Comprehensive Medication Analysis: paracetamol

Generated:

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Analysis Confidence: 0.75

Evidence Quality: moderate

Analysis Cost: $0.0043

Duration: 200.0s

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Overview

Drug Classification

Drug Class:

Non-opioid analgesic and antipyretic (p-aminophenol derivative)

Mechanism of Action

Exact mechanism not fully elucidated. Primarily inhibits cyclooxygenase (COX) enzymes in the central nervous system, possibly a COX-3 variant, reducing prostaglandin E2 synthesis and hypothalamic fever response. Weak peripheral COX-1/COX-2 inhibition. Additional actions include activation of descending serotonergic inhibitory pathways, transient receptor potential vanilloid 1 (TRPV1) modulation, and inhibition of fatty acid amide hydrolase (FAAH), enhancing endocannabinoid signaling.

Pharmacology

Absorption

Rapidly absorbed from gastrointestinal tract; oral bioavailability 70-90%; onset of analgesia 15-60 minutes; peak plasma concentration 0.5-2 hours.

Distribution & Metabolism

Hepatic phase II conjugation predominant: glucuronidation (50-60%), sulfation (25-35%); minor CYP2E1, CYP1A2, CYP3A4 oxidation to N-acetyl-p-benzoquinone imine (NAPQI), detoxified by glutathione.

Elimination

Primarily renal excretion of metabolites (90-100% within 24 hours); <5% excreted unchanged in urine.

Half-Life:

1.5-3 hours in adults (prolonged to 4-8 hours in hepatic impairment or neonates).

Clinical Use

Approved Indications

1. Relief of mild to moderate pain
2. Reduction of fever

Off-Label Uses

1. Postoperative pain (intravenous formulation)
2. Osteoarthritis pain
3. Headache and migraine
4. Dysmenorrhea

Standard Dosing

Adults: 500-1000 mg orally or rectally every 4-6 hours as needed; maximum 4000 mg/day. Children (≥2 years): 10-15 mg/kg/dose every 4-6 hours; maximum 75 mg/kg/day (not exceeding adult maximum).

Dose Adjustments

Renal Impairment:

CrCl 10-50 mL/min: every 6 hours; CrCl <10 mL/min or hemodialysis: every 8 hours; maximum 3000 mg/day.

Hepatic Impairment:

Mild-moderate: maximum 3000 mg/day; severe (Child-Pugh C): avoid or maximum 2000 mg/day with close monitoring.

Interactions

Drug-Drug Interactions

Ethanol (chronic heavy use) (SEVERE)

Mechanism:

PK: Induction of CYP2E1, increasing toxic NAPQI metabolite formation

Clinical Effect:

Hepatotoxicity, potentially fulminant liver failure

Management:

Avoid concurrent use; if necessary, use minimal effective paracetamol dose and monitor LFTs closely

Evidence Level:

moderate

Warfarin (MODERATE)

Mechanism:

PD/PK: Possible inhibition of warfarin metabolism or enhanced anticoagulant effect

Clinical Effect:

Elevated INR, increased bleeding risk

Management:

Monitor INR frequently, particularly with high-dose or prolonged paracetamol use

Evidence Level:

moderate

Lamotrigine (MODERATE)

Mechanism:

PK: Paracetamol induces lamotrigine glucuronidation

Clinical Effect:

Decreased lamotrigine plasma concentrations, reduced efficacy

Management:

Monitor lamotrigine levels and clinical response; titrate dose as needed

Evidence Level:

moderate

Probenecid (MODERATE)

Mechanism:

PK: Inhibits renal excretion and glucuronidation of paracetamol

Clinical Effect:

Increased paracetamol exposure, risk of toxicity

Management:

Monitor for hepatotoxicity; consider paracetamol dose reduction

Evidence Level:

moderate

Isoniazid (MODERATE)

Mechanism:

PK/PD: Additive hepatotoxicity; possible CYP2E1 induction

Clinical Effect:

Elevated liver enzymes, hepatotoxicity

Management:

Monitor LFTs regularly

Evidence Level:

moderate

Metoclopramide (MINOR)

Mechanism:

PK: Enhanced gastric emptying accelerates absorption

Clinical Effect:

Faster onset of action, no change in overall exposure

Management:

No dose adjustment required

Evidence Level:

moderate

Cholestyramine (MINOR)

Mechanism:

PK: Physical binding in gastrointestinal tract

Clinical Effect:

Reduced paracetamol absorption if co-administered

Management:

Administer paracetamol at least 1 hour before or 4 hours after cholestyramine

Time Separation:

1 hour before or 4 hours after

Evidence Level:

moderate

Activated charcoal (MINOR)

Mechanism:

PK: Adsorption in gastrointestinal tract

Clinical Effect:

Decreased paracetamol bioavailability

Management:

Separate administration by at least 1 hour

Time Separation:

1 hour

Evidence Level:

moderate

Food & Lifestyle Interactions

No significant food interactions identified.

Safety Profile

Adverse Effects

Recommendations

What TO DO: Evidence-Based Recommendations

Monitoring Requirements

Analysis Completed:

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Reasoning Steps: 4

Cost Analysis

Total Cost:

$0.0043

Total Duration: 200.0s

Phase Breakdown

- **Phase 1: Pharmacology Analysis**: $0.0004 (10.3%) - 16.7s
- **Phase 2: Interaction Analysis**: $0.0015 (34.6%) - 114.5s
- **Phase 3: Safety Profile Assessment**: $0.0007 (17.3%) - 20.5s
- **Phase 4: Recommendation Synthesis**: $0.0012 (27.6%) - 31.6s
- **Phase 5: Monitoring Requirements**: $0.0004 (10.1%) - 16.7s

IMPORTANT DISCLAIMER:

This analysis is for educational and research purposes only.
It does not constitute medical advice. Always consult qualified healthcare professionals for
medication decisions, dosing, and management of health conditions.

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