Paracetamol: special dosing advice

Paracetamol is in widespread use as a first-line analgesic across all age groups. This is despite evidence of limited efficacy when compared with placebo in common conditions such as chronic low back pain and osteoarthritis.

In this article, we consider special situations where we may need to adjust the dosing of paracetamol, drawing on several DTB reviews and guidance from the British Hepatology Pharmacy Group (DTB 2018;56:69, DTB 2022;60:84, BHPG Paracetamol position statement 2022).

However, the most important questions initially are: do they need it at all, and, if so, is it helping?

- The standard dose of paracetamol is 0.5–1g four times daily, with a maximum daily dose of 4g.
- In overdose, it can cause liver and, less frequently, renal damage – the therapeutic window is relatively narrow, with 5g over 24h sufficient to cause liver damage, particularly if there are additional risk factors, e.g. alcohol consumption, malnutrition, long-term enzyme-inducing drugs.
- There is no national standard prescribing guidance for paracetamol in higher-risk groups.

Dosing in liver disease

Doses of up to 2g per day are acceptable in cirrhosis (Lancet 2021;398:1359).

(see 'Liver disease and cirrhosis' article for guidance on prescribing in liver disease).

Dosing in renal disease

Irrespective of weight, if eGFR <30ml/min, the interval between doses should be a minimum of 6 hours (BHPG Paracetamol position statement 2022 (BASL)).

Dosing in epilepsy

The BNF reminds us that co-administration of enzyme-inducing antiepileptic medications can increase the risk of hepatotoxicity, and paracetamol doses should be reduced in this group (BNF Online 2022, BNF online - paracetamol, accessed November 2022).

Dosing in the frail elderly

The DTB reviewed the risks of hepatotoxicity at 'standard doses' of paracetamol in the frail elderly (DTB 2018;56:69).

Most trials which have considered the safety and efficacy of paracetamol in a range of settings have excluded those aged 65y or over, or those with multimorbidity. The DTB could not identify any large-scale trials considering these groups.

- Observational studies have suggested that increasing age and frailty reduce clearance of paracetamol, and so higher plasma levels are seen, even if the dose is reduced.
- Case reports have identified elderly patients with elevated trough paracetamol levels above the threshold for *N*-acetylcysteine treatment, despite standard dosing. These events are rare.
- No dose adjustment is required for older people in good health who weigh >50kg.
- The British Geriatric Society guidance on the management of pain in older people suggests 'caution' for elderly patients who are malnourished or weigh less than 50kg (Age and ageing 2013;42 Suppl1:i1).

Dosing for low body weight?

The UK Healthcare Safety Investigation Branch (HISB) reported on the death from hepatotoxicity of a hospitalised patient weighing 40kg who was given standard paracetamol doses (DTB 2022;60:84). The report called for national prescribing guidance for clinicians to avoid risk of iatrogenic harm.

The BNF advises *"clinical judgement should be used to adjust the dose"* of patients with a body weight of under 50kg (BNF online – paracetamol, accessed November 2022).

The summary of product characteristics (SPC) for oral paracetamol does not include any guidance on doses for low body weight (SPC EMC 2022 – paracetamol tablets 500mg (POM)).

The DTB makes the following practical recommendations (DTB 2018;56:69):

- **For very frail patients or those who weigh <50kg (where paracetamol clearance may be affected), dose reduction to either 500mg four times daily or 1g three times daily may be appropriate.**
- **With lower doses, it is important to reassess the effectiveness of the analgesia in this situation (and, indeed, whether it is having any effect at all).**

The British Hepatology Pharmacy Group (a branch of the British Association for the Study of the Liver) has produced a position statement on prescribing weight-adjusted oral paracetamol in adults, which has been taken up by many hospital trusts as guidance (BHPG Paracetamol position statement 2022 (BASL)). We reproduce their quoted figures here precisely, but we recognise some small gaps in the guidance, e.g. at 40.5kg.

	Weight ≤40kg	**Weight 41–49kg**	**Weight >50kg**
Oral dosing	500mg 4 times daily	500mg–1g 3 times daily	500mg–1g 4 times daily
Maximum daily dose	2g	3g	4g

Irrespective of weight, if eGFR <30ml/min, the interval between doses should be a minimum of 6 hours.

Paediatric dosing

The MHRA adjusted the dosing recommendations for paracetamol in children to take better account of their weight and age (DTB 2011;49:74). This change is to more accurately reflect the wide variation in size of children of similar ages. Note that there are two different strengths of paracetamol suspension available.

If we prescribe paracetamol to children, we should use the BNFc age-band doses OR prescribe by weight (15–20mg/kg) up to four times daily (BNFc – paracetamol: indications and dose 2022).

Paracetamol and hypertension

A small British Heart Foundation-funded, double-blind placebo controlled trial assessed the impact of paracetamol on blood pressure control (DTB 2022 60;10:147). Participants with controlled hypertension were enrolled. Exclusions included use of regular paracetamol, NSAIDs or anticoagulants, or those who had existing cardiovascular or liver disease. They were prescribed 1g paracetamol 4 times daily for 2 weeks, or a matching placebo, and then crossed over to the other treatment arm for a further 2 weeks.

- Paracetamol 4g/day for 2 weeks increased systolic blood pressure by 5mmHg compared with placebo.

The authors speculated that prolonged use could impact on cardiovascular risk. However, the MHRA felt the study population was too narrow for this finding to be extrapolated to the general population and did not recommend any regulatory action or update to the product information.

	**Paracetamol: special dosing advice** • First, ask: do they need it? Is it helping? • Consider adjusting the dose and frequency of paracetamol for frail or <50kg elderly patients. • Prescribe paracetamol for children by weight or the narrower age-band dosing regimen. • Be cautious in liver and renal disease.
	How many patients do you have on a regular repeat prescription for paracetamol? Are they taking it? Does it help? Consider auditing paracetamol use in patients <50kg and updating doses in line with guidance.