SUMMARY OF PRODUCTS CHARACTERISTICS

1.NAME OF THE FINISHED PHARMACEUTICAL PRODUCT :

1.1 Brand Name : Ibuplus Tablets
1.2 Generic Name : Ibuprofen and Paracetamol Tablets
1.3 Strength : Ibuprofen 400mg & Paracetamol 325mg per tablet
1.4 Pharmaceutical Form: Tablet

2. QUALITATIVE & QUANTITATIVE COMPOSITION :

Each uncoated tablet contains:

Ibuprofen	BP	400mg
Paracetamol	BP	325mg

3. PHARMACEUTICAL FORM

Tablet

White coloured elongated biconvex uncoated tablet having central breakline on face of each tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Ankylosing spondylosis, Lumbar, Cervical spondylosis, Rheumatoid arthritis, Osteo - arthritis.

Dentistry -Painful root-abscesses, after tooth extraction.

Urology -Balanitis, Cystitis, Prostatitis, Pyelonephritis.

Gynaec -Vulvovaginitis , Vaginitis.

4.2 Posology and method of administration

One tablet three times a day or as prescribed by the Physician.

4.3 Contraindications:

Blood dyscrasias, peptic and duodenal ulcers, asthma, visual disturbances and hepatic dysfunction. Paracetamol is hepatotoxic in large doses. As NSAIDs Ibuprofen blocks cyclo oxygenase enzyme, they inhibit PG-synthesis in the inflammed tissues, and also inhibits PG-synthesis elsewhere, namely prostaglandins in gastric mucosa which has a cyto-protective effect. Its simultaneous blockade gives rise to gastrointestinal side effects hence NSAIDs should be administered with food.

Prostaglandins maintain renal blood flow, inhibition reduces it and hence glomerular filtration rate in patients with CCF, hepatic cirrhosis or renal failure reduces. Prostaglandins assist platelet aggregation, inhibition causes increased bleeding. Leukotrienes also contribute to inflammation, biosynthesized from arachidonic acid by enzyme lipo-oxygenase. Blocking of PG synthesis diverts arachidonic acid to leukotrienes in some intolerant individuals, manifested as vasomotor rhinitis, asthma, shock and can worsen bronchial asthma.

4.4 Special warnings and special precautions for use:

Bronchospasm may be precipitated in patients suffering from or with a previous history of bronchial asthma. Ibuprofen should not be given to patients in whom Aspirin and other non-steroidal anti-inflammatory induce the symptoms of asthma, rhinitis or urticaria.

Caution for Paracetamol: Overdose may be injurious to liver.

4.5 Interaction with other FPPs and Other forms of Interaction

IBUPROFEN:

- **Acetylsalicylic acid:** Concomitant administration of ibuprofen and acetylsalicylic acid is not generally recommended because of the potential of increased adverse effects, unless low-dose acetylsalicylic acid (not above 75 mg daily) has been advised by a doctor. Experimental data suggest that Ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce

the cardioprotective effect of low-dose acetylsalicylic acid cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use.

- **Other NSAIDs including cyclo-oxygenase-2 selective inhibitors** as these may increase the risk of adverse effects

PARACETAMOL:

Anticoagulants: Prolonged regular use of paracetamol possibly enhances anticoagulant effect of Coumarins.

Antidiabetics: Absorption of paracetamol possibly reduced when given 1 to 4 hours after Lixisenatide.

Antiepileptics: Metabolism of paracetamol possibly accelerated by Carbamazepine, Fosphenytoin, Phenobarbital, Phenytoin and Primidone (also isolated reports of hepatotoxicity)

Antifungals: Avoidance of paracetamol advised by manufacturer of Ketoconazole.

Cytotoxics: Paracetamol possibly inhibits metabolism of intravenous Busulfan.

Lipid-regulating Drugs: Absorption of paracetamol reduced by Colestyramine.

Metoclopramide: Rate of absorption of paracetamol increased by Metoclopramide.

4.6 Pregnancy and lactation

Pregnancy: Congenital abnormalities have been reported in association with NSAID administration in man; however these are low in frequency and do not appear to follow any discernible pattern. In view of the known affects of NSAIDs on the fetal cardiovascular system (risk of closure of ductus arteriosus), use in the last trimester is contraindicated. The onset of labour may be delayed and duration increased with an increased bleeding tendency in both mother and child. NSAIDs should not be used during the first two trimesters of pregnancy or labor unless the potential benefit to the patient outweighs the potential risk to the foetus. Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol use at the recommended dosage. Therefore if possible, the use of this product should be avoided in the first six months of pregnancy and contraindicated in the last three months of pregnancy.

Breast feeding: Ibuprofen and its metabolites can pass in very small amounts (0.0008% of the maternal dose) into the breast milk. No harmful effects to infants are known. Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breastfeeding. Therefore it is not necessary to interrupt breastfeeding for short-term treatment with the recommended dose of this product.

4.7 Effects on ability to drive and use machines

Undesirable effects such as dizziness, drowsiness, fatigue and visual disturbances are possible after taking NSAIDs. If affected patients should not drive or operate machinery.

4.8 Undesirable effects

Very Rare: Haematopoietic disorders, Confusion, depression and hallucinations, Visual disturbance, Tinnitus and vertigo, Cardiac failure and oedema, Hypertension, Respiratory

reactivity including: asthma, exacerbation of asthma, bronchospasm and dyspnoea, Abnormal liver function, hepatitis and jaundice, Nephrotoxicity etc.

Uncommon: Hypersensitivity with urticaria and pruritus**,** Headache and dizziness, peptic ulcer, gastrointestinal perforation or gastrointestinal haemorrhage, melaena, haematemesis, mouth ulceration, exacerbation of colitis and Crohn's disease gastritis, pancreatitis, flatulence and constipation, skin rashes etc.

Common: Abdominal pain, vomiting, diarrhoea, nausea, dyspepsia and abdominal discomfort, Hyperhidrosis, Alanine aminotransferase increased, gamma-glutamyltransferase increased and liver function tests abnormal with paracetamol, Blood creatinine increased, blood urea increased.

4.9 Overdose

Paracetamol

Liver damage is possible in adults who have taken 10 g (equivalent to 20 tablets) or more of paracetamol. Ingestion of 5 g (equivalent to 10 tablets) or more of paracetamol may lead to liver damage if the patient has one or more of the risk factors below:

a) Is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.

b) Regularly consumes alcohol in excess of recommended amounts.

c) Is likely to be glutathione depleted e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia

Ibuprofen

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesic; Antipyretic

Mechanism of action:

IBUPLUS is a rational combination of Ibuprofen and Paracetamol in rational concentration provides full therapeutic doses of anti-inflammatory and analgesic agents. Analgesic and anti-inflammatory activities are potentiated when Acetaminophen (PARACETAMOL) is combined with NSAIDs, which are the inhibitors of prostaglandin formation. A combination of peripherally acting Ibuprofen and centrally acting Paracetamol produces anti-inflammatory, antipyretic and analgesic effect. Ibuprofen acts peripherally at tissue level and Paracetamol acts centrally at heat regulation centre in hypothalamus. IbuPlus - a combination thus ensures a better analgesic action than Ibuprofen alone.

5.2 Pharmacokinetic properties

Ibuprofen: A non-steroidal anti-inflammatory drug which is very well-tolerated acts by inhibiting cyclo-oxygenase enzyme responsible for biosynthesis of prostaglandins.

Paracetamol: It is a non-narcotic, non-opoid analgesic which produces analgesia by raising pain threshold in the brain and is particularly suitable as a day time analgesic. Encompasses complete pyrexia when given in combination with Ibuprofen.

5.3 Preclinical safety data

None Known

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

SN	Ingredients	Spec.
01.	Starch (Maize)	BP
02.	Dibasic Calcium Phosphate	BP
03.	Sodium Methyl Hydroxybenzoate (Sodium Methylparaben)	BP
04.	Sodium Propyl Hydroxybenzoate (Sodium Propylparaben)	BP
05.	Gelatin	BP
06.	Purified Talc (Talcum)	BP
07.	Magnesium Stearate	BP
08.	Sodium Starch Glycolate	BP
09.	Colloidal Anhydrous Silica (Colloidal Silicon Dioxide)	BP
10.	Purified water	BP

6.2 Incompatibilities

Not Known

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at temperature not exceeding 30^0C. Protect from light. Keep away from moisture. Keep out of reach of children.

6.5 Nature and contents of container

1 Strip of 15 Tablets in a monopack & such 10 mono packs in an outer carton.
15's x 2 x 20 Tablets in an E-flute carton.

6.6 Instructions for use and handling

Please see the package insert.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESS

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8. MARKETING AUTHORISATION NUMBER

AMD/12/2002 & AMD/6/2002

9. DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION

AMD/12/2002& AMD/6/2002:

a) Date of first authorization: 21/01/1989.

b) Date of latest renewal: 01/01/2018.

10. DATE OF REVISION OF THE TEXT

01/01/2023