1.6 PRODUCT INFORMATION

1.6.1 SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT
PHARMADOL (Paracetamol Caplets 500 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each caplet contains:
Paracetamol BP 500 mg
Excipients QS

3. PHARMACEUTICAL FORM
Tablet, Solid dosage form

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
PHARMADOL can be used for the relief of mild to moderate pain and febrile conditions, eg headache, toothache, colds, influenza, rheumatic pain and dysmenorrhoea.

4.2 Posology and method of administration
Adult: 1 to 2 caplets
Children 12 years and over: 1 Caplet
Repeat dosage three or four times a day if necessary or
As directed by the Physician

Method of administration:
Oral use.

4.3 Contraindications
Contraindicated in Hypersensitivity to the active substance or to any of the excipients

4.4 Special warnings and precaution for use
Where analgesics are used long term (>3 months) with administration every two days or more frequently, headache may develop or worsen. Headache induced by overuse of analgesics (MOH-medication- overuse headache) should not be treated by dose increase. In such cases, the use of analgesics should be discontinued in consultation with the doctor.
Care is advised in the administration of Paracetamol to patients with alcohol dependency, severe renal or severe hepatic impairment. The hazards of overdose are greater in those with non cirrhotic alcoholic liver disease
Label Warnings:
Do not exceed the recommended dose.
If symptoms persist consult your doctor.
Donot take with any other paracetamol containing products.
Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage

4.5 Interaction with other medicinal products and other forms of interaction
The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.
Metoclopramide- may increase speed of absorption of Paracetamol.
Domperidone- may increase speed of absorption of Paracetamol
Colestyramine-may reduce absorption if given within one hour of Paracetamol
Imatinib- restriction or avoidance of concomitant regular Paracetamol use should be taken with Imatinib

4.6 Pregnancy and Lactation
Epidemiological studies in human pregnancy have shown no effects due to paracetamol used in the recommended dosage.
However Paracetamol should be avoided in pregnancy unless considered essential by the Physician
Breast feeding:
Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast-feeding.

4.7 Effects on ability to drive and use machines
None

4.8 Undesirable effects
Adverse effects of paracetamol are rare but Hypersensitivity including skin rash, urticaria or angioedema may occur. There have been reports of blood dyscrasias including thrombocytopenia, Leucopenia, neutropenia, pancytopenia and agranulocytosis, but these were not necessarily causally related to paracetamol.
Very rare cases of serious skin reactions.

4.9 Overdose
Liver damage is possible in adults who have taken 10g or more of paracetamol. Ingestion of 5g or more of paracetamol may lead to liver damage if the patient has risk factors (see below).
Risk Factors.
If the patient:
a. Is on long term treatment with carbmazepine, phenobarbital, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.
Or
b. Regularly consumes ethanol in excess of recommended amounts
Or
Is likely to be glutathione depleted e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

5. PHARMACOLOGICAL PROPERTIES
Pharmacotherapeutic group: Analgesics and Antipyretics
ATC code: N02BE01

5.1 Pharmacodynamic properties
Mechanism of action
Paracetamol is an effective analgesic and antipyretic agent, but has only weak anti-inflammatory properties. Its mechanism of action is not fully understood. It has been suggested that it may act predominantly by inhibiting prostaglandin synthesis in the CNS and to a lesser extent through a peripheral action by blocking pain-impulse generation. The peripheral action may also be due to

inhibition of prostaglandin synthesis or to inhibition of the synthesis or actions of other substances that sensitise pain receptors to mechanical or chemical stimulation. Paracetamol probably produces an antipyretic action by a central effect on the hypothalamic heat-regulating centre to produce peripheral vasodilatation resulting in increased blood flow through the skin, sweating and heat loss. The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus. The drug has no effect on the cardiovascular and respiratory systems, and unlike salicylates it does not cause gastric irritation or bleeding.

5.2 Pharmacokinetic properties
Absorption and Distribution: Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion.

Metabolism: Metabolized in the liver (90-95%)

Excretion: excreted in the urine mainly as the glucuronide and sulphate conjugates.
Less than 5% is excreted as unchanged paracetamol. The elimination half-life varies from about 1 to 4 hours. Plasma protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.
A minor hydroxylated metabolite (N-acetyl-p-benzoquinoneimine) which is usually produced in very small amounts by mixed-function oxidases in the liver and which is usually detoxified by conjugation with liver glutathione may accumulate following paracetamol over dosage and cause liver damage. The time to peak plasma concentration of paracetamol is 0.5 to 2 hours, the time to peak effect 1 to 3 hours and the duration of action 3 to 4 hours.

5.3 Preclinical safety data
There are no preclinical data of relevance to the prescribe which are additional to that already included in other sections

6. PHARMACEUTICAL PARTICULARS
6.1 List of Excipients
Sodium Starch Glycolate BP
Maize starch BP#
Maize starch BP
Gelatin BP
Methyl Paraben BP
Propyl Paraben BP
Purified Water
Purified Talc BP
Colloidal Silicon dioxide BP
Sodium Starch Glycolate BP
Magnesium Stearate BP

6.2 Incompatibilities
Not applicable

6.3 Shelf life
36 months

6.4 Special precautions for storage
Store below 30^0 C. Protect from light and moisture.

Keep Medicine Out of Reach of Children

6.5 Nature and contents of container
10 Blisters of 10 tablets each are packed in carton along with Product insert. (10×10's Alu-PVC Blisters pack)

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER
Not Applicable

9. DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION
Not Applicable