1. NAME OF THE MEDICINAL PRODUCT

Alfen Capsules B.P 30/200/325mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains:

Ibuprofen B.P.....200mg
Paracetamol B.P.....325mg
Caffeine B.P.....30mg

Excipients with known effect:

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

- Capsules, hard
- Deep blue and Sky blue capsules printed with 'ALBEN".

4. Clinical Particulars

4.1 Therapeutic indications

Alfen is indicated for the treatment of:

- Non-articular rheumatic conditions
- Osteo-arthritis
- Cervical spondylosis
- Infective inflammation
- Dental & traumatic inflammation
- Pain and fever associated with inflammation

4.2 Posology and method of administration

Dosage: 1-2 capsules three times per day or as prescribed by Physician.

Route of Administration: Capsules (Oral)

Condition of Administration: Capsules are to be taken with food or after meals with sufficient water or as prescribed by the physician.

Method of administration: Oral use.

4.3 Contraindications

Alfen is contraindicated in patients with impaired kidney or liver function, cardiac arrhythmias, active peptic ulcer and gastrointestinal bleeding.
Alfen is also not suitable for the patients with known hypersensitivity to any of the ingredients of the drug.

4.4 Special warnings and precaution for use

Alfen is to be advocated with caution in liver & kidney damage, elderly, patients requiring Surgery, anemia, bronchial asthma, stomatitis, compromised cardiac function, heart failure, Pre-existing edema, and systemic lupus erythematosus. Safe use of Alfen in pregnancy and lactation has not been established. Alfen should not be preferably co-administered with other NSAIDs, corticosteroids, hypoglycemics, digoxin, lithium, methotrexate, cyclosporine, coagulants & anticoagulants, bone marrow suppressants as well as probenecid. Abrupt stoppage of Caffeine-containing products is not advisable since it could cause withdrawal symptoms such as headache, anxiety, or muscle tension within 12 to 18 hours.

4.5 Interactions with other medicinal products and other forms of interaction

- Cholestyramine: Reduces absorption of Alfen.
- Activated charcoal: if administered immediately after administration of Alfen, reduces absorption of Alfen.
- Domperidone & metoclopramide: Enhance absorption of Alfen.
- Alcohol: Chronic excessive ingestion of alcohol potentiates hepatotoxicity of Alfen.
- Zidovudine: Effects of zidovudine may be decreased.
- Lithium: Raised blood lithium levels.
- Aspirin and other NSAIDs: Increased risk of bleeding and or peptic ulcers.
- Methotrexate: Alfen increases the risk of toxicity.
- Diazepam: Alfen induces impairment of cognitive skills & relaxation of extra ocular muscles.
- Pentobarbital: Alfen activates the hypnotic effect of Pentobarbital.

4.6 Pregnancy and Lactation

Safe use of Alfen in pregnancy and lactation has not been established. Alfen should not be preferably co-administered with other NSAIDs, corticosteroids, hypoglycemics, digoxin, lithium, methotrexate, cyclosporine, coagulants & anticoagulants, bone marrow suppressants as well as probenecid.
Abrupt stoppage of Caffeine-containing products is not advisable since it could cause withdrawal symptoms such as headache, anxiety, or muscle tension within 12 to 18 hours.
Alfen is not safe in pregnancy & in nursing mothers.

4.7 Effects on ability to drive and use machines

Alfen may cause side effects which could affect your ability to drive. Alfen Tablet may cause headaches, blurred vision, dizziness or drowsiness in some patients. This may affect your ability to drive.

4.8 Undesirable effects

Long-term use may lead to gastric ulcer, anti-inflammatory drug induced allergy, asthma, hypertension, hepatic, renal dysfunction, insomnia, vertigo and abdominal pain. Large doses may cause restlessness,

excitement, muscle tremor, tachycardia, liver damage & renal failure with acute tubular necrosis.

4.9 Overdose

Ibuprofen: Symptoms include nausea, vomiting, epigastric pain, and headache. Gastric lavage or induced emesis may be used for the treatment. Treatment is supportive.

Paracetamol: Symptoms of paracetamol overdosage in the first 24 hours are pallor, nausea, vomiting, diarrhoea, anorexia, abdominal pain and increased sweating. Liver damage may become apparent 12 to 48 hours after ingestion. Gastric lavage or induced emesis may be used for the treatment. Specific therapy with an antidote such as acetylcysteine or methionine may be necessary.

Caffeine: symptoms include recurrent coffee ground emesis, diuresis, tachycardia, and CNS stimulation.

5. Pharmacological properties:

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:

Ibuprofen BP Analgesic & Anti-inflammatory, ATC code: M01AE01
Paracetamol BP: Analgesic & Antipyretic, ATC code: N02BE01
Caffeine BP: Central Nervous System Stimulant, ATC code: N06BC01

Pharmacological Category:
Ibuprofen BP: Analgesic & Anti-inflammatory
Paracetamol BP: Analgesic & Antipyretic
Caffeine BP: Central Nervous System Stimulant

Pharmacological Action:
In Alfen, Paracetamol exhibits analgesic action by peripheral blockage of pain impulse generation. It produces anti-pyresis by inhibiting the hypothalamic heat-regulating centre. Ibuprofen inhibits prostaglandin production around the body by blocking the cyclooxygenase enzymes known as COX-1 and COX-2. Caffeine acts as Central nervous system stimulant due to a blockade of receptors for the neurotransmitter / neuromodulator adenosine.

5.2 Pharmacokinetic properties

Ibuprofen:
Ibuprofen is well absorbed from the gastrointestinal tract and is extensively bound to plasma Proteins. Ibuprofen diffuses into the synovial fluid. Plasma levels of ibuprofen from this product are detected from 5 minutes with peak plasma concentrations achieved within 1 2 hours after ingestion on an empty stomach. When this product was taken with food peak ibuprofen plasma levels were lower and delayed by a median of 25 minutes, but overall extent of absorption was equivalent. Ibuprofen is metabolised in the liver to two major metabolites with primary excretion via the Kidneys, either as such or as major conjugates, together with a negligible amount of unchanged ibuprofen. Excretion by the kidney is both rapid and complete. The elimination halflife is approximately 2 hours. In limited studies, ibuprofen appears in the breast milk in very low concentrations. No significant differences in ibuprofen pharmacokinetic profile are observed in the elderly. The bioavailability and pharmacokinetic profiles of ibuprofen and paracetamol taken as this Product is not altered when taken in combination as a single or repeat dose.
Paracetamol:
Paracetamol is readily absorbed from the gastrointestinal tract. Plasma protein binding is Negligible at usual therapeutic concentrations, although this is dose dependent. Plasma levels of paracetamol from this product are detected from 5 minutes with peak plasma concentrations occurring at 0.5-0.67 hours after ingestion on an empty stomach. When this product was taken with food peak paracetamol plasma levels were lower and delayed by a median of 55 minutes, but overall extent of absorption was equivalent. Paracetamol is

metabolised in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates, with about 10% as glutathione conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half-life is approximately 3 hours. A minor hydroxylated metabolite, which is usually produced in very small amounts by mixed function oxidases in the liver and detoxified by conjugation with liver glutathione, may accumulate following paracetamol overdose and cause liver damage. No significant differences in the paracetamol pharmacokinetic profile are observed in the elderly.
Caffeine:
Caffeine is absorbed readily after oral administration, maximal plasma concentration is acheived within one hour and the plasma half-life is about 3.5 hours. 65 – 80 % of administered Caffeine is excreted in the urine as 1-Methyluric acid and 1-methylxanine.

5.3 Preclinical safety data

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

1. Pharmaceutical particulars

6.1 List of excipients

- Starch
- Magnesium stearate

6.2 Incompatibilities

- None relevant known.

6.3 Shelf life

- 36 Months

6.4 Special precautions for storage

- Store below 30°C
- Store in a cool dry place protected from light and out of reach of children.

6.5 Nature and contents of container<and special equipment for use, administration or implantation>

2 PVC/Al Blisters of 10 capsules in a monocarton and such 10 monocartons in a box.

6.6 Special precautions for disposal<and other handling>

- None.

7. Applicant/Manufacturer

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