SUMMARY OF PRODUCT CHARACTERISTICS

RONMAX EXTRA EFFER

(Paracetamol, Diclofenac and Caffeine Effervescent Tablets)

1. NAME OF THE MEDICINAL PRODUCT: RONMAX EXTRA EFFER

Generic Name of Product : Paracetamol, Diclofenac and Caffeine Effervescent Tablets

Strength (formula) : Each Effervescent tablet contains:

Paracetamol BP 500 mg
Diclofenac Sodium BP 50 mg
Caffeine (Anhydrous) BP 30 mg
Excipients q.s.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

2.1 Qualitative & Quantitative Composition Declaration:

Sr. No.	Approved name	Label claim / tablet (In mg)	Overages Added (In %)	Qty / tablet (in mg)	Specifications	Reason for inclusion of ingredient
1.	Paracetamol	500.00	---	500.00	BP	Active
2.	Diclofenac Sodium	50.00	---	50.00	BP	Active
3.	Caffeine	30.00	---	30.00	BP	Active
4.	Citric acid	---	10	668.5	BP	Effervescent system
5.	Sodium Bicarbonate	---	10	1000	BP	Effervescent system
6.	PVP K-30	---	---	25	USP	Binder
7.	Sodium Saccharine	---	---	10	BP	Taste masking
8.	Tween 80	---	---	1.5	BP	Stabilizer
9.	Purified water	---	---	0.03 ml	BP	Vehicle
10.	Sodium Bicarbonate	---	---	160	BP	Effervescent system
11.	Simethicone	---	---	10	BP	Effervescent system
12.	IPA	---		0.01 ml	BP	Solvent
13.	Orange flavour	---		20	IH	Flavour
14.	Sucralose	---		20	USP	Sugar
15.	Sodium Carbonate	---		45	BP	Effervescent system

16.	Sodium benzoate	---		60	BP	Antimicrobial preservative
	Total weight of tablet			**2600 mg**		

BP: - British Pharmacopoeia

IH :- Inhouse Pharmacopoeia

USP :- United state Pharmacopoeia

3. PHARMACEUTICAL FORM:

White to off-white colour, round flat faced beveled edge tablets with orange odour.

4. CLINICAL PARTICULARS:

4.1 Therapeutic Indications:

RONMAX EXTRA EFFER is indicated for:

RONMAX EXTRA EFFER is indicated in the treatment of painful rheumatic disorders such as rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and acute gout. Acute musculoskeletal disorders and soft tissue inflammation such as periarthritis, sprains, strains, tenosynovitis, bursitis, pain in fractures and dislocation. Relief of pain and inflammation associated with orthopedic, dental, gynecological and other minor surgical procedures.

4.2 Posology and Method of Administration:

Posology:

Paracetamol, Diclofenac & Caffeine Soluble Tablets should be dissolved in at least half a tumbler of water.

Dosage

Adults

One to two tablets dissolved in water not more frequently than every 4-6 hours when necessary to a maximum of 8 tablets in 24 hours.

Elderly

Same as adult dose. A reduced dose may be required

Paediatric population:

Children aged 16-18 years:

One to two tablets dissolved in water every 4-6 hours when necessary to a maximum of 8 tablets in 24 hours.

Children aged 12-15 years:

One tablet dissolved in water every 6 hours when necessary to a maximum of 4 tablets in 24 hours.

Children aged less than 12 years:

Not recommended for children under 12years.

Method of Administration:

Oral administration

4.3 Contra – Indications:

RONMAX EXTRA EFFER is contraindicated in:

Hypersensitivity to paracetamol, Diclofenac, caffeine and/or other constituents.
This medicine should not be used by people who have been diagnosed with hypertension or who are receiving antihypertensive medication, or who have a history of cardiac arrhythmia.
This medicine should not be used by patients recovering from chronic alcoholism who are taking disulfiram.
This medicine should not be used if antidepressants (including lithium carbonate), anxiolytics (including clozapine) and sedatives are being used, or by persons with anxiety disorders.
This medicine should not be used by any persons who are also taking ephedrine.
NSAIDs should not be administered to patients with a history of, or active peptic ulceration.
NSAIDs are contraindicated in patients who have previously shown hypersensitivity reactions (e.g., asthma, rhinitis or urticaria) in response to ibuprofen, aspirin or other non-steroidal anti-inflammatory drugs.

Caffeine shares the same metabolic pathway as theophylline and therefore this medicine should not be used concurrently with theophylline.

4.4 Special Warning and Precautions for Use:

- If symptoms persist consult your doctor
- Do not exceed the stated dose
- Keep all medicines out of the reach and sight of children
- Do not 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.
- Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.
- Caution is required if administrated to patients suffering from, or with a previous history of, bronchial asthma since NSAIDs have been reported to cause bronchospasm in such patients.
- NSAIDs should only be given with care to patients with a history of gastrointestinal disease.

- Undesirable effects may be minimised by using the minimum effective dose for the shortest possible duration.
- Side effects are generally more serious in the elderly and if serious, diclofenac sodium should be withdrawn.
- Patients on long term treatment should be monitored and patients with severe hepatic, cardiac or renal insufficiency should be kept under close surveillance as the use of NSAIDs may result in deterioration of renal function. Patients with impaired cardiac or renal function or recovering from major surgery or being treated with diuretics should be considered because of the importance of prostaglandins in maintaining blood flow. The dose should be kept as low as possible and renal function should be monitored in these patients.
- NSAIDs should be given with care to patients with a history of heart failure or hypertension since oedema has been reported in association with NSAID administration.

4.5 Interaction with other medicinal products and other forms of interaction

As caffeine is found naturally in tea, coffee and chocolate, and in some carbonated drinks there is the potential for users to take more than the recommended 520 mg/day of caffeine (8 tablets) per day. Therefore users should take account of dietary and other medicinal sources of caffeine and ensure that they do not exceed the stated dose.

Xanthine derivatives such as caffeine can weaken the vasodilating effect of substances used for myocardial imaging such as adenosine and dipyridamole. Therefore, caffeine should be avoided for 24 hours before myocardial imaging.

Caffeine, a CNS stimulant, has an antagonistic effect towards the action of sedatives and tranquilizers.
Caffeine may enhance the tachycardic effect of phenylpropanolamine.
Caffeine exerts a competitive inhibition of the metabolism of clozapine. Therefore clozapine and caffeine must not be used concurrently (see contraindications).
Caffeine can increase blood pressure and counters the hypotensive action of beta blockers such as atenolol, metoprolol, oxprenolol and propranolol. This medicine should not be used at the same time as beta blockers.
Disulfiram increases caffeine clearance by up to 50%. Concomitant use of disulfiram and caffeine should be avoided (see contraindications).
Use of lithium carbonate and caffeine may cause a small to moderate rise in serum lithium levels. Concomitant use should be avoided (see contraindications).
Monoamine oxidase inhibitors may increase the stimulant effects of caffeine.
Methoxsalen reduces clearance of caffeine and may increase the effects of caffeine.
Phenytoin doubles caffeine clearance, although caffeine does not affect the metabolism of phenytoin.
Pipemidic acid reduces caffeine clearance, enhancing the effects of caffeine.

Theophylline and caffeine share the same metabolic pathway, leading to increased clearance times for theophylline when used concurrently with caffeine. Concomitant use should be avoided (see contraindications).
Levothyroxine, like caffeine can increase blood pressure, and therefore these two active ingredients should not be used concurrently.
Ephedrine and caffeine interact to produce significant cardiovascular effects. Therefore caffeine should be avoided when ephedrine is being taken.
The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine.
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.

4.6 Pregnancy and lactation

Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol used in the recommended dosage, but patients should follow the advice of their doctor regarding its use.

Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding.

Diclofenac sodium should be used in pregnancy only if the benefits outweigh the risk, when the lowest effective dose should be employed. Use of prostaglandin synthetase inhibitors may result in premature closure of the foetal ductus arteriosus or uterine inertia and therefore are not recommended during the last trimester of 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.
Traces have been detected in breast milk but the level is so low as to be thought not to affect the infant.

Caffeine appears in breast milk. Irritability and poor sleeping pattern in the infant have been reported.

4.7 Effects on ability to drive and use machine:

Must not drive vehicles when taken RONMAX EXTRA EFFER .

4.8 Undesirable effects

Adeverse effects of diclofenac are Gastro-intestinal disorders (rarely with bleeding) and lower intestinal disorders, in some cases with exacerbation of existing conditions such as ulcerative colitis, may occur. These include nausea, vomiting, diarrhoea, dyspepsia, abdominal pain, melaena, haematemesis and gastrointestinal haemorrhage. Less frequently, gastritis, duodenal ulcer, gastric ulcer and gastrointestinal perforation have been observed. Pancreatitis, aphthous stomatitis, glossitis and constipation may occur.

Occasionally there are effects on the CNS such as headaches, dizziness, vertigo, drowsiness, disturbance of taste, vision, hearing and sensation. There may be malaise, fatigue, insomnia, confusion, anxiety or depression, tremor or psychotic reactions.
Skin reactions, including loss of hair and photosensitivity reactions occur occasionally.

4.9 Overdoses:

PARACETAMOL

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 carbamazepine, phenobarbitone, 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
c, Is likely to be glutathione deplete e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.
Symptoms
Symptoms of paracetamol overdosage in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema, and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

Management

Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention. Symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines, see BNF overdose section.
Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after this time. If required the patient should be given intravenous N-acetylcysteine, in line with the established dosage schedule. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital. Management of patients who present with serious hepatic dysfunction beyond 24h from ingestion should be discussed with the NPIS or a liver unit.

DICLOFENAC

Symptoms include headache, vomiting, drowsiness, dizziness and fainting.

Treatment should be symptomatic and supportive. Gastric lavage and treatment with active charcoal, as soon as possible, to prevent absorption together with symptomatic measures to treat gastro-intestinal irritation and other complications such as hypotension, convulsions, respiratory disorders and renal failure are indicated. Correction of severe electrolyte abnormalities may need to be considered.

The extensive metabolism and high rate of protein binding of NSAIDs obviate the use of specific therapies such as forced diuresis, haemoperfusion or dialysis.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties

Paracetamol

ANALGESIC:

The mechanism of analgesic action has not been fully determined. Paracetamol may act predominantly by inhibiting a prostaglandin synthesis in the central nervous system (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 sensitize pain receptors to mechanical or chemical stimulation.

ANTIPYRETIC:

Paracetamol probably produces antipyresis by acting centrally on the hypothalamic heat-regulating centre to produce peripheral vasodilation resulting in increased blood flow through the skin, sweating, and heat loss. The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus.

Diclofenac Sodium:

Diclofenac sodium is a non-steroidal anti-inflammatory agent which has analgesic and antipyretic properties. It is a prostaglandin synthetase (cyclo-oxygenase) inhibitor.

Caffeine:

Central nervous system stimulant – Caffeine stimulates all levels of the CNS, although its cortical effects are milder and of shorter duration than those of amfetamines.

5.2 Pharmacokinetic properties

Paracetamol

Paracetamol is rapidly and almost completely absorbed from the gastro- intestinal tract, it is relatively uniformly distributed throughout most body fluids and exhibits variable protein binding. Excretion is almost exclusively renal, in the form of conjugated metabolites.

Caffeine

Caffeine is absorbed readily after oral administration, maximal plasma concentrations are achieved 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-methylxanthine.

Diclofenac Sodium:

Following ingestion, diclofenac sodium is completely absorbed from the intestinal tract but undergoes first pass metabolism and peak plasma concentrations occur in about 2 to 4 hours; at therapeutic concentrations it is more than 99% bound to plasma proteins. Diclofenac is almost entirely metabolised in the liver and the terminal plasma half-life is about 1-2 hours, with metabolic excretion mainly via the kidneys and also in the bile.

5.3 Preclinical safety data

Not available

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients

Citric acid, Sodium bicarbonate, PVP K-30, Sodium Sacharine, PVP K-30, Purified water, Simethicone, Isopropyl alcohol, Orange flavour, Sucralose, Sodium Carbonate & Sodium benzoate.

6.2 Incompatibilities:

Not Applicable.

6.3 Shelf – life:

36 Months.

6.4 Special Precautions for Storage:

Store below 30°C. Protected from light & moisture.

6.5 Nature and Contents of Container:

4 Tablets are packed in a ALU-PVC Strip such a 3 strip is placed in a carton with package insert.

(3 x 4 tablets Alu-Alu strip).

6.6 Special Precautions for disposal:

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder

(Company) Name:	RONAK EXIM PRIVATE LIMITED
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	Police Station, Baroda – 390 001, GUJARAT
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8. Marketing authorization number(s)

Not applicable.

9. Date of first authorization/renewal of the authorization

Not applicable.

10. Date of revision of the text

Not applicable.

RONAK EXIM PVT. LTD. INDIA