SUMMARY OF PRODUCT CHARACTERISTICS

KLAXON
(Diclofenac Sodium Injection)

1 NAME OF THE FINISHED PHARMACEUTICAL PRODUCT
KLAXON
(Diclofenac Sodium Injection)

2 QUALITATIVE AND QUANTITATIVE COMPOSITIONS
Each mL contains:
Diclofenac Sodium BP……25 mg
For excipients, see 6.1.

3 PHARMACEUTICAL FORM
Injection

4 CLINICAL PARTICULARS
4.1 Therapeutic Indications
Acute, severe pain due to inflammatory and degenerative form of rheumatism; rheumatoid arthritis; ankylosing spondylitis; osteoarthrosis.
Painful post traumatic inflamma-tion and swelling.
Pain following dental surgery.
Acute attack of gout.

4.2 Posology and method of administration
Adults: For adults the dosage is generally one ampoule daily injected deep intragluteally into the upper outer quadrant, by way of exception, in severe cases two injections, separated by an interval of few hours, can be given per day (one into each buttock). Alternatively it is possible to combine ampoule with Klaxon tablets upto a maximum daily dosage of 150 mg. Klaxon ampoules should not be given for more than 2 days; if necessary, the treatment can be continued with Klaxon tablets.
Children: Klaxon ampoules are not suitable for children.

4.3 Contraindications
Peptic ulcer, Hypersensitivity to the active substance or excipients. Like other non-steroidal anti-inflammatory agents, Klaxon is also contraindicated in asthmatic patients, in whom attacks of asthma, urticaria, or acute rhinitis are precipitated by acetylsalicylic acid or by other drugs with prostaglandin synthetase inhibiting activity.

4.4 Special warnings and special precautions for use
Strict accuracy of diagnosis and close medical surveillance are imperative in-patients with symptoms indicative of gastro-intestinal disorder, with a case history suggestive of gastro-intestinal ulceration, with ulcerative colitis, or with Crohn's disease, as well as in patients suffering from severe impairment of hepatic function. Owing to the importance of prostaglandins or maintaining renal blood flow, particular caution is called for when

using Klaxon in cases of impaired cardiac or renal function, in patients being treated with diuretic, and in those recovering from major surgical operations.
In the rare instances where peptic ulceration or gastro-intestinal bleeding occur in patients receiving the medication, the drug should be withdrawn.
In patients of advanced age, caution is indicated on basic of medical grounds.
During prolonged treatment with Klaxon as with other highly active non-steroidal anti-inflammatory agents blood counts and monitoring of hepatic and renal function are indicated as precautionary measures.

Mutagenicity, carcinogenicity and reproduction toxicity studies:
Diclofenac showed no mutagenic, carcinogenic or teratogenic effects in the studies conducted.

Use during pregnancy and lactation:
Insufficient data are available as yet on the use of Klaxon ampoules during pregnancy and lactation. For this reason, their use is not recommended during pregnancy and lactation.

Effects on ability to drive or use machines:
Patients experiencing dizziness or other central nervous disturbances should refrain from driving a vehicle or operating machines.

4.5 Interaction with other FPPs and other forms of interaction
When given together with preparation containing lithium or digoxin, Klaxon may raise their plasma concentrations: but no clinical signs of overdosage in such cases have yet been encountered.
Various non-steroidal anti-inflammatory agents are liable to inhibit the activity of diuretics and to potentiate the effect of potassium-sparring diuretics, thus making it necessary to monitor the serum potassium levels.
Concomitant administration of systemic non-steroidal anti-inflammatory agents may increase the occurrence of side effects.
Clinical investigations would appear to indicate that Klaxon has no influence on the effect of oral anticoagulants. As a precaution, however, it is recommended that, when giving concomitant treatment with Klaxon and anticoagulants laboratory tests should be performed in order to check that the desired response to the anticoagulant is being maintained. As with other non-steroidal anti-flammatory agents, diclofenac in a high dose (200 mg) can temporarily inhibit platelet aggregation.
Clinical studies have showed that Klaxon can be given together with oral antidiabetic agents without influencing their clinical effect.
Caution should be excercised when diclofenac is administered less than 24 hours before or after treatment with methotrexate, since the blood concentration of methotrexate may rise and the toxicity of this substance be increased.

4.6 Pregnancy and lactation
None known.

4.7 Effects on ability to drive and use machines
None known.

4.8 Undesirable effects
Gastro-intestinal tract:
Occasional: epigastric pain, other gastro-intestinal disorders (e.g. nausea, vomiting, diarrhoea)
Rare : Gastro-intestinal bleeding, peptic ulcer.
In isolated cases : peptic ulcer with perforation, lower gut disorders (e.g. non-specific haemorrhagic colitis and exacerbations ulcerative colitis)
Central Nervous System :
Occasional: Headache, dizziness, or vertigo
Rare: Drowsiness
In isolated cases:Disturbances of sensation or vision (blurred vision, diplopia), tinnitus, insomnia, irritability, convulsions.
Skin :
Occasional: Rashes or skin eruptions
Rare: Urticaria
In isolated cases: Bulious eruptions, eczema multiforme, Stevens-Johnson Syndrome, Lyell's Syndrome, loss of hair.
Kidney :
In isolated cases: acute renal insufficiency, urinary abnormalities (e.g. haematuria), intestinal nephritis, nephrotic syndrome.
Liver :
Rare: Liver function disorders including hepatitis with or without jaundice, in isolated cases, fulminant.
Blood :
In isolated cases: thrombocytopenia, leucopenia, agranulocytosis, haemolytic anaemia, aplastic anaemia.
Other organ systems :
Rare: odema, hypersensitivity reactions (e.g bronchospasm, anaphylactic/anaphylactoid systematic reactions including hypotension), injection site disorders (e.g. local pain and induration; in isolated cases: abscesses and local necrosis.

4.9 Overdose
Management of acute poisoning with non-steroidal anti-inflammatory agents consists of supportive and symptomatic measures. There is no typical picture resulting from an overdosage of diclofenac.
The therapeutic measures to be taken in case of overdosage are as follows: Supportive and symptomatic treatment should be given for complications, such as hypotension, renal failure, convulsions, gastro-intestinal irritation, and respiratory depression.
Specific therapies, such as forced diuresis, dialysis or haemoperfusion are probably of no help in eliminating non-steroidal anti-inflammatory agents, because of their high protein binding rate and extensive metabolism.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Klaxon contains a non-steroidal compound with pronounced anti-inflammatory, and analgesic properties.

Inhibition of prostaglandin biosynthesis, which has been demonstrated experimentally, is regarded as having an important bearing on its mechanism of action. Prostaglandin plays an important role in the causation of inflammation, pain, fever.

In rheumatic diseases, the anti-inflammatory and analgesic properties of Klaxon elicit a clinical response characterised by marked releif from signs and symptoms such as pain at rest, pain on movement, morning stiffness, post-traumatic inflammatory conditions.

Klaxon rapidly relieves both spontaneous pain and pain on movement and diminishes inflammatory swelling and wound oedema.

Klaxon ampoules are particularly suitable as initial therapy for inflammatory and degenerative rheumatic diseases.

5.2 Pharmacokinetic properties

Approximately 20 minutes after intramuscular injection of 75 mg diclofenac, a mean peak plasma concentration of 2.5 µg/ml (8 µmol/litre) is attained.

The plasma concentration is in linear reaction to the dose. The area under the concentration curve (AUC) is about twice as large as it is following oral dose of equal size, because about half the active substance is metabolised during its first passage through the liver ("first pass" effect) when administered via the oral route.

Diclofenac becomes bound to serum proteins are at a rate of 99.7% chiefly to albumin (99.4%).

The total systemic clearance of diclofenac in plasma is 263 ± 56ml/min, (mean value ± SD). The terminal half-life in plasma is 1-2 hours.

Pharmacokinetic behaviour remains unchanged following repeated administration.

No accumulation occurs provided the recommended dosage intervals are observed. Diclofenac enters the synovial fluid where maximum concentrations are measured 2-4 hours after the peak plasma values have been attained.

The apparent half-life for elimination from the synovial fluid is 3-6 hours.

Only 4-6 hours after administration therefore, concentration of active substance are already higher in the synovial fluid than they are in the plasma and remain higher for up to 12 hours.

The biotransformation of diclofenac involves partly glucordination of the intact molecules but mainly single and multiple hydroxylation followed by glucordination. About 60% of the administered dose is excreted in the urine in the form of metabolites from one of the two process : less then 1% is excreted as unchanged substance. The remainder of the dose is eliminated as metabolites through the bile in the faeces.

The age of the patient has no influence on the absorption, metabolism, or excretion of diclofenac.

In-patients suffering from renal impairment, no accumulation of the unchanged active substance can be inferred from the single-dose kinetics when applying the usual dosage schedule. At a creatinine clearance of 10ml/min, the theoretical steady-state plasma levels of metabolites are about 4 times higher than in normal subjects. However, the metabolites are ultimately cleared through the bile.

In the presence of impaired hepatic function (chronic hepatitis, non-decompensated cirhosis), the kinetics and metabolism of diclofenac are the same as in patients without liver disease.

5.3 Preclinical safety data
None known.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Mannitol BP
Sodium Metabisulphite BP
Benzyl Alcohol BP
Propylene Glycol BP
Sodium Hydroxide BP
Water for Injection BP

6.2 Incompatibilities
As a rule Klaxon ampoules for intramuscular use should not be mixed with other injections solutions.

6.3 Shelf Life
36 Months

6.4 Special precautions for storage
Store below 30°C. Do not freeze. Protect from light.

6.5 Nature and contents of container
Ampoule of 3 mL.

6.6 Instructions for use and handling
Even invisible damage to bottle caused during storage or transit, may result in contamination. Do not use if leak found on squeezing, or contents not clear, and return for replacement.

7. MARKETING AUTHORISATION HOLDER

UNIQUE PHARMACEUTICAL LABORATORIES.
(A. Division of J. B. Chemicals and Pharmaceuticals Ltd.)
Plot No.4, Phase IV, GIDC, Industrial Area, Panoli 394 116. India

8. NUMBER (S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS
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9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION:
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10 DATE OF REVISION OF THE TEXT:
