AKNO-10

Isotretinoin USP 10mg Soft Capsule

WARNING FOR FEMALE PATIENTS

Isotretinoin (Akno-10) will damage an unborn baby. You must not take Akno-10 if you are pregnant, or think you may be pregnant. You must use an effective birth control for one month before treatment, during treatment and for one month after treatment ends.

Composition : Each Soft Gelatin Capsule Contains Isotretinoin USP 10mg.

Indication : It is indicated in severe forms of acne (such as nodular or conglobate acne or acne at risk of permanent scarring) resistant to adequate courses of standard therapy with systemic anti-bacterials and topical therapy.

Dosage and Administration : The capsules should be taken with food once or twice daily. Isotretinoin should only be prescribed by or under the supervision of physicians with expertise in the use of systemic retinoids for the treatment of severe acne and a full understanding of the risks of Isotretinoin therapy and monitoring requirements. *Adults including adolescents and the elderly :* Isotretinoin therapy should be started at a dose of 0.5 mg/kg daily. The therapeutic response to Isotretinoin and some of the adverse effects are dose-related and vary between patients. This necessitates individual dosage adjustment during therapy. For most patients, the dose ranges from 0.5-1.0 mg/kg per day. Long-term remission and relapse rates are more closely related to the total dose administered than to either duration of treatment or daily dose. It has been shown that no substantial additional benefit is to be expected beyond a cumulative treatment dose of 120-150 mg/kg. The duration of treatment will depend on the individual daily dose. A treatment course of 16-24 weeks is normally sufficient to achieve remission. In the majority of patients, complete clearing of the acne is obtained with a single treatment course. In the event of a definite relapse a further course of Isotretinoin therapy may be considered using the same daily dose and cumulative treatment dose. As further improvement of the acne can be observed up to 8 weeks after discontinuation of treatment, a further course of treatment should not be considered until at least this period has elapsed.

Patients with severe renal impairment : In patients with severe renal insufficiency treatment should be started at a lower dose (e.g. 10 mg/day). The dose should then be increased up to 1 mg/kg/day or until the patient is receiving the maximum tolerated dose.

Patients with intolerance: In patients who show severe intolerance to the recommended dose, treatment may be continued at a lower dose with the consequences of a longer therapy duration and a higher risk of relapse. In order to achieve the maximum possible efficacy in these patients the dose should normally be continued at the highest tolerated dose. Or, as directed by the registered physician.

Contraindication : Isotretinoin is contraindicated in women who are pregnant or breastfeeding . Isotretinoin is contraindicated in women of childbearing potential unless all of the conditions of the Pregnancy Prevention Programme are met.Isotretinoin is also contraindicated in patients with hypersensitivity to Isotretinoin or to any of the excipients. Isotretinoin is also contraindicated in patients with hepatic insufficiency, with excessively elevated blood lipid values, with hypervitaminosis A, receiving concomitant treatment with tetracyclines.

Precaution : *Special warnings and precautions for use in pregnancy :* Pregnancy Prevention Programme: This medicinal product is TERATOGENIC. Isotretinoin is contraindicated in women of childbearing potential unless all of the following conditions of the Pregnancy Prevention Programme are met : She has severe acne (such as nodular or conglobate acne or acne at risk of permanent scarring) resistant to adequate courses of standard therapy with systemic antibacterials and topical therapy. She understands the teratogenic risk. She understands the need for rigorous follow-up on a monthly basis . She understands and accepts the need for effective contraception, without interruption, 1 month before starting treatment, throughout the entire duration of treatment and for 1 month after the end of treatment. At least one highly effective method of contraception (i.e. a user-independent form) or two complementary user-dependent forms of contraception should be used. Even if she has amenorrhea she must follow all of the advice on effective contraception. She is informed and understands the potential consequences of pregnancy and the need to rapidly consult if there is a risk of pregnancy. She understands the need and accepts to undergo regular pregnancy testing before, ideally monthly during treatment and 1 month after stopping treatment. She has acknowledged that she has understood the hazards and necessary precautions associated with the use of isotretinoin. These conditions also concern women who are not currently sexually active unless the prescriber considers that there are compelling reasons to indicate that there is no risk of pregnancy . The prescriber must ensure that : The patient complies with the conditions for pregnancy prevention as listed above, including confirmation that she has an adequate level of understanding. The patient has acknowledged the above mentioned conditions.The patient understands that she must consistently and correctly use one highly effective method of contraception (i.e. a user-independent form) or two complementary user-dependent forms of contraception, for at least 1 month prior to starting treatment and is continuing to use effective contraception throughout the treatment period and for at least 1 month after cessation of treatment. Negative pregnancy test results have been obtained before, during and 1 month after the end of treatment. The dates and results of pregnancy tests should be documented. *Contraception :* Female patients must be provided with comprehensive information on pregnancy prevention and should be referred for contraceptive advice if they are not using effective contraception. As a minimum requirement, female patients of childbearing potential must use at least one highly effective method of contraception. Contraception should be used for at least 1 month prior to starting treatment, throughout treatment and continue for at least 1 month after stopping treatment with isotretinoin, even in patients with amenorrhea.*Pregnancy testing :* According to local practice, medically supervised pregnancy tests with a minimum sensitivity of 25 mIU/mL are recommended to be performed, as follows . *Prior to starting therapy :* At least one month after the patient has started using contraception, and shortly (preferably a few days) prior to the first prescription, the patient should undergo a medically supervised pregnancy test. This test should ensure the patient is not pregnant when she starts treatment with Isotretinoin.*Follow-up visits :* Follow-up visits should be arranged at regular intervals, ideally monthly. The need for repeated medically supervised pregnancy tests every month should be determined according to local practice including consideration of the patient's sexual activity, recent menstrual history (abnormal menses, missed periods or amenorrhea). Where indicated, follow-up pregnancy tests should be performed on the day of the prescribing visit or in the 3 days prior to the visit to the prescriber . *End of treatment :* One month after stopping treatment, women should undergo a final pregnancy test. *Prescribing and dispensing restrictions :* For women of childbearing potential should be limited to 30 days in order to support regular follow up, including pregnancy testing and monitoring. Ideally, pregnancy testing, issuing a prescription and dispensing of Isotretinoin should occur on the same day. Dispensing of isotretinoin should occur within a maximum of 7 days of the prescription. *Male patients :* The available data suggest that the level of maternal exposure from the semen of the patients receiving Isotretinoin, is not of a sufficient magnitude to be associated with the teratogenic effects of Isotretinoin . Male patients should be reminded that they must not share their medication with anyone, particularly not females. *Additional precautions:*Patients should be instructed never to give this medicinal product to another person, and to return any unused capsules to their pharmacist at the end of treatment.Patients should not donate blood during therapy and for 1 month following discontinuation of isotretinoin because of the potential risk to the foetus of a pregnant transfusion recipient . *Psychiatric disorders:* Depression, depression aggravated, anxiety, aggressive tendencies, mood alterations, psychotic symptoms, and very rarely, suicidal ideation, suicide attempts and suicide have been reported in patients treated with isotretinoin . Particular care needs to be taken in patients with a history of depression and all patients should be monitored for signs of depression and referred for appropriate treatment if necessary . However, discontinuation of isotretinoin may be insufficient to alleviate symptoms and therefore further psychiatric or psychological evaluation may be necessary . *Skin and subcutaneous tissues disorders:* Acute exacerbation of acne is occasionally seen during the initial period but this subsides with continued treatment, usually within 7-10 days, and usually does not require dose adjustment . Exposure to intense sunlight or to UV rays should be avoided . Where necessary a sun- protection product with a high protection factor of at least SPF 15 should be used . Aggressive chemical dermabrasion and cutaneous laser treatment should be avoided in patients on isotretinoin for a period of 5-6 months after the end of the treatment because of the risk of hypertrophic scarring in atypical areas and more rarely post inflammatory hyper or hypopigmentation in treated areas . Wax depilation should be avoided

in patients on isotretinoin for at least a period of 6 months after treatment because of the risk of epidermal stripping . Concurrent administration of isotretinoin with topical keratolytic or exfoliative anti-acne agents should be avoided as local irritation may increase . Patients should be advised to use a skin moisturising ointment or cream and a lip balm from the start of treatment as isotretinoin is likely to cause dryness of the skin and lips . There have been post-marketing reports of severe skin reactions (e.g. erythema multiforme (EM), Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) associated with isotretinoin use . As these events may be difficult to distinguish from other skin reactions that may occur, patients should be advised of the signs and symptoms and monitored closely for severe skin reactions . If a severe skin reaction is suspected, isotretinoin treatment should be discontinued . *Allergic reactions:*Anaphylactic reactions have been rarely reported, in some cases after previous topical exposure to retinoids . Allergic cutaneous reactions are reported infrequently . Serious cases of allergic vasculitis, often with purpura (bruises and red patches) of the extremities and extra cutaneous involvement have been reported. Severe allergic reactions necessitate interruption of therapy and careful monitoring . *Eye disorders:* Dry eyes, corneal opacities, decreased night vision and keratitis usually resolve after discontinuation of therapy . 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 . Decreased night vision has also been reported and the onset in some patients was sudden . Withdrawal of isotretinoin may be necessary. *Musculo-skeletal and connective tissue disorders :* Myalgia, arthralgia and increased serum creatine phosphokinase values have been reported in patients receiving isotretinoin, particularly in those undertaking vigorous physical activity . Bone changes including premature epiphyseal closure, hyperostosis, and calcification of tendons and ligaments have occurred after several years of administration at very high doses for treating disorders of keratinisation. The dose levels, duration of treatment and total cumulative dose in these patients generally far exceeded those recommended for the treatment of acne . *Benign intracranial hypertension :* Cases of benign intracranial hypertension have been reported, some of which involved concomitant use of tetracyclines . Signs and symptoms of benign intracranial hypertension include headache, nausea and vomiting, visual disturbances and papilloedema . Patients who develop benign intracranial hypertension should discontinue isotretinoin immediately. *Hepatobiliary disorders :* Liver enzymes should be checked before treatment, 1 month after the start of treatment, and subsequently at 3 monthly intervals unless more frequent monitoring is clinically indicated . Transient and reversible increases in liver transaminases have been reported . In many cases these changes have been within the normal range and values have returned to baseline levels during treatment. However, in the event of persistent clinically relevant elevation of transaminase levels, reduction of the dose or discontinuation of treatment should be considered. *Renal insufficiency :* Renal insufficiency and renal failure do not affect the pharmacokinetics of isotretinoin . Therefore, isotretinoin can be given to patients with renal insufficiency . However, it is recommended that patients are started on a low dose and titrated up to the maximum tolerated dose. *Lipid Metabolism :* Serum lipids (fasting values) should be checked before treatment, 1 month after the start of treatment, and subsequently at 3 monthly intervals unless more frequent monitoring is clinically indicated. Elevated serum lipid values usually return to normal on reduction of the dose or discontinuation of treatment and may also respond to dietary measures.Isotretinoin has been associated with an increase in plasma triglyceride levels . Isotretinoin should be discontinued if hypertriglyceridaemia cannot be controlled at an acceptable level or if symptoms of pancreatitis occur. Levels in excess of 800 mg/dL or 9 mmol/L are sometimes associated with acute pancreatitis, which may be fatal . *Gastrointestinal disorders:* Isotretinoin has been associated with inflammatory bowel disease (including regional ileitis) in patients without a prior history of intestinal disorders. Patients experiencing severe (haemorrhagic) diarrhoea should discontinue isotretinoin immediately.*High Risk Patients :* In patients with diabetes, obesity, alcoholism or a lipid metabolism disorder undergoing treatment with isotretinoin, more frequent checks of serum values for lipids and/or blood glucose may be necessary. Elevated fasting blood sugars have been reported, and new cases of diabetes have been diagnosed during isotretinoin therapy.

Side effects : 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). The incidence of the adverse reactions calculated from pooled clinical trial data involving 824 patients and from post-marketing data. 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).

Infections : Very Rare: Gram positive (mucocutaneous) bacterial infection.*Blood and lymphatic system disorders:*Very Common: Thrombocytopenia, anaemia, thrombocytosis, red blood cell sedimentation rate increased; *Common:* Neutropenia; Very Rare: Lymphadenopathy. *Immune system disorders : Rare :* Anaphylactic reactions, hypersensitivity, allergic skin reaction.

Metabolism and nutrition disorders: Very Rare:Diabetes mellitus,hyperuricaemia. *Psychiatric disorders*: Rare: Depression, depression aggravated, aggressive tendencies, anxiety, mood alterations. *Very Rare:* Suicide, suicide attempt, suicidal ideation, psychotic disorder, abnormal behavior. *Nervous system disorders :* Common: Headache; Very Rare: Benign intracranial hypertension, convulsions, drowsiness, dizziness.*Eye disorders:* Very Common : Blepharitis, conjunctivitis, dry eye, eye irritation; Very Rare : 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:* Very Rare:Hearing impaired.*Vascular disorders :* Very Rare : Vasculitis (for example Wegener's granulomatosis, allergic vasculitis). *Respiratory, thoracic and mediastinal disorders :* Common : Nasopharyngitis, epistaxis, nasal dryness ; Very Rare : Bronchospasm (particularly in patients with asthma), hoarseness. *Gastrointestinal disorders :* Very Rare : Inflammatory bowel disease, colitis, ileitis, pancreatitis, gastrointestinal haemorrhage, haemorrhagic diarrhoea, nausea, dry throat. *Hepatobiliary disorders :* Very Common: Transaminase increased ; Very Rare : Hepatitis. *Skin and subcutaneous tissues disorders :* Very Common: Pruritus, rash erythematous, dermatitis, cheilitis, dry skin, localised exfoliation, skin fragility (risk of frictional trauma); Rare: Alopecia; Very Common: Acne fulminans, acne aggravated (acne flare), erythema (facial), exanthema, hair disorders, hirsutism, nail dystrophy, paronychia, photosensitivity reaction, pyogenic granuloma, skin hyperpigmentation, sweating increased.*Musculo-skeletal and connective tissue disorders :* Very Common: Arthralgia, myalgia, back pain (particularly in children and adolescent patients); Very Rare: Arthritis, calcinosis (calcification of ligaments and tendons), epiphyses premature fusion, exostosis, (hyperostosis), reduced bone density, tendonitis.*Renal and urinary disorders:* Very Rare: Glomerulonephritis. *General disorders and administration site conditions*: Very Rare: Granulation tissue (increased formation of), malaise.

Use in pregnancy and lactation : Pregnancy is an absolute contraindication to treatment with isotretinoin · If pregnancy does occur in spite of these precautions during treatment with Isotretinoin or in the month following, there is a great risk of very severe and serious malformation of the foetus.If pregnancy occurs in a woman treated with isotretinoin, treatment must be stopped and the patient should be referred to a physician specialised or experienced in teratology for evaluation and advice · 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 mother's milk, Isotretinoin is contraindicated during breast-feeding.

Use in Child : 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.

Overdose : Isotretinoin is a derivative of vitamin A. Although the acute toxicity of isotretinoin is low, signs of hypervitaminosis A could appear in cases of accidental overdose. Manifestations of acute vitamin A toxicity include severe headache, nausea or vomiting, drowsiness, irritability and pruritus. Signs and symptoms of accidental or deliberate overdosage with isotretinoin would probably be similar. These symptoms would be expected to be reversible and to subside without the need for treatment.

Storage : Store below 30°C in a dry place.

Packing : Each box contains 15's soft capsules in blister pack.

Manufactured by
DRUG INTERNATIONAL LTD.
Tongi, Gazipur, Bangladesh

12/2022/Nil