mg
Tufacne® 20

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Tufacne® 10
Each soft gelatin capsule contains:
Isotretinoin I.P. 10 mg
Excipients q.s.
Capsule Shell Contain Colours: Sunset Yellow FCF, Ponceau 4R & Titanium Dioxide I.P.
Tufacne® 20
Each soft gelatin capsule contains:
Isotretinoin I.P. 20 mg
Excipients q.s.
Capsule Shell Contain Colours: Red Oxide of Iron, Black Oxide of Iron & Yellow Oxide of Iron.

3. DOSAGE FORM AND STRENGTH

Refer section 1 & 2

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATION

Isotretinoin is used to treat cystic & conglobate acne, severe nodular acne unresponsive to antibiotic therapy.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

- Children Up to 12 Years: Not recommended.
- Children 12 Years and Older and Adults: The dose of isotretinoin is 0.5 to 1 mg/kg/day and the average length of treatment should be 15 to 20 weeks.

  Method of Administration: Oral route, to be taken with water.

4.3 CONTRAINDICATIONS:

- Hypersensitivity to isotretinoin or any component of the formulation; sensitivity to parabens, vitamin A, or other retinoids; pregnancy.
- Isotretinoin must not be used by female patients who are or may become pregnant. There is an extremely high risk that severe birth defects will result if pregnancy occurs while taking Isotretinoin in any amount, even for short period of time. Potentially any fetus exposed during

pregnancy can be affected. There are no accurate means of determining whether an exposed fetus has been affected.

- Birth defects which have been documented following Isotretinoin exposure include abnormalities of the face, eyes, ears, skull, central nervous system, cardiovascular system and thymus and parathyroid glands. Cases of IQ scores less than 85 with or without other abnormalities have been reported. There is an increased risk of spontaneous abortion and premature births have been reported.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE:

- It is a Pregnancy Category X. Women who are pregnant must not use Tufacne. Women must avoid becoming pregnant while taking this medication. Serious (sometimes fatal) birth defects, miscarriages and premature births have occurred when this drug has been used during pregnancy.
- For female patients, two effective forms of birth control (or complete avoidance of sexual intercourse) must be used for 1 month before starting Tufacne, during use and for 1 month after stopping this drug. You must also have monthly pregnancy-avoidance counseling from your doctor. Do not use "minipills" for birth control (non-estrogen-containing pills) since they may not work as well with isotretinoin. If you are late in having your menses, or if you have sexual intercourse at any time without using two effective forms of birth control, stop taking this medication and contact your doctor immediately. You should also avoid pregnancy for 6 months after stopping the treatment.

PRECAUTIONS:

- Before taking Tufacne, tell your doctor if you are allergic to it; or to soybean, peanuts, soya lecithin, or parabens; or if you have any other allergies.
- Before using this medication, tell your doctor about your medical history, especially of: diabetes, family or personal history of high blood fats (triglycerides), family or personal history of psychiatric disorders (including depression), suicidal thoughts and behavior, aggressive and/or violent behavior, liver disease, obesity, eating disorders (e.g., anorexia nervosa), alcohol abuse, pancreatitis, bone loss conditions (e.g., osteoporosis/osteomalacia, decreased bone density).
- Do not donate blood while you are taking isotretinoin and for at least 1 month after you stop taking it.
- This medication may make you more sensitive to the sun. Avoid prolonged sun exposure, tanning booths and sunlamps. Use a sunscreen and wear protective clothing when outdoors.
- Isotretinoin can affect your night vision. Be cautious when driving or operating any machinery after dark.
- lf you wear contact lenses, you may not tolerate them as well as usual while using this medication. Contact your doctor for more information.
- Do not have cosmetic procedures to smooth your skin (e.g., waxing, laser, dermabrasion) during and for 6 months after isotretinoin therapy. Skin scarring may occur.
- Pseudotumor cerebri, some cases with concomitant tetracyclines.
- Serious skin reactions: Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN).

- Acute pancreatitis, rarely fatal hemorrhagic pancreatitis, in patients with either elevated or normal serum triglyceride levels.
- Lipid Abnormalities: Triglyceridemia, low HDL and elevation of cholesterol. Monitor lipid levels at regular intervals.
- Impaired hearing has been reported in patients taking isotretinoin; in some cases.
- Hepatotoxicity: Monitor liver function tests at regular intervals.
- Isotretinoin has been associated with inflammatory bowel disease (including regional ileitis) in patients without a prior history of intestinal disorders.
- Skeletal Abnormalities: Arthralgias, back pain, decreases in bone mineral density and premature epiphyseal closure.
- Ocular Abnormalities: corneal opacities, decreased night vision.
- Glucose: Some patients receiving isotretinoin have experienced problems in the control of their blood sugar level.
- CPK: Some patients undergoing vigorous physical activity while on isotretinoin therapy have experienced elevated CPK levels; however, the clinical significance is unknown.
- Further details can be obtained from your prescribing Dermatologist.

4.5 DRUGS INTERACTIONS

- The concurrent use of Tufacne with tetracycline antibiotics or vitamin A supplementation is not recommended. Concurrent use of Tufacne with tetracyclines significantly increases the risk of idiopathic intracranial hypertension. Concurrent intake of Vitamin A supplementation increases the risk of vitamin A toxicity.
- Concurrent use of Tufacne with methotrexate increases the risk of hepatotoxicity and may increase methotrexate levels. The combination is used with caution and close monitoring of adverse effects and liver function tests.
- Systemic Corticosteroids: Systemic corticosteroids are known to cause osteoporosis. No formal clinical studies have been conducted to assess if there is an interactive effect on bone loss between systemic corticosteroids and Isotretinoin. Therefore, caution should be exercised when using these drugs together.

4.6 USE IN SPECIAL POPULATIONS (SUCH AS PREGNANT WOMEN, LACTATING WOMEN, PAEDIATRIC PATIENTS, GERIATRIC PATIENTS ETC.)

- Pregnancy category X. Isotretinoin is a teratogen - that is, if taken by pregnant women, it may cause serious harm to the developing baby, even if taken only for a short period. The possibility of pregnancy must be excluded before a woman of child-bearing potential can begin isotretinoin and measures must be taken to ensure women taking isotretinoin, or who have recently stopped isotretinoin, do not become pregnant.
- Lactation- Isotretinoin is highly lipophilic, therefore the passage of isotretinoin into human milk is very likely. Due to the potential for adverse effects in the child exposed via mothers' milk, Isotretinoin is contraindicated during breast-feeding.
- Paediatric Population- Isotretinoin should not be used for the treatment of prepubertal acne and is not recommended in children less than 12 years of age due to a lack of data on efficacy and safety.

- Geriatric - Appropriate studies performed to date have not demonstrated geriatric-specific problems that would limit the usefulness of isotretinoin in the elderly. However, elderly patients are more likely to have serious unwanted effects, which may require caution in patients receiving isotretinoin.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Isotretinoin could potentially have an influence on the ability to drive and use machines.

A number of cases of decreased night vision have occurred during isotretinoin therapy and in rare instances have persisted after therapy (see section 4.4 and section 4.8). Because the onset in some patients was sudden, patients should be advised of this potential problem and warned to be cautious when driving or operating machines.

Drowsiness, dizziness and visual disturbances have been reported very rarely. Patients should be warned that if they experience these effects, they should not drive, operate machinery or take part in any other activities where the symptoms could put either themselves or others at risk.

4.8 UNDESIRABLE EFFECTS

- The most common side effects of isotretinoin are dry skin, itching, dry nose, back pain, dry eye, dry lip, nasopharyngitis, dermatitis, blood creatine kinase increased, musculoskeletal discomfort, upper respiratory track, chapped lips, pain nosebleeds (epistaxis), cracks in the corners of the mouth (chilitis), dry mouth and visual acuity reduced, minor swelling of the eyelids or lips, crusty skin, nosebleeds, upset stomach, or thinning of hair may occur. Joint aches also are common. Patients may develop an increase in blood cholesterol and triglycerides. If any of these effects persist or worsen, tell your doctor promptly.
- Dry eyes, corneal opacities, decreased night vision and keratitis usually resolve after discontinuation of therapy. Cases of dry eyes not resolving after discontinuation of therapy have been reported. Dry eyes can be helped by the application of a lubricating eye ointment or by the application of tear replacement therapy. Intolerance to contact lenses may occur which may necessitate the patient to wear glasses during treatment.
- Remember that your doctor has prescribed this medication because he or she has judged that the benefit to you is greater than the risk of side effects. Many people using this medication do not have serious side effects.
- Tell your doctor immediately if you have any of these unlikely but serious side effects: mental/mood changes (e.g., depression, aggressive or violent behavior and in rare cases, thoughts of suicide), tingling feeling in the skin, quick/severe sunburn (sun sensitivity), back/joint/muscle pain, signs of infection (e.g., fever, persistent sore throat), painful swallowing, peeling skin on palms/soles.
- Isotretinoin may infrequently cause disease of the pancreas (pancreatitis) that may rarely be fatal. Stop taking this medication and tell your doctor immediately if you develop: severe stomach pain, severe or persistent nausea/vomiting.
- Stop taking this medication and tell your doctor immediately if you develop these unlikely but very serious side effects: severe headache, vision changes, ringing in the ears, hearing loss, chest pain, yellowing eyes/skin, dark urine, severe diarrhea, rectal bleeding.

- A very serious allergic reaction to this drug is rare. However, seek immediate medical attention if you notice any symptoms of a serious allergic reaction, including: rash, itching, swelling, severe dizziness, trouble breathing.
- This is not a complete list of possible side effects. If you notice other effects not listed above, contact your doctor.
- The most feared complication of isotretinoin is its teratogenicity, i.e., the ability to cause birth defects.

4.9 OVERDOSE:

- In humans, overdosage has been associated with vomiting, facial flushing, cheilosis, abdominal pain, headache, dizziness and ataxia. These symptoms quickly resolve without apparent residual effects.
- Isotretinoin causes serious birth defects at any dosage. Female patients of childbearing potential who present with isotretinoin overdose must be evaluated for pregnancy. Patients who are pregnant should receive counseling about the risks to the fetus. Non-pregnant patients must be warned to avoid pregnancy for at least one month and receive contraceptive counseling as described in *Warnings and Precautions*. Further information can be obtained from your prescribing doctor.
- Patients should not donate blood for at least 30 days following overdose. Male patients should use a condom or avoid sexual activity for 30 days following overdose.

ADVERSE EFFECTS:

Summary of safety profile

- Some of the side effects associated with the use of isotretinoin are dose-related. The side effects are generally reversible after altering the dose or discontinuation of treatment, however some may persist after treatment has stopped. The following symptoms are the most commonly reported undesirable effects with isotretinoin: dryness of the skin, dryness of the mucosae e.g. of the lips (cheilitis), the nasal mucosa (epistaxis) and the eyes (conjunctivitis).

Tabulated list of adverse reactions

- The incidence of the adverse reactions calculated from pooled clinical trial data involving 824 patients and from post-marketing data are presented in the table below. The adverse reactions are listed below by MedDRA system organ class (SOC) and categories of frequency. Frequency categories are defined as Very common (≥1/10), Common (≥1/100 to <1/10), Uncommon (≥1/1,000 to <1/100), Rare (≥1/10,000 to <1/1,000), Very rare (< 1/10,000) and not known (cannot be estimated from the available data). Within each frequency grouping and SOC, adverse reactions are presented in order of decreasing seriousness.

- **Table 1 Tabulated list of adverse reactions in patients treated with isotretinoin**

System Organ Class	**Very Common**	**Common**	**Rare**	**Very Rare**	**Not known***
Infections				Gram positive (mucocutaneous) bacterial infection	

Blood and lymphatic system disorders	Thrombocytopenia, anaemia, thrombocytosis, red blood cell sedimentation rate increased	Neutropenia		Lymphadenopathy	
Immune system disorders			Anaphylactic reactions, hypersensitivity, allergic skin reaction		
Metabolism and nutrition disorders				Diabetes mellitus, hyperuricaemia	
Psychiatric disorders			Depression, depression aggravated, aggressive tendencies, anxiety, mood alterations.	Suicide, suicide attempt, suicidal ideation, psychotic disorder, abnormal behaviour	
Nervous system disorders		Headache		Benign intracranial hypertension, convulsions, drowsiness, dizziness	
Eye disorders	Blepharitis, conjunctivitis, dry eye, eye irritation			Papilloedema (as sign of benign intracranial hypertension), cataract, colour blindness (colour vision deficiencies), contact lens intolerance, corneal opacity, decreased	

				night vision, keratitis, photophobia, visual disturbances, blurred vision.	
Ear and labyrinth disorders				Hearing impaired	
Vascular disorders				Vasculitis (for example Wegener's granulomatosis, allergic vasculitis)	
Respiratory, thoracic and mediastinal disorders		Nasopharyngitis, epistaxis, nasal dryness		Bronchospasm (particularly in patients with asthma), hoarseness	
Gastrointestinal disorders				Inflammatory bowel disease, colitis, ileitis, pancreatitis, gastrointestinal haemorrhage, haemorrhagic diarrhoea, nausea dry throat	
Hepatobiliary disorders	Transaminase increased			Hepatitis	
Skin and subcutaneous tissues disorders	Pruritus, rash erythematous, dermatitis, cheilitis, dry skin, localised exfoliation, skin fragility (risk of frictional trauma)		Alopecia	Acne fulminans, acne aggravated (acne flare), erythema (facial), exanthema, hair disorders, hirsutism, nail dystrophy, paronychia, photosensitivity reaction, pyogenic granuloma, skin hyperpigmentation, sweating increased	Erythema multiforme, Stevens-Johnson Syndrome, toxic epidermal necrolysis
Musculo-skeletal and connective tissue disorders	Arthralgia, myalgia, back pain (particularly in children and adolescent patients)			Arthritis, calcinosis (calcification of ligaments and tendons), epiphyses premature fusion, exostosis, (hyperostosis),	Rhabdomyolysis Sacroiliitis a type of inflammatory back pain causing pain in your buttocks or lower back has been reported in patients

				reduced bone density, tendonitis	exposed to isotretinoin. To differentiate sacroiliitis from other causes of back pain, in patients with clinical signs of sacroiliitis, further evaluation may be needed including imaging modalities such as MRI. In cases reported post-marketing, sacroiliitis improved after discontinuation of <product name> and appropriate treatment.
Renal and urinary disorders				Glomerulonephritis	Urethritis-Inflammation of the urethra
Reproductive system and breast disorders					Sexual dysfunction including erectile dysfunction and decreased libido, gynaecomastia, Vulvovaginal dryness
General disorders and administration site conditions				Granulation tissue (increased formation of), malaise	
Investigations	Blood triglycerides increased, high density lipoprotein decreased	Blood cholesterol increased, blood glucose increased, haematuria, proteinuria		Blood creatine phosphokinase increased	

- cannot be estimated from the available data
- Reporting of suspected adverse reactions
- Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

5. PHARMACOLOGICAL PROPERTIES

5.1 MECHANISM OF ACTION

- Isotretinoin is a stereoisomer of all-trans retinoic acid (tretinoin). The exact mechanism of action of isotretinoin has not yet been elucidated in detail, but it has been established that the improvement observed in the clinical picture of severe acne is associated with suppression of sebaceous gland activity and a histologically demonstrated reduction in the size of the sebaceous glands. Furthermore, a dermal anti-inflammatory effect of isotretinoin has been established.

5.2 PHARMACODYNAMICPROPERTIES

- Hypercornification of the epithelial lining of the pilosebaceous unit leads to shedding of corneocytes into the duct and blockage by keratin and excess sebum. This is followed by formation of a comedone and, eventually, inflammatory lesions. Isotretinoin inhibits proliferation of sebocytes and appears to act in acne by re-setting the orderly program of differentiation. Sebum is a major substrate for the growth of Propionibacterium acnes so that reduced sebum production inhibits bacterial colonisation of the duct.

5.3 PHARMACOKINETIC PROPERTIES

- **Absorption**
  - The absorption of isotretinoin from the gastro-intestinal tract is variable and dose-linear over the therapeutic range. The absolute bioavailability of isotretinoin has not been determined, since the compound is not available as an intravenous preparation for human use, but extrapolation from dog studies would suggest a fairly low and variable systemic bioavailability. When isotretinoin is taken with food, the bioavailability is doubled relative to fasting conditions.

- **Distribution**
  - Isotretinoin is extensively bound to plasma proteins, mainly albumin (99.9 %). The volume of distribution of isotretinoin in man has not been determined since isotretinoin is not available as an intravenous preparation for human use. In humans little information is available on the distribution of isotretinoin into tissue. Concentrations of isotretinoin in the epidermis are only half of those in serum. Plasma concentrations of isotretinoin are about 1.7 times those of whole blood due to poor penetration of isotretinoin into red blood cells.

- **Biotransformation**
  - After oral administration of isotretinoin, three major metabolites have been identified in plasma: 4-oxo-isotretinoin, tretinoin, (all-trans retinoic acid), and 4-oxo-tretinoin. These metabolites have shown biological activity in several in vitro tests. 4-oxo-isotretinoin has been shown in a clinical study to be a significant contributor to the activity of isotretinoin (reduction in sebum excretion rate despite no effect on plasma levels of isotretinoin and tretinoin). Other minor metabolites include glucuronide conjugates. The major metabolite is 4-oxo-isotretinoin with plasma concentrations at steady state, that are 2.5 times higher than those of the parent compound.

- Isotretinoin and tretinoin (all-trans retinoic acid) are reversibly metabolised (interconverted), and the metabolism of tretinoin is therefore linked with that of isotretinoin. It has been estimated that 20-30 % of an isotretinoin dose is metabolised by isomerisation.

- Enterohepatic circulation may play a significant role in the pharmacokinetics of isotretinoin in man. In vitro metabolism studies have demonstrated that several CYP enzymes are involved in the metabolism of isotretinoin to 4-oxo-isotretinoin and tretinoin. No single isoform appears to have a predominant role. Isotretinoin and its metabolites do not significantly affect CYP activity.

- **Elimination**
- After oral administration of radiolabelled isotretinoin approximately equal fractions of the dose were recovered in urine and faeces. Following oral administration of isotretinoin, the terminal elimination half-life of unchanged drug in patients with acne has a mean value of 19 hours. The terminal elimination half-life of 4-oxo-isotretinoin is longer, with a mean value of 29 hours.

- Isotretinoin is a physiological retinoid and endogenous retinoid concentrations are reached within approximately two weeks following the end of isotretinoin therapy.

- **Hepatic impairment**
- Since isotretinoin is contraindicated in patients with hepatic impairment, limited information on the kinetics of isotretinoin is available in this patient population.

- **Renal impairment**
- Renal failure does not significantly reduce the plasma clearance of isotretinoin or 4-oxo-isotretinoin.

6. NONCLINICAL PROPERTIES
6.1 ANIMAL TOXICOLOGY OR PHARMACOLOGY

- **Acute toxicity**
- The acute oral toxicity of isotretinoin was determined in various animal species. LD50 is approximately 2000 mg/kg in rabbits, approximately 3000 mg/kg in mice, and over 4000 mg/kg in rats.

- **Chronic toxicity**
- A long-term study in rats over 2 years (isotretinoin dosage 2, 8 and 32 mg/kg/d) produced evidence of partial hair loss and elevated plasma triglycerides in the higher dose groups. The side effect spectrum of isotretinoin in the rodent thus closely resembles that of vitamin A, but does not include the massive tissue and organ calcifications observed with vitamin A in the rat. The liver cell changes observed with vitamin A did not occur with isotretinoin.

- All observed side effects of hypervitaminosis A syndrome were spontaneously reversible after withdrawal of isotretinoin. Even experimental animals in a poor general state had largely recovered within 1–2 weeks.

- **Teratogenicity**
  - Like other vitamin A derivatives, isotretinoin has been shown in animal experiments to be teratogenic and embryotoxic.

- **Mutagenicity**
  - Isotretinoin has not been shown to be mutagenic in in vitro or in vivo animal tests.

7. DESCRIPTION

Tufacne 10:

TUFACNE 10 is supplied for oral administration, as a soft gelatin capsule of Isotretinoin. Each soft gelatin capsule of TUFACNE 10 contains Isotretinoin 10 mg.

Tufacne 20:

TUFACNE 20 is supplied for oral administration, as a soft gelatin capsule of Isotretinoin. Each soft gelatin capsule of TUFACNE 20 contains Isotretinoin 20 mg.

8. PHARMACEUTICAL PARTICULARS

8.1 INCOMPATIBILITIES

Not Applicable

8.2 SHELF-LIFE

Refer pack

8.3 PACKAGING INFORMATION

Refer pack

8.4 STORAGE CONDITION AND HANDING INSTRUCTIONS

Refer pack

9. PATIENT COUNSELLING INFORMATION

- Patients should be informed that the most common reasons that contraception fails, and the importance of using 2 forms of effective contraception when taking teratogenic drugs and comprehensive information about types of potential birth defects which could occur if a female patient who is pregnant takes Tufacne at any time during pregnancy.
- Male patients and Female patients not of childbearing potential must understand the risks and benefits of Tufacne. Female patients of childbearing potential must be instructed that they must not be pregnant when Tufacne therapy is initiated or plan to become pregnant while receiving Tufacne therapy. Additionally, they must use 2 forms of effective contraception simultaneously for 1 month before starting Tufacne, while taking Tufacne, and for 1 month after Tufacne has been stopped, unless they commit to continuous abstinence from heterosexual intercourse. They should also sign a Patient Information/Informed Consent form and Patient Information/Informed Consent About Birth Defects (for female patients who can get pregnant) form prior to beginning Tufacne therapy.
- Female patients should be seen by their prescribers monthly and have a urine or serum pregnancy test, in a certified laboratory, performed each month during treatment to confirm

negative pregnancy status before another Tufacne prescription is written. Additionally, a pregnancy test must be completed at the end of the entire course of Tufacne therapy and 1 month after discontinuation of therapy.

- Advise the patient that isotretinoin is found in the semen of male patients taking isotretinoin, but the amount delivered to a female partner would be about one million times lower than an oral dose of 40 mg. While the no-effect limit for isotretinoin induced embryopathy is unknown, 20 years of post-marketing reports include four with isolated defects compatible with features of retinoid exposed fetuses; however two of these reports were incomplete and two had other possible explanations for the defects observed.

- Prescriber should be alert to the warning signs of psychiatric disorders to guide patients to receive the help they need. Therefore, prior to initiation of Tufacne treatment, patients and family members should be asked about any history of psychiatric disorder, and at each visit during treatment patients should be assessed for symptoms of depression, mood disturbance, psychosis, or aggression to determine if further evaluation may be necessary. Inform patients that symptoms of depression include sad mood, hopelessness, feelings of guilt, worthlessness or helplessness, loss of pleasure or interest in activities, fatigue, difficulty concentrating, change in sleep pattern, change in weight or appetite, suicidal thoughts or attempts, restlessness, irritability, acting on dangerous impulses, and persistent physical symptoms unresponsive to treatment. Patients should stop treatment and the patient or a family member should promptly contact their prescriber if the patient develops depression, mood disturbance, psychosis, or aggression, without waiting until the next visit. Discontinuation of Tufacne treatment may be insufficient; further evaluation may be necessary. While such monitoring may be helpful, it may not detect all patients at risk. Patients may report mental health problems or family history of psychiatric disorders. These reports should be discussed with the patient and/or the patient's family. A referral to a mental health professional may be necessary. The physician should consider whether Tufacne therapy is appropriate in this setting; for some patients the risks may outweigh the benefits of Tufacne therapy.

- Patients must be informed that some patients, while taking isotretinoin or soon after stopping isotretinoin, have become depressed or developed other serious mental problems. Symptoms of depression include sad, "anxious" or empty mood, irritability, acting on dangerous impulses, anger, loss of pleasure or interest in social or sports activities, sleeping too much or too little, changes in weight or appetite, school or work performance going down, or trouble concentrating. Some patients taking isotretinoin have had thoughts about hurting themselves or putting an end to their own lives (suicidal thoughts), some have tried to end their own lives, and some have ended their own lives. There were reports that some of these people did not appear depressed. There have been reports of patients on isotretinoin becoming aggressive or violent. There have also been reports of psychotic symptoms, which indicate a loss of contact with reality. Psychotic symptoms include feelings of suspiciousness toward others, strange beliefs, hearing voices or other noises without an obvious source, and seeing unusual objects or people with no explanation. No one knows if isotretinoin caused these behaviors and symptoms or if they would have happened even if the person did not take isotretinoin. If any of these behaviors or symptoms occur, the patient should stop treatment and the patient or family member should contact the prescriber promptly without waiting until the next visit. Some people have had other signs of depression while taking isotretinoin.

- Patients must be informed that they must not share Tufacne with anyone else because of the risk of birth defects and other serious adverse reactions.
- Patients must be informed not to donate blood during therapy and for 1 month following discontinuation of the drug because the blood might be given to a pregnant female patient whose fetus must not be exposed to Tufacne. Tufacne may be taken without regard to meals. To decrease the risk of esophageal irritation, patients should swallow the capsules with a full glass of liquid.
- Patients should be informed that inflammatory bowel disease (including regional ileitis) may occur without a prior history of intestinal disorders. In rare instances, symptoms have been reported to persist after treatment has stopped. Patients should be informed that if they experience abdominal pain, rectal bleeding or severe diarrhea, they should discontinue Tufacne immediately.
- Patients should be informed that transient exacerbation (flare) of acne has been seen, generally during the initial period of therapy.
- Wax epilation and skin resurfacing procedures (such as dermabrasion, laser) should be avoided during Tufacne therapy and for at least 6 months thereafter due to the possibility of scarring.
- Patients should be advised to avoid prolonged exposure to UV rays or sunlight.
- Patients should be informed that they may experience dry eye, corneal opacities, and decreased night vision. Contact lens wearers may experience decreased tolerance to contact lenses during and after therapy.
- Patients should be informed that 16% of patients treated with isotretinoin in a clinical trial developed musculoskeletal symptoms (including arthralgia) during treatment. In general, these symptoms were mild to moderate, but occasionally required discontinuation of the drug. Transient pain in the chest has been reported less frequently. In the clinical trial, these symptoms generally cleared rapidly after discontinuation of therapy, but in some cases persisted.
- There have been rare postmarketing reports of rhabdomyolysis, some associated with strenuous physical activity.
- Pediatric patients and their caregivers should be informed that approximately 17% to 29% of pediatric patients treated with isotretinoin developed back pain. In a clinical trial, back pain was severe in 13.5% of the cases and occurred at a higher frequency in female patients than male patients. Arthralgias were experienced in 22% (79/358) of pediatric patients. Arthralgias were severe in 7.6% (6/79) of patients. Appropriate evaluation of the musculoskeletal system should be done in patients who present with these symptoms during or after a course of treatment. Consideration should be given to discontinuation of isotretinoin if any significant abnormality is found.
- Neutropenia and rare cases of agranulocytosis have been reported in patients treated with isotretinoin. Tufacne should be discontinued if clinically significant decreases in white cell counts occur.

- Patients should be advised that severe skin reactions (Stevens-Johnson syndrome and toxic epidermal necrolysis) have been reported in post marketing data in patients treated with isotretinoin. Treatment with Tufacne should be discontinued if clinically significant skin reactions occur.
- Adolescent patients who participate in sports with repetitive impact should be informed that isotretinoin use may increase their risk of spondylolisthesis or hip growth plate injuries. There are spontaneous reports of fractures and/or delayed healing in patients while on therapy with isotretinoin or following cessation of therapy with isotretinoin while involved in these activities.

10. DETAILS OF MANUFACTURER
Refer Pack for manufacturer details.

Marketed by:
Abbott Healthcare Pvt. Ltd.
Angel Space, Bldg. D-4, Gala No. 1 to 6 &
11 to 16 Ground Floor, 101 to 106 &
111 to 116 First Floor, 201 to 206 & 211 to 216
2nd Floor, Pimplas, Dist. Thane, Bhiwandi - 421 302, India.

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11. DETAILS OF PERMISSION OR LICENCE NUMBER
Refer Pack for Permission/License details.

12. DATE OF REVISION
Version 4.0, dated 07/09/2023

For Product Complaints/Adverse events or Queries please write to **webmasterindia@abbott.com**