1. Name of the medicinal product

Khairafen Suspension (Ibuprofen Oral Suspension BP)

2. Qualitative and quantitative composition

Each 5 ml contains

Ibuprofen BP 100 mg

3. PHARMACEUTICAL FORM

Oral Liquid

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Prescription and OTC:

Khairafen Suspension is used as an analgesic for relief of mild to moderate muscular pain, post-immunisation pyrexia, symptomatic relief of headache, earache, dental pain and backache. It can also be used in minor injuries such as sprains and strains. Khairafen Suspension is effective in the relief of feverishness and symptoms of colds and influenza.

Prescription Only:

Khairafen Suspension is indicated for its analgesic and anti-inflammatory effects in the treatment of dysmenorrhoea, neuralgia, post–operative pain, rheumatoid arthritis (including juvenile rheumatoid arthritis or Still's disease), ankylosing spondylitis, osteoarthritis and other non-rheumatoid (seronegative) arthropathies.

In the treatment of non-articular rheumatic conditions, Khairafen Suspension is indicated for periarticular conditions such as frozen shoulder (capsulitis), bursitis, tendonitis, tenosynovitis and low back pain. Khairafen Suspension can also be used in soft tissue injuries such as sprains and strains.

4.2 Posology and method of administration

For oral administration and short-term use only.

Adults, the elderly and children over 12 years:

The lowest effective dose should be used for the shortest duration necessary to relieve symptoms. The patient should consult a doctor if symptoms persist or worsen, or if the product is required for more than 10 days.

Adults, the elderly and children over 12 years:

The recommended dose is 200mg-400mg (10-20ml), up to three times a day as required.

Leave at least four hours between doses and do not take more than 1200mg (60ml) in any 24 hour period.

Children: For pain and fever - 20mg/kg/day in divided doses (including OTC use).

Infants 3-6 months weighing more than 5 kg:	One 2.5 ml dose may be taken 3 times in 24 hours. Do not use for more than 24 hours
Infants 6 months-1 year:	2.5ml three to four times a day.
Children 1-4 years:	5ml three times a day
Children 4-7 years:	7.5ml three times a day
Children 7-12 years:	10ml three times a day.

Post-immunisation fever: 2.5ml (50mg) followed by one further dose of 2.5ml (50mg) six hours later if necessary. No more than 2 doses in 24 hours. If fever is not reduced, consult a doctor.

For Juvenile Rheumatoid Arthritis (prescription only use): Doses up to 30-40mg/kg/day may be taken in three or four divided doses.

Elderly: No special dosage modifications are required unless renal or hepatic function is impaired, in which case dosage should be assessed individually.

Do not give to children under 3 months of age.

If the child's (aged over 6 months) symptoms persist for more than 3 days, consult your doctor promptly.

For children under 6 months medical advice should be sought promptly after 24 hours use (3 doses) if the symptoms persist.

4.3 Contraindications

Hypersensitivity to Ibuprofen or any of the constituents in the product.

Patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema or urticaria) in response to aspirin or other non-steroidal anti-inflammatory drugs.

Active or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding)

History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.

Severe hepatic failure, renal failure or heart failure.

Last trimester of pregnancy.

Patients with rare hereditary problems of fructose intolerance should not take this medicine.

4.4 Special warnings and precautions for use

The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal.

Systemic lupus erythematosus and mixed connective tissue disease – increased risk of aseptic meningitis.

Renal impairment as renal function may further deteriorate

Hepatic dysfunction

Chronic inflammatory intestinal disease (ulcerative colitis, Crohn's disease) – as these conditions may be exacerbated.

The use of Khairafen Suspension with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided.

Undesirable effects may be minimised by using the minimum effective dose for the shortest possible duration.

There is limited evidence that drugs which inhibit cyclo-oxygenase/prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible upon withdrawal of treatment.

GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at anytime during treatment, with or without warning symptoms or a previous history of serious GI events.

Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.

Caution should be advised in patients receiving concomitant medications which could increase the risk of gastrotoxicity or bleeding, such as corticosteroids, or anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as aspirin.

When GI bleeding or ulceration occurs in patients receiving ibuprofen, the treatment should be withdrawn.

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation, and in the elderly. These patients should commence treatment on the lowest dose available.

Administration of NSAID'S such as Ibuprofen may cause dose dependent renal toxicity in patients with reduced renal blood flow or blood volume where renal prostaglandins support the maintenance of renal perfusion. Patients at risk of this reaction include those with impaired renal function, heart failure or liver dysfunction. This is of particular importance in hypertension and/or cardiac impairment as renal function may deteriorate and/or fluid retention occur. Caution is therefore required in the use of Ibuprofen in such patients.

Ibuprofen should be used with caution in patients with bronchial asthma or allergic disease, since such patients may have NSAID – sensitive asthma which has been associated with severe bronchospasm.

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms.

Cardiovascular and cerebrovascular effects:

Caution is required prior to starting treatment in patient with history of hypertension and/or heart failure as fluid retention; hypertension and oedema have been reported in association with NSAIDs therapy.

Clinical trial and epidemiological data suggest that use of ibuprofen, particularly at high doses (2400mg daily) and in long-term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). Overall, epidemiological studies do not suggest that low dose ibuprofen is associated with an increased risk of myocardial infarction.

4.5 Interaction with other medicinal products and other forms of interaction

Dermatological:

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs. Patients appear to be at highest risk for these reactions early in the course of therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. Khairafen Suspension should be discontinued at the first appearance of skin rash, mucosal lesion, or any other sign of hypersensitivity.

The label will include:

Read the enclosed leaflet before taking this product.

Do not give this product if your baby or child

• Has or has ever had a stomach ulcer, perforation or bleeding

• Is allergic to ibuprofen or any other ingredient of the product, aspirin or other related painkillers

• Is taking other NSAIDs painkillers, or aspirin with a daily dose above 75 mg

Speak to a pharmacist or your doctor before giving this product if your baby or child

• Has or has had asthma, diabetes, high cholesterol, high blood pressure, a stroke, liver, heart, kidney or bowel problems.

If you are an adult taking this product:

Do not take it; if you are pregnant.

Consult your doctor or pharmacist before taking if; you are trying to get pregnant; are elderly; are a smoker.

Additional Warnings for OTC use

Do not give to babies aged 3-6 months for more than 24 hours.

Do not give to children aged 6 months and older for more than 3 days.

Consult your doctor promptly if symptoms persist or worsen.

Do not exceed the stated dose.

Not recommended for children under 3 months.

Ibuprofen should be avoided in combination with:

Aspirin: Unless low-dose aspirin (not above 75 mg daily) has been advised by a doctor, as this may increase the risk of adverse reactions.

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. However, the limitations of these data and the uncertainties regarding extrapolation of ex-vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use

Other NSAIDs including cyclooxygenase-2 selective inhibitors: avoid concomitant use of two or more NSAIDs as this may increase the risk of adverse effects

Ibuprofen should be used with caution in combination with:

Anticoagulants: NSAIDs may enhance the effects of anticoagulants, such as warfarin.

Antihypertensives and diuretics: NSAIDs may diminish the effect of these drugs. Diuretic can increase risk of nephrotoxicity of NSAIDs.

Corticosteroids: increased risk of gastrointestinal ulceration or bleeding.

Anti-platelets agents and selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding.

Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increased plasma glycoside levels.

Ciclosporin: Increased risk of nephrotoxicity.

Mifepristone: NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

Tacrolimus: Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.

Lithium: There is evidence for potential increase in plasma levels of lithium.

Methotrexate: There is potential of an increase in plasma methotrexate.

Zidovudine : Increased risk of haematological toxicity when NSAIDs are given with zidovudine. There is evidence of an increased risk of haemarthroses and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

Quinolone antibiotics : Animal data indicate that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAIDs and quinolone may have increased risk of developing convulsions.

4.6 Pregnancy and Breastfeeding

Whilst no teratogenic effects have been demonstrated in animal experiments the use of Khairafen Suspension, should, if possible, be avoided during the first 6 months of pregnancy.

During the 3rd trimester, ibuprofen is contraindicated as there is a risk of premature closure of the foetal ductus arteriosis with possible persistent pulmonary hypertension. The onset of labour may be delayed and the duration increased with an increased bleeding tendency in both mother and child

In limited studies, ibuprofen appears in the breast milk in very low concentration and is unlikely to affect breast-fed infants adversely.

4.7 Effects on ability to drive and use machines

None expected at recommended doses and duration of therapy.

4.8 Undesirable Effects

Hypersensitivity reactions have been reported and these may consist of:

A) Non-specific allergic reactions and anaphylaxis

B) Respiratory tract reactivity, e.g. asthma, aggravated asthma, bronchospasm, dyspnoea.

C) Various skin reactions, e.g. pruritis, urticaria, angioedema and more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).

The following list of adverse effects relates to those experienced with ibuprofen at OTC doses, for short-term use. In the treatment of chronic conditions, under long-term treatment, additional adverse effects may occur.

Hypersensitivity reactions:

Uncommon: Hypersensitivity reactions with urticaria and pruritis.

Very rare: Severe hypersensitivity reactions. Symptoms could be: facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock).

Exacerbation of asthma and bronchospasm.

Gastrointestinal : The most commonly-adverse events are gastrointestinal in nature.

Uncommon : Abdominal pain, nausea and dyspepsia.

Rare : Diarrhoea, flatulence, constipation and vomiting.

Very rare: Peptic ulcer, perforation or gastrointestinal haemorrhage, sometimes fatal, particularly in the elderly. Exacerbation of ulcerative colitis and Crohn's disease

Nervous System :

Uncommon : Headache

Renal :

Very Rare : Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema.

Hepatic :

Very Rare : Liver disorders.

Haematological :

Very Rare : Haematopoietic disorders (anaemia, leucopoenia, thrombocytopenia, panytopenia, agranulocytosis). First signs are: fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising.

Dermatological :

Uncommon: Various skin rashes

Very rare: Severe forms of skin reactions such as bullous reactions, including Stevens- Johnson Syndrome, erythema multiforme and toxic epidermal necrolysis can occur.

Immune System:

In patients with existing auto-immune disorders (such as systemic lupus erythematosus, mixed connective tissue disease) during treatment with ibuprofen, single cases of symptoms of aseptic meningitis, such as stiff neck, headache, nausea, vomiting, fever or disorientation have been observed.

Cardiovascular and Cerebrovascular:

Oedema, hypertension, and cardiac failure, have been reported in association with NSAID treatment. Clinical trial and epidemiological data suggest that use of ibuprofen (particularly at high doses 2400 mg daily) and in long-term treatment may be associated with a small increased risk of arterial thrombotic events.

Reporting of suspected adverse reactions.

4.9 Overdose

In children ingestion of more than 400 mg/kg may cause symptoms. In adults the dose response effect is less clear cut. The half-life in overdose is 1.5 – 3 hours.

Symptoms

Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, vomiting, epigastric pain, or more rarely diarrhoea. Tinnitus, headache and gastrointestinal bleeding are also possible. In more serious poisoning, toxicity is seen in the central nervous system, manifesting as drowsiness, occasionally excitation and disorientation or coma. Occasionally patients develop convulsions. In serious poisoning metabolic acidosis may occur and the prothrombin time/INR may be prolonged, probably due to interference with the actions of circulating clotting factors. Acute renal failure and liver damage may occur. Exacerbation of asthma is possible in asthmatics.

Management

Management should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable. Consider oral administration of activated charcoal if the patient presents within 1 hour of ingestion of a potentially toxic amount. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Give bronchodilators for asthma.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacological Action :

Ibuprofen is a propionic acid derivative NSAID that has demonstrated its efficacy by inhibition of prostaglandin synthesis. In humans ibuprofen reduces inflammatory pain, swelling and fever. Furthermore, ibuprofen reversibly inhibits platelet aggregation.

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. In one study, when a single dose if ibuprofen 400mg was taken within 8 hours before or within 30 minutes after immediate release aspirin dosing (81mg), a decreases effect of aspirin on the formation of thromboxane or platelet aggregation occurred. However, the limitation of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effects is considered to be likely for occasional ibuprofen use.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipient

Sorbitol Solution 70% BP,Sucrose BP ,Propylene Glycol BP,Sodium Methyl Paraben ,Sodium Propyl Paraben BP,Di-Sodium EDTA BP,Xanthan Gum BP (Plain),Arrow Gum Super /CRT,MCC,Enisweet EP Powder Polysorbate 80 BP (Tween 80),Aerosil ,Sodium Saccharin BP

Sodium Hydroxide BP,Citric Acid ,Colour Erythrosine,Colour Carmoisine,Coconut Oil,Strawberry NTL 8778 Flavour,Purified Water BP etc.

6.2 Incompatibilities

None reported

6.3 Shelf life

36 months from the date of manufacturing.

6.4 Special precautions for storage

Store in a cool and dark place. Protect from light. Keep out of reach of children.

Do not use after the expiry date shown on the pack.

Keep out of reach of children.

6.5 Nature and contents of container

Pink coloured, homogenous suspension with characteristic flavour in a 100 ml pet bottle, sealed with 25 mm Golden Aluminium P. P Caps.

6.6 Special precautions for disposal and other Special handling

Shake well before use.

7. Marketing authorization holder

KHAIRAT Pharmacy & Vet Co. Ltd.

No.54 Kirimbo Challawa Ind. Area,

Kano.

08. Marketing authorisation number(s)

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9. Date of first authorisation/renewal of the authorisation

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10. Date of revision of the text
