COMPOSITION :

Each tablet contains

Ferrous Ascorbate	……..	37.5 mg
Paracetamol	……..	325 mg.

PHARMACOLOGICAL ACTION :

Tramadol is a centrally acting synthetic analgesic compound whose analgesic profile can be attributed to the binding of parent and 0-demethylated (M1) metabolite to μ-opioid receptors as well as the weak inhibition of neuronal re-uptake of noradrenaline and serotonin.

Paracetamol also has centrally acting analgesic effects.

Tramadol is well absorbed after oral administration, reaching peak activity in 2 to 3 hours. The mean absolute bioavailability of a single 100 mg oral dose is approximately 75%, increasing to approximately 90% with multiple dosing. Oral absorption of paracetamol following administration of OPITRAL-P gives a peak plasma concentration of paracetamol within one hour and is not affected by co-administration with tramadol.

Tramadol and paracetamol are both extensively metabolised in the liver. Approximately 30% of tramadol is excreted unchanged in the urine. Tramadol and its metabolites are eliminated primarily by the kidney. The plasma elimination half-lives of tramadol and its M1 metabolite are approximately 6 and 7 hours respectively. Paracetamol is eliminated from the body primarily by formation of glucuronide and sulfate conjugates in a dose-dependent manner.

The half-life of paracetamol is about 2-3 hours in adults. Less than 9% of paracetamol is excreted unchanged in the urine.

INDICATIONS :

OPITRAL-P is indicated for the short-term treatment (i.e. three days or less) of mild to moderate acute pain.

CONTRA-INDICATIONS :

OPITRAL-P is contra-indicated in patients with a known hypersensitivity to tramadol, paracetamol or other opioids such as codeine. It is also contraindicated in cases of severe liver function impairment and in acute intoxication with alcohol, hypnotics, centrally acting analgesics, opioids or psychotropic medicines. It should not be administered to patients who are receiving monoamine oxidase inhibitors or within two weeks of their withdrawal.

OPITRAL-P must not be used for narcotic withdrawal treatment.

OPITRAL-P should not be given to patients with respiratory depression especially in the presence of cyanosis and excessive bronchial secretions.

OPITRAL-P should not be given to patients with increased intracranial pressure or central nervous system depression due to head injury or cerebral disease.

Safety during pregnancy and lactation has not been established. Tramadol has been shown to cross the placenta.

DOSAGE AND DIRECTIONS FOR USE :

To be used in adults and children over 16 years of age. Do not exceed the recommended dose.
Acute pain:
2 tablets every 4 to 6 hours as needed for pain relief. Do not exceed 8 tablets per day. Renal impairment:
For patients with creatinine clearance <30 mL/min, the dosing interval of OPITRAL-P should be increased not to exceed 2 tablets every to 12 hours.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS :

The most frequently reported side effects were of the gastrointestinal and central nervous systems. These include:
Gastrointestinal system:
Nausea; abdominal pain, constipation, flatulence, vomiting; dry mouth; dyspepsia and diarrhoea.

Central Nervous System and Psychiatric:
Dizziness, headache, nervousness, anxiety, agitation, euphoria, emotional lability, hallucinations, hypertonia and tremor. Somnolence, insomnia, anorexia, anxiety, confusion, euphoria and nervousness.

Other reported side-effects include pruritus, fatigue, upper respiratory tract infection, increased sweating, hot flushes, rashes and asthenia.

Other side-effects reported with the use of tramadol include: anaphylaxis, increased liver enzyme values, postural hypotension or cardiovascular

collapse and the potential for Toxic Epidermal Necrolysis and Stevens-Johnson Syndrome.

Paracetamol may cause allergic reactions and skin rash. The rash usually appears as red areas or allergic wheals, and may be accompanied by fever and involvement of the mucous membranes. The use of paracetamol has been associated with the occurrence of neutropenia, pancytopenia and leucopenia.

SPECIAL PRECAUTIONS :

Do not co-administer OPITRAL-P with other tramadol or paracetamol containing products. OPITRAL-P should not be taken with alcohol containing beverages.

The administration of OPITRAL-P concurrently with central nervous system (CNS) depressants such as alcohol, opioids, anaesthetic agents, phenothiazines, tranquilizers or sedative hypnotics is likely to intensify and prolong CNS effects.

OPITRAL-P should be used with caution in patients with impaired renal function and in patients prone to convulsive disorders or in shock.

DRUG INTERACTIONS :

Concomitant administration of OPITRAL-P and carbamazepine may cause significantly decreased tramadol and M1 concentrations. Patients receiving carbamazepine may have significantly reduced analgesic effect from the tramadol component of OPITRAL-P.

Concomitant administration with inhibitors of CYP2D6 such as fluoxetine, paroxetine, quinidine and amitriptyline could result in some inhibition of the metabolism of tramadol.

Simultaneous administration with cimetidine is associated with clinically insignificant changes in serum concentrations of tramadol. Therefore, no alteration of the OPITRAL-P dosage regimen is recommended for patients receiving chronic cimetidine therapy.

OPITRAL-P must not be combined with a MAO-inhibitor, or within 14 days of discontinuation of it, as potentiation of serotonergic and noradrenergic effects may result.

Post-marketing surveillance of tramadol has revealed rare reports of digoxin toxicity and rare alterations of warfarin effect including elevation of prothrombin times.

Periodic evaluation of prothrombin time should be performed when OPITRAL-P is administered concurrently with warfarin like compounds.

Concomitant administration of diflunisal and paracetamol produces a 50% increase in paracetamol plasma levels in normal volunteers. OPITRAL-P should be used cautiously and patients should be monitored carefully.

PRESENTATION :

Available in a strip of 10 Tablets.