For the use of a Registered Medical Practitioner or Hospital or a Laboratory only

XTPARA 650

1. Generic Name

Paracetamol Tablets I.P. 650mg

2. Qualitative and quantitative Composition:

Each uncoated tablet contains:

Paracetamol I.P. ……..650 mg

Excipients……..q.s.

The excipients used are Maize Starch, PVPK-30, Microcrystalline Cellulose, Talc, Sodium Starch Glycolate and Magnesium Stearate.

3. Dosage form and strength

Dosage form: Uncoated Tablets

Strength: Paracetamol - 650 mg

4. Clinical particulars

4.1. Therapeutic indication

Paracetamol are mild analgesic and antipyretic, and are recommended for the treatment of most painful and febrile conditions, for example, headache including migraine and tension headaches, toothache, backache, rheumatic and muscle pains, dysmenorrhoea, sore throat, and for relieving the fever, aches and pains of colds and flu. Also recommended for the symptomatic relief of pain due to non-serious arthritis.

4.2. Posology and method of administration

Posology

Dose: One tablet 4-6 times a day or as directed by the Physician. Taking more than daily dose of paracetamol may cause serious liver damage.

Method of administration

Paracetamol 650 mg uncoated tablets should be administered orally.

4.3. Contraindications

Hypersensitivity to paracetamol or any of the other constituents.

4.4. Special warnings and precautions for use

Contains paracetamol. Do not use with any other paracetamol-containing products.

Underlying liver disease increases the risk or paracetamol related liver damage. Patients who have been diagnosed with liver or kidney impairment must seek medical advice before taking this medication.

Do not exceed the stated dose. Patients should be advised to consult their doctor if their headaches become persistent. Patients should be advised to consult a doctor if they suffer from non-serious arthritis and need to take painkillers every day.

Caution should be exercised in patients with glutathione depleted states, as the use of paracetamol may increase the risk of metabolic acidosis .

Use with caution in patients with glutathione depletion due to metabolic deficiencies. If symptoms persist, medical advice must be sought.

Keep out of the sight and reach of children.

Pack Label:

Talk to a doctor at once if you take too much of this medicine even if you feel well. Do not take anything else containing paracetamol while taking this medicine.

Patient Information Leaflet:

Talk to a doctor at once if you take too much of this medicine even if you feel well. This is because too much paracetamol can cause delayed, serious liver damage.

4.5. Drugs interactions

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 daily use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

4.6. Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, paracetamol can be used during pregnancy if clinically needed, however, as with any medicine it should be used at the lowest effective dose for the shortest possible time.

Breast-feeding

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

4.7. Effects on ability to drive and use machines

There is no information found.

4.8. Undesirable effects

Adverse events of paracetamol from historical clinical trial data are both infrequent and from small patient exposure. Accordingly, events reported from extensive post-marketing experience at therapeutic/labelled dose and considered attributable are tabulated below by system class and frequency.

The following convention has been utilised for the classification of the undesirable effects: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare

(≥1/10,000 to <1/1000) and very rare (<1/10,000), not known (cannot be estimated from available data).

Adverse event frequencies have been estimated from spontaneous reports received through post-marketing data.

Body System	Undesirable effect	Frequency
Blood and lymphatic system disorders	Thrombocytopenia Agranulocytosis	Very rare
Immune system disorders	Anaphylaxis Cutaneous hypersensitivity reactions including, among others, skin rashes and angioedema. Very rare cases of serious skin reactions	Very rare
Respiratory, thoracic and mediastinal disorders	Bronchospasm*	Very rare
Hepatobiliary disorders	Hepatic dysfunction	Very rare

* There have been cases of bronchospasm with paracetamol, but these are more likely in asthmatics sensitive to aspirin or other NSAIDs.

Reporting of adverse reactions

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: https://www.torrentpharma.com/index.php/site/info/adverse_event_reporting By reporting side effects, you can help provide more information on the safety of this medicine.

4.9. Overdose

Paracetamol overdose may cause liver failure which may require liver transplant or lead to death.

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 Nacetylcysteine, 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.

5. Pharmacological properties

5.1. Mechanism of Action

Paracetamol produces analgesic and antipyretic as main effects and it has been also reported that paracetamol has a weak anti-inflammatory effect. Analgesic action: The central analgesic action of Paracetamol resembles that of aspirin. It produces analgesia by raising pain threshold. Antipyretic effect: The antipyretic effect of Paracetamol is attributed to its ability to inhibit COX in the brain where peroxide tone is low. Recent evidence suggests inhibition of COX-3 (believed to be splice variant product of the COX-1 gene) could represent a primary central mechanism by which Paracetamol decreases pain and possibly fever. Paracetamol is a peripherally acting analgesic with antipyretic activity.

5.2. Pharmacodynamic properties

Paracetamol is an antipyretic analgesic. The mechanism of action is probably similar to that of aspirin and dependant on the inhibition of prostaglandin synthesis. This inhibition appears, however to be on a selective basis.

Clinical Efficacy

In two dental pain reported studies, pain relief was observed at a median time of 15 minutes following administration of the 1000 mg dose of Paracetamol tablets.

Paracetamol tablets demonstrated superior pain relief at 1000 mg dose compared to placebo and to Paracetamol tablets at 500 mg dose. Paracetamol tablets 500 mg dose also demonstrated superior efficacy compared to placebo.

5.3. Pharmacokinetic properties

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. The concentration in plasma reaches a peak in 30 to 60 minutes and the plasma half-life is 1 - 4 hours after therapeutic doses.

Paracetamol is relatively uniformly distributed throughout most body fluids. Binding of the drug to plasma proteins is variable; 20 to 30% may be bound at the concentrations encountered during acute intoxication. Following therapeutic doses 90 - 100% of the drug may be recovered in the urine within the first day. However, practically no paracetamol is excreted unchanged and the bulk is excreted after hepatic conjugation.

Paracetamol Tablets contain a disintegrant system which accelerates tablet dissolution compared to standard paracetamol tablets.

Human scintigraphy data demonstrate that Paracetamol tablets generally start to disintegrate by 5 minutes post dose in the stomach. There is also less between-subject and less within-subject variability ($p<0.0001$) in early absorption of paracetamol from paracetamol 500 mg Tablets compared to standard paracetamol tablets.

Human pharmacokinetic data demonstrate that the time taken to reach plasma paracetamol therapeutic threshold (4-7mcg/ml) is at least 37% faster with Paracetamol 500 mg Tablets compared to standard paracetamol tablets ($P < 0.05$).

Total extent of absorption of paracetamol from Paracetamol 500 mg Tablets is equivalent to that from standard paracetamol tablets.

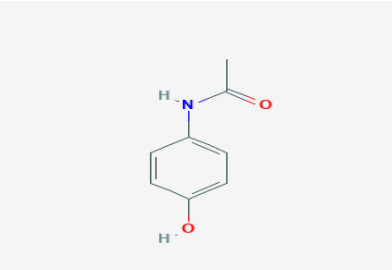
6. Nonclinical properties

6.1. Animal Toxicology or Pharmacology

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

7. Description

Paracetamol is 4-hydroxyacetanilide having molecular formula of $C_8H_9NO_2$ and molecular weight is 151.2 and the chemical structure is:



Paracetamol is white crystals or white, crystalline powder which is freely soluble in ethanol (95%) and in acetone; sparingly soluble in water; very slightly soluble in dichloromethane and in ether.

Paracetamol Tablets are White to off white, oval shaped, uncoated tablet, having break line on one side and plain on other side. The excipients used are Maize Starch, PVPK-30, Microcrystalline Cellulose, Talc, Sodium Starch Glycolate and Magnesium Stearate.

8. Pharmaceutical particulars

8.1. Incompatibilities

Not applicable

8.2. Shelf-life

Do not use later than the date of expiry

8.3. Packaging information

XTPARA 650 is available in strip of 10 Tablets

8.4. Storage and handing instructions

Store in a cool and dry place. Protect from light. Keep out of reach of children.

9. Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies
- Have kidney or liver problems
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illness
- Are taking any medicines (prescription, over-the-counter, vitamins, or herbal products)

10. Details of manufacturer

Manufactured in India by:

Acme Generics LLP

Plot No. 115, HPSIDC, Industrial Area, Davni, P.O. Gurumajra,

Tehsil Nalagarh, Distt. Solan, Himachal Pradesh – 174101.

11. Details of permission or licence number with date

Mfg Lic No. MNB/15/880 issued on 28.09.2015.

12. Date of revision

OCT 2023

MARKETED BY

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