



# Centamol<sup>TM</sup> Plus

Suspension

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Each 5ml contain

Paracetamol                      125mg

Mefenamic acid                50mg

### **Pharmacokinetic properties:**

Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 10 to 60 minutes after oral doses. Paracetamol is distributed into most body tissues. It crosses the placenta and is present in breast milk. Plasma-protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations. The elimination half-life of paracetamol varies from about 1 to 3 hours. Paracetamol is metabolised mainly in the liver and excreted in the urine mainly as the glucuronide and sulfate conjugates. Less than 5% is excreted as unchanged paracetamol. A minor hydroxylated metabolite (Nacetyl-p-benzoquinoneimine), is usually produced in very small amounts by cytochrome P450 isoenzymes (mainly CYP2E1 and CYP3A4) in the liver and kidney. It is usually detoxified by conjugation with glutathione but may accumulate after paracetamol over dosage and cause tissue damage.

Mefenamic acid is absorbed from the gastrointestinal tract. Peak plasma concentrations occur about 2 to 4 hours after ingestion. The plasma elimination half-life is reported to be about 2 to 4 hours. Mefenamic acid is more than 90% bound to plasma proteins. It is distributed into breast milk. Mefenamic acid is metabolised by the cytochrome P450 isoenzyme CYP2C9 to 3-hydroxymethyl Mefenamic acid, which may then be oxidised to 3-carboxymefenamic acid. Over 50% of a dose may be recovered in the urine, as unchanged drug or, mainly, as conjugates of Mefenamic acid and its metabolites.

### **Mechanism of Action**

Paracetamol act primarily in the CNS, increasing the pain threshold by inhibiting both isoforms of cyclooxygenase, COX-1, COX-2, and COX-3 enzymes involved in prostaglandin (PG) synthesis. The antipyretic properties of acetaminophen are likely due to direct effects on the heat-regulating centres of the hypothalamus resulting in peripheral vasodilation, sweating and hence heat dissipation.

Mefenamic acid binds the prostaglandin synthetase receptors COX-1 and COX-2, inhibiting the action of prostaglandin synthetase. As these receptors have a role as a major mediator of inflammation and/or a role for prostanoid signaling in activity-dependent plasticity, the symptoms of pain are temporarily reduced.

### **Other pharmacodynamic properties:**



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Paracetamol is a widely used analgesic and antipyretic drug that is used for the relief of fever, headaches, and other minor aches and pains. It is a major ingredient in numerous cold and flu medications and many prescription analgesics. It is extremely safe in standard doses, but because of its wide availability, deliberate or accidental overdoses are not uncommon. Paracetamol, unlike other common analgesics such as aspirin and ibuprofen, has no anti-inflammatory properties or effects on platelet function, and it is not a member of the class of drugs known as non-steroidal anti-inflammatory drugs or NSAIDs. At therapeutic doses Paracetamol does not irritate the lining of the stomach nor affect blood coagulation, kidney function, or the fetal ductus arteriosus (as NSAIDs can). Like NSAIDs and unlike opioid analgesics, Paracetamol does not cause euphoria or alter mood in any way. Paracetamol and NSAIDs have the benefit of being completely free of problems with addiction, dependence, tolerance and withdrawal. Paracetamol is used on its own or in combination with pseudoephedrine, dextromethorphan, chlorpheniramine, diphenhydramine, doxylamine, codeine, hydrocodone, or oxycodone.

Mefenamic acid, an anthranilic acid derivative, is a member of the fenamate group of nonsteroidal anti-inflammatory drugs (NSAIDs). It exhibits anti-inflammatory, analgesic, and antipyretic activities. Similar to other NSAIDs, mefenamic acid inhibits prostaglandin synthetase.

**Indication:**

Centamol Plus suspension is licensed for treatment of pain and fever in children.

**Contraindication:**

The use of Centamol Plus suspension is contraindicated in patients with:

- Hypersensitivity to any of the ingredients of the formulation.
- Patients with severe hepatic dysfunction

**Drug Interaction:**Paracetamol

- Anticoagulant drugs (warfarin) - dosage may require reduction if paracetamol and anticoagulants are taken for a prolonged period of time
- Paracetamol absorption is increased by substances that increase gastric emptying, e.g. metoclopramide
- Paracetamol absorption is decreased by substances that decrease gastric emptying, e.g. propantheline, antidepressants with anticholinergic properties, and narcotic analgesics
- Paracetamol may increase chloramphenicol concentrations
- The risk of paracetamol toxicity may be increased in patients receiving other potentially hepatotoxic drugs or drugs that induce liver microsomal enzymes such as alcohol and anticonvulsant agents
- Paracetamol excretion may be affected and plasma concentrations altered when given with probenecid
- Colestyramine reduces the absorption of paracetamol if given within 1 hour.



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- Antivirals: Regular use of paracetamol possibly reduces metabolism of Zidovudine (increased risk of neutropenia).

### Mefenamic Acid

- Mefenamic Acid enhances activity of oral anticoagulants but rarely significant.
- Increased cyclosporine, lithium toxicity and convulsions reported with ciprofloxacin.
- Absorption is increased by Magnesium Hydroxide antacids.

### **Adverse effects:**

The most commonly reported adverse effects are feeling or being sick, hypersensitivity reactions, skin rashes, diarrhea, nausea.

### **Warnings and Precautions:**

- In case a hypersensitivity reaction occurs which is rare, Centamol Plus suspension should be discontinued.
- Centamol Plus suspension contains Paracetamol and therefore should not be used in conjunction with other Paracetamol containing products.
- Centamol Plus suspension should be used with caution in patients with renal or hepatic dysfunction, diabetes mellitus, hyperthyroidism, cardiovascular problems, epilepsy and closed angle glaucoma.
- Chronic heavy alcohol abusers may be at increased risk of liver toxicity from excessive paracetamol use, although reports of this event are rare. These reports usually involve cases of severe chronic alcoholics and dosages of paracetamol that most often exceed recommended doses. Chronic alcoholics should not exceed 2 g/day of paracetamol.

### **Use in special population:**

1. **Pediatric:** Centamol Plus suspension is safe in children.
2. **Geriatric:** Elderly population may be at greater risk for the side-effects.
3. **Liver impairment:** Use with caution.
4. **Renal failure:** Use with caution.
5. **Pregnancy and lactation:** Centamol Plus suspension is not recommended for Women who are in their late stages of pregnancy. Since Mefenamic acid is distributed into breast milk, use in lactating mothers should be avoided.

### **Dosage:**

The usual recommended dose of Centamol Plus in children is as under:

- 6 months-2 years age: 1 table spoonful three times a day.
- 2-5 years age: 1- 2 table spoonful three times a day.

### **Presentation:**

Centamol Plus suspension is available bottle of 60ml with a measuring cup.



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**Storage and handling:**

Store below 25°C. Protect from light



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