

APPENDIX 2

Case details for TGA ADRS reports for modified release paracetamol products and overdose (accidental and intentional), hepatotoxicity and liver injury, incorrect dosing and abnormal liver function (searched on 25 June 2018)

ADR reference	Date reported	Date of ADR	Gender/age	Case details
	9/8/2005	Not reported		Patient took up to 8 tablets daily for 5 months. Experienced GI bleeding
	16/6/2008	7/7/2008		Patient developed elevated liver function tests when she received paracetamol (Panadol Osteo) for treatment of arthritis
	12/5/2009	Not reported		Presented with dyspnoea, found to have profound metabolic acidosis; elevated pyroglutamic acid identified in urine
	18/8/2009	9/2/2009		Patient developed paracetamol induced liver impairment and jaundice after treatment with Panadol Osteo (dose 2.6g daily). Other suspected medicines include Lipitor.
	20/8/2009	19/2/2009		Patient developed abnormal hepatic function after receiving Panadol Osteo (6 dose units daily) over a period of 83 days.
	9/9/2009	Not reported		Literature report. Intentional overdose with paracetamol and mirtazapine with hepatic injury. Treated with acetylcysteine
	19/1/2011	20/12/2010		Patient developed nausea and liver injury. Co-suspected medicines included Panadol Osteo, pariet, trimethoprim, Zolof, 'co-arathon' herbal medicine. LFTs improved on ceasing these.

ADR reference	Date reported	Date of ADR	Gender/age	Case details
	27/8/2014	6/8/2014		Patient developed drug induced liver injury after taking Panadol Osteo. LFTs improved after ceasing Panadol osteo. Also taking perindopril and sertraline.
	10/2/2015	1/12/2014		Patient developed possible liver problem after taking Panadol Osteo. Reported by pharmacist, referred to GP for investigation.
	4/4/2017	Not reported		Overdose involving Panadol Osteo, Cymbalta, lamotrigine and cocaine
	4/4/2017	Not reported		The patient experienced an overdose with Panadol Osteo with increased transaminases. Treated with N-acetylcysteine. Took overdose almost 12 hours before acetylcysteine started. Toxicologist advice sought.
	4/4/2017	Not reported		Overdose with multiple agents.
	5/4/2017	Not reported		Overdose with elevated transaminases
	5/4/2017	Not reported		Overdose with Panadol Osteo and epilim. Elevated transaminases, treated with acetylcysteine.
	5/4/2017	Not reported		Overdose with Panadol Osteo and nurofen. Treated with acetylcysteine.
	5/4/2017	Not reported		Overdose with Panadol Osteo. Treated with acetylcysteine.
	5/4/2017	Not reported		Overdose with Panadol Osteo. Treated with acetylcysteine.
	5/4/2017	Not reported		Overdose with Panadol Osteo. Nausea, vomiting and epigastric tenderness.

ADR reference	Date reported	Date of ADR	Gender/age	Case details
	5/4/2017	8/6/2016		Overdose with Panadol Osteo. Transaminases increased, treated with acetylcysteine.
	5/4/2017	Not reported		Overdose with Panadol Osteo. Treated with acetylcysteine.
	5/4/2017	Not reported		Overdose with Panadol Osteo and diazepam. Treated with acetylcysteine.
	5/4/2017	Not reported		Overdose with Panadol Osteo – 30 tablets at 10.00pm presented at 2.00pm the following day. Treated with acetylcysteine 16 hours post. Normal ALT and paracetamol < 10mg/L. Repeat bloods normal. Continued acetylcysteine and retested in 6-8 hours based on large dose ingested and SR form.
	5/4/2017	Not reported		Overdose with Panadol Osteo and temazepam. Treated with acetylcysteine.
	5/4/2017	Not reported		Overdose with Panadol Osteo.
	5/4/2017	Not reported		Overdose with Panadol Osteo and alprazolam. Resulted in metabolic acidosis and hepatotoxicity.
	5/4/2017	Not reported		Overdose with Panadol Osteo. Treated with acetylcysteine.
	5/4/2017	Not reported		Overdose with Panadol Osteo – 96 tablets. Report via Poisons Information Centre Qld. Treated with acetylcysteine. Acidosis but resolved. Referred to tox as over 40g.
	5/4/2017	Not reported		Overdose with Panadol Osteo. Treated with acetylcysteine.

ADR reference	Date reported	Date of ADR	Gender/age	Case details
	5/4/2017	Not reported		Overdose with Panadol Osteo. Treated with acetylcysteine. Advice sought re treatment of MR paracetamol.
	5/4/2017	Not reported		Overdose with Panadol Osteo, 110 tablets. Treated with acetylcysteine.
	5/4/2017	13/9/2015		Overdose with Panadol Osteo 60g. Treated with acetylcysteine.
	5/4/2017	Not reported		Overdose with Panadol Osteo 32 tablets. Treated with acetylcysteine.
	5/4/2017	Not reported		Overdose with Panadol Osteo (10 tablets) and paroxetine 20mg (30 tablets).
	5/4/2017	Not reported		Overdose with Panadol Osteo. Developed anaphylactoid reaction
	5/4/2017	Not reported		Overdose with Panadol Osteo, amitriptyline and diazepam.
	5/4/2017	Not reported		Overdose with Panadol Osteo, ibuprofen and diazepam.
	5/4/2017	Not reported		Overdose with Panadol Osteo and carbimazole. Treated with acetylcysteine.
	5/4/2017	Not reported		Overdose with Panadol Osteo. Treated with acetylcysteine.
	5/4/2017	Not reported		Overdose with Panadol Osteo. Approx 24g, treated with acetylcysteine.
	5/4/2017	Not reported		Overdose with Panadol Osteo. Treated with acetylcysteine.

ADR reference	Date reported	Date of ADR	Gender/age	Case details
	5/4/2017	Not reported		Reported via Poisons Information Centre Qld. Overdose with Panadol Osteo. Presented 5 days after ingesting overdose. Hepatotoxicity, advice sought from paediatrics and hepatology.
	5/4/2017	Not reported		Child overdose with Panadol Osteo. Transaminitis, paracetamol level >10. Treated with acetylcysteine.
	5/4/2017	Not reported		Overdose with Panadol Osteo (240 tablets). Delayed presentation, nausea, haematemesis, hepatotoxicity, thrombocytopenia and coagulopathy (INR 6.6). Treated with acetylcysteine. Advised to seek advice from liver unit and toxicology.
	5/4/2017	Not reported		Overdose with Panadol Osteo 84 tablets. Developed vomiting and liver tenderness.
	5/4/2017	5/10/2012		Overdose with Panadol Osteo (36 tablets) and phenylephrine. Information from Poisons Information Centre Qld.
	5/4/2017	Not reported		Overdose with Panadol Osteo 36 tablets. Nausea, abdominal discomfort, dizziness, malaise. Treated with acetylcysteine. Information from Poisons Information Centre Qld.
	5/4/2017	Not reported		Overdose with Panadol Osteo and methotrexate.
	5/4/2017	Not reported		Overdose with Panadol Osteo. Developed drowsiness, vomiting and elevated transaminases. Treated with acetylcysteine.

ADR reference	Date reported	Date of ADR	Gender/age	Case details
	28/3/2017	16/2/2017		Developed hepatitis. Thought probable statin induced hepatitis, also taking Panadol Osteo. Medications subsequently ceased.
	15/5/2017	Not reported		Patient suffered myocardial infarction elevated BP and leg pain. Patient reported taking Pandol osteo 1.5 tablets four times per day (6 total), incorrect dosing.
	3/11/2017	Not reported		Patient reported taking Panadol Osteo. Dose and period of administration were not reported. Patient developed pain, headache, decreased mobility, eye pain, pain in extremity, chest pain, leg swelling, hallucination and excessive sleep. It was also reported that incorrect dosage was administered but no further information provided on this.
	20/11/2017	Not reported		Patient was taking Pandol osteo three times per day for an unknown duration of time. It was reported that she subsequently developed addiction and product used in unapproved indication.
	22/11/2017	5/11/2017		Patient was taking Panadol Osteo. She later experienced an increase in pain, product label confusion and accidental overdose and liver disorder. No further details provided.
	16/5/2018	Not reported		Patient vomiting after taking 12-14 tabs of paracetamol in total for pain due to new dental braces. Referred to hospital by PIC for blood test given symptoms. ?4x Panamax + 8x Panadol Osteo, definitely no more than 14 tabs - no doses in previous 24h Below toxic dose even if all MR formulation.