

PELADOL EXTRA (Paracetamol 325 mg + Diclofenac Sodium 50 mg + Caffeine 30 mg Tablets)	
Summary of Product Characteristics	

1. Name of the product: PELADOL EXTRA

2. Qualitative and Quantitative formula:

Sr. No.	Ingredients	Specification	Label Qty/ Tablet (mg)	Over ages	Qty. / batch (In kg)
1.	Paracetamol	BP	325.00	--	132.925
2.	Diclofenac Sodium	BP	50.00	--	20.45
3.	Caffeine	BP	30.00	--	12.27
4.	Sodium Starch Glycolate	BP	55.00	--	22.495
5.	Dicalcium Phosphate	BP	13.692	--	5.600
6.	**Maize Starch	BP	111.332	5.0	47.812
7.	*Maize Starch	BP	16.00	--	6.544
8.	*PVP K-30	BP	3.00	--	1.227
9.	*Methyl Paraben	BP	1.00	--	0.409
10.	*Propyl Paraben	BP	0.08	--	0.033
11.	Colour Tartrazine Supra	IH	1.896	--	0.775
Lubrication					
12.	Purified Talcum	BP	6.50	--	5.317
13.	Magnesium Stearate	BP	6.50	--	5.317
14.	Sodium Starch Glycolate	BP	18.0	--	14.724
15.	Sodium Lauryl Sulphate	BP	2.00	--	1.636
16.	Croscarmellose Sodium	BP	10.00	--	8.18
	Average weight		650.00		

* Marked material for paste preparation

** Material With 5.0 % excess to compensate loss on drying

3. a) Pharmaceutical Form: Uncoated Tablet.

b) Presentation: A yellow coloured, caplet shaped biconvex tablet having embossing "SPPL" on one side & plain on other side.

c) Dosage

Adults : 1 Tablet every 8 hours. Do not exceed 3 tablets in 24 hours.

Children over 12 years of Age: 1 Tablet every 24 hours or as directed by Physician.

Not recommended for use in children below 12 years of age.

4. Clinical Data:

4.1. Therapeutic Indications:

For the relief of pains of minor and middle intensity such as headaches, neuralgia, myalgia, arthralgia, toothache, dysmenorrhoea.

As antipyretic, it is used for relief from signs and symptoms of rheumatoid arthritis and osteoarthritis.

4.2. Dosage and Instructions:

Adults : 1 tablet every 8 hours. Do not exceed 3 tablets in 24 hours.

Children over 12 years of Age: 1 Tablet every 24 hours or as directed by Physician.

PELADOL EXTRA (Paracetamol 325 mg + Diclofenac Sodium 50 mg + Caffeine 30 mg Tablets)	
Summary of Product Characteristics	

Not recommended for use in children below 12 years of age.

4.3. Contraindications:

PELADOL EXTRA should not be used in patients who have previously exhibited hypersensitivity to Diclofenac Sodium, Paracetamol and Caffeine, or in individuals with the syndrome of nasal polyps, angio-oedema and bronchospastic reactivity to aspirin or other non-steroidal anti-inflammatory agents

4.4. Warning & Special Precautions for administration:

PELADOL EXTRA 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, systemic lupus erythematosus.

PELADOL EXTRA 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. Drug Interactions:

Diclofenac Sodium

The products that may interact with Diclofenac Sodium include: aliskiren, ACE Inhibitors (such as lisinopril), angiotensin II receptor blockers (such as valsartan, losartan), corticosteroids (such as prednisone), cidofovir, cyclosporine, lithium, methotrexate, pemetrexed. This medication may increase the risk of bleeding when taken with other drugs that also may cause bleeding. Examples include anti-platelet drugs such as clopidogrel, "blood thinners" such as dabigatran/enoxaparin/warfarin.

Many medications contain pain relievers/fever reducers (aspirin, NSAIDs such as celecoxib, ibuprofen, or ketorolac). These drugs are similar to diclofenac and may increase your risk of side effects if taken together.

Paracetamol

Absorption rate of paracetamol may increase when using metoclopramide and domperidone and may decrease when using cholestyramine. Anticoagulant effect of warfarin and other coumarins may increase in concomitant regular daily use of paracetamol, with an increased risk of bleeding. When administered periodically, it has no significant effect.

Barbiturates reduce the antipyretic effect of paracetamol. Anticonvulsants (including phenytoin, barbiturates, carbamazepine) which stimulate the activity of microsomal liver enzymes may increase the toxic effects of paracetamol on the liver due to increased metabolism of the drug into hepatotoxic metabolites. In concomitant use of paracetamol with hepatotoxic agents, their toxic effect on the liver increases. Concomitant use of high doses of paracetamol and isoniazid, rifampicin increases the risk of hepatotoxic syndrome. Paracetamol reduces the efficacy of diuretics. Do not use with alcohol.

Caffeine:

Aspirin, clozapine, theophylline

Plasma levels of these agents may be elevated by caffeine, increasing their pharmacologic effects and adverse reactions.

PELADOL EXTRA (Paracetamol 325 mg + Diclofenac Sodium 50 mg + Caffeine 30 mg Tablets)	
Summary of Product Characteristics	

Cimetidine, disulfiram, fluoroquinolones, mexiletine, oral contraceptives

May increase caffeine levels, enhancing the effects.

Lithium

Plasma levels may be reduced by caffeine, decreasing the pharmacologic effect.

Phenytoin, smoking

May decrease caffeine levels.

4.6. Pregnancy & Breastfeeding:

It is risk to use this drug during pregnancy & Breastfeeding.

4.7. Side – Effects:

Abdominal pain or cramps, constipation, diarrhea, flatulence, GI bleeding, GI perforation, peptic ulcer, vomiting, dyspepsia, nausea, dizziness, headache liver function test abnormalities, renal function abnormalities, anemia, prolonged bleeding time, pruritus, rash, tinnitus, edema, rash, allergic reaction.

5. Pharmacological characteristics:

5.1. Pharmacodynamic characteristics:

PELADOL EXTRA is a combined drug with a pronounced anti-inflammatory, analgesic and antipyretic effect. Pharmacological activity of the drug is due to the properties of Diclofenac, caffeine and paracetamol, which are the components of the drug. Diclofenac sodium has a pronounced anti-inflammatory and analgesic, and a moderate antipyretic effect. Paracetamol has a pronounced analgesic, slight antipyretic and anti-inflammatory effect. Caffeine has analeptic effect. The mechanism of action is associated with inhibition of prostaglandin synthesis.

5.2. Pharmacokinetics characteristics:

After the intake, the drug is rapidly and completely absorbed. Food has no effect on absorption of the drug.

Plasma concentrations of active substances are linearly dependent on the dose; the maximum levels are reached in 60-90 minutes after ingestion.

Binding of diclofenac to plasma proteins (mainly albumin) reaches 99.7%. The expected volume of distribution is 0.12-0.17 L/kg. Diclofenac penetrates into synovial liquid, where its maximum concentration is reached 2-4 hours later than in blood plasma. The half-life for elimination from the synovial fluid is 3-6 hours.

Diclofenac is metabolized by glucuronidation of unchanged molecule and methoxylation, which forms several phenolic metabolites, the biological activity of which is considerably inferior to the activity of the parent substance.

General plasmatic clearance of diclofenac is approximately 300 mL/min. Terminal half-life is 1-2 hours. 60% of the administered dose is excreted in the urine as glucuronic conjugates of unchanged diclofenac; the rest is excreted in the bile and feces.

Paracetamol is metabolized in the liver and is mainly excreted in the urine.

Caffeine is 99% absorbed orally, Rapidly distributed throughout tissues; crosses the blood-brain barrier and placenta; excreted in breast milk. 17% to 36% protein bound, Rapidly metabolized in the liver to 1-methyluric acid, 1-methylxanthine, and 7-methylxanthine; CYP1A2 is involved in the biotransformation, The $t_{1/2}$ is 3 to 5 h. Approximately 1% is excreted in the urine as unchanged drug.

PELADOL EXTRA (Paracetamol 325 mg + Diclofenac Sodium 50 mg + Caffeine 30 mg Tablets)	
Summary of Product Characteristics	

After repeated administration of the drug, pharmacokinetic parameters of active substances remain unchanged. No accumulation occurs provided the recommended dosage intervals are observed.

5.3. Pre – Clinical Safety Data:

Reference: Serum paracetamol concentration: an alternative to X-rays to determine feeding tube location in the critically ill.

Berger MM, Werner D, Revelly JP, Cayeux MC, Tappy L, Bachmann C, Chiolerio RL.
Soins Intensifs Chirurgicaux, Lausanne, Switzerland.

Background: Placement of enteral feeding tubes is an important clinical issue.

Previous studies suggest that paracetamol absorption is very fast after jejunal administration. The aim was to determine whether paracetamol serum concentration measured by immunoassay can determine the tip position of the feeding tube.

Methods: Thirty-three critically ill patients requiring enteral nutrition with either gastric or post-pyloric feeding tubes were enrolled prospectively in the surgical intensive care unit of a university hospital.

Paracetamol was administered in the feeding tube (15 mg/kg) after a baseline blood sample (T0). Thereafter, 8 blood samples were taken between 2.5 and 240 minutes. Paracetamol was analyzed using an automated homogenous immune assay.

Results: The patients did not differ with respect to age or severity of disease. Peak paracetamol concentrations were significantly higher after post-pyloric administration with 42.6 +/- 13.5 versus 20.5 +/- 7.5 mg/L ($p < .0001$). Time-to-peak paracetamol concentration was significantly shorter with post-pyloric tubes (median, 5 versus 60 minutes; $p < .0001$). The receiver operating characteristic (ROC) curves showed the highest sensitivity and specificity at 5 minutes with 94.1% and 100%, respectively, for discriminating between gastric and post-pyloric location.

Conclusions: Because of paracetamol's rapid absorption after jejunal administration, the test seems to be a safe and inexpensive alternative to X-ray control for assessment of the enteral feeding tube location. Its value in clinical practice remains to be established.

Single dose oral Paracetamol (acetaminophen) for postoperative pain in adults.

Toms L, McQuay HJ, Derry S, Moore RA.

Pain Research and Nuffield Department of Anaesthetics, University of Oxford, West Wing (Level 6), John Radcliffe Hospital, Oxford, Oxfordshire, UK, OX3 9DU.

BACKGROUND: This is an updated version of the original Cochrane review published in Issue 1, 2004 - this original review had been split from a previous title on 'Single dose paracetamol (acetaminophen) with and without codeine for postoperative pain'. The last version of this review concluded that paracetamol is an effective analgesic for postoperative pain, but additional trials have since been published. This review sought to evaluate the efficacy and safety of paracetamol using current data, and to compare the findings with other analgesics evaluated in the same way.

OBJECTIVES: To assess the efficacy of single dose oral paracetamol for the treatment of acute postoperative pain.

SEARCH STRATEGY: We searched The Cochrane Library, MEDLINE, EMBASE, the Oxford Pain Relief Database and reference lists of articles to update an existing version of the review in July 2008.

PELADOL EXTRA (Paracetamol 325 mg + Diclofenac Sodium 50 mg + Caffeine 30 mg Tablets)	
Summary of Product Characteristics	

SELECTION CRITERIA: Randomised, double-blind, placebo-controlled clinical trials of paracetamol for acute postoperative pain in adults.

DATA COLLECTION AND ANALYSIS: Two review authors independently assessed trial quality and extracted data. Area under the "pain relief versus time" curve was used to derive the proportion of participants with paracetamol or placebo experiencing at least 50% pain relief over four to six hours, using validated equations. Number-needed-to-treat-to-benefit (NNT) was calculated, with 95% confidence intervals (CI). The proportion of participants using rescue analgesia over a specified time period, and time to use, were sought as measures of duration of analgesia. Information on adverse events and withdrawals was also collected.

MAIN RESULTS: Fifty-one studies, with 5762 participants, were included: 3277 participants were treated with a single oral dose of paracetamol and 2425 with placebo.

About half of participants treated with paracetamol at standard doses achieved at least 50% pain relief over four to six hours, compared with about 20% treated with placebo. NNTs for at least 50% pain relief over four to six hours following a single dose of paracetamol were as follows: 500 mg NNT 3.5 (2.7 to 4.8); 600 to 650 mg NNT 4.6 (3.9 to 5.5); 975 to 1000 mg NNT 3.6 (3.4 to 4.0). There was no dose response. Sensitivity analysis showed no significant effect of trial size or quality on this outcome. About half of participants needed additional analgesia over four to six hours, compared with about 70% with placebo. Five people would need to be treated with 1000 mg paracetamol, the most commonly used dose, to prevent one needing rescue medication over four to six hours, who would have needed it with placebo. Adverse event reporting was inconsistent and often incomplete. Reported adverse events were mainly mild and transient, and occurred at similar rates with 1000 mg paracetamol and placebo. No serious adverse events were reported. Withdrawals due to adverse events were uncommon and occurred in both paracetamol and placebo treatment arms. **AUTHORS' CONCLUSIONS:** A single dose of paracetamol provides effective analgesia for about half of patients with acute postoperative pain, for a period of about four hours, and is associated with few, mainly mild, adverse events.

PMID: 18843665 [PubMed - indexed for MEDLINE]

6. Pharmaceutical Data:

6.1. List of excipients

Sr. No.	Ingredients	Specification
1	Sodium Starch Glycolate	BP
2	Dicalcium Phosphate	BP
3	**Maize Starch	BP
4	*Maize Starch	BP
5.	*PVP K-30	BP
6	*Methyl Paraben	BP
7.	*Propyl Paraben	BP
8	Colour Tartrazine Supra	IH
9	Purified Talcum	BP
10.	Magnesium Stearate	BP
11.	Sodium Starch Glycolate	BP
12.	Sodium Lauryl Sulphate	BP
13.	Croscarmellose Sodium	BP

PELADOL EXTRA (Paracetamol 325 mg + Diclofenac Sodium 50 mg + Caffeine 30 mg Tablets)	
Summary of Product Characteristics	

6.2. Incompatibilities: Not Applicable

6.3. Duration of Storage: 36 Months (3 years)

6.4. Special precautions for Storage:

Store in a cool & dry place below 30°C.

Keep all medicines away from reach of children.

6.5. Nature and content of the external packaging: Each Alu- Pvc blister of 10 tablets packed in a catch cover. Such a 20 catch covers packed in one outer carton along with insert.

6.6 Instructions for use and handling and disposal

No special requirements.

7. Marketing authorisation holder

SOCOMED PHARMA PVT. LTD.

No.3, Maruti Paradies/Plot 93-95, Sector 15,

CBD Belapur/ Navi Mumbai- 400 614.

Tel: +91 22 2758 3001/3.

8. Number(s) in the national register of finished pharmaceutical products

Mfg. Lic. No. In India: MH/102380A

9. Renewal Of the Authorisation

17th Feb /2015 – 16th Feb 2020

10. Date Of Revision of The Text

17th Feb 2015 – 16th Feb 2020