

01 - Psychotropics in overdose

Psychotropics in overdose

The Maudsley® Prescribing Guidelines in Psychiatry, Fifteenth Edition. David M. Taylor, Thomas R. E. Barnes and Allan H. Young. © 2025 David M. Taylor. Published 2025 by John Wiley & Sons Ltd. Chapter 13 Psychotropics in overdose Suicide attempts and suicidal gestures are frequently encountered in psychiatric and general practice, and psychotropic drugs are often taken in overdose (Table 13.1). This section gives brief details of the toxicity in overdose of commonly used psychotropics. It is intended to help guide drug choice in those thought to be at risk of suicide, to give some indication of safe quantities to prescribe and to help identify symptoms of overdose. This section gives no information on the treatment of psychotropic overdose and readers are directed to specialist poisons centres. In all cases of suspected overdose, urgent referral to acute medical facilities is, of course, strongly advised. Psychotropic drugs in special conditions Table 13.1 Psychotropic drugs in overdose. Drug or drug group Toxicity in overdose* Smallest dose likely to cause death Signs and symptoms of overdose Antidepressants Agomelatine^{1,2} Low No deaths reported. In early trials, 800mg was maximum tolerated dose. EU SPC reports no serious effects from 2.45g overdose. A mixed overdose of 7.5g caused only drowsiness and mild tachycardia. Sedation, agitation, stomach pains, dizziness Brexanolone³ Not known No deaths reported. Two cases of accidental overdose due to pump malfunction. Sudden loss of consciousness (Continued)

914 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 13 Table 13.1 (Continued) Drug or drug group Toxicity in overdose* Smallest dose likely to cause death Signs and symptoms of overdose Bupropion⁴⁻⁷ Moderate Around 4.5g, although largest overdose of 15g was not fatal.^{3,8} Tachycardia, seizures, QRS prolongation, QT prolongation, arrhythmia. Agitation and toxic psychosis also reported. Fatal serotonin syndrome may occur if taken with venlafaxine.⁹ Dextromethorphan and bupropion³ Probably moderate Unclear. Bupropion inhibits metabolism of the dextromethorphan which may result in more severe/persistent overdose. Bupropion: as above Dextromethorphan: nausea, vomiting, stupor, coma, respiratory depression, seizures, tachycardia, hyperexcitability, toxic psychosis Duloxetine¹⁰⁻¹³ Low Unclear - no deaths from single overdose reported but involved in numerous mixed overdose deaths. Drowsiness, bradycardia, hypotension May be asymptomatic Esketamine¹⁴ Not known Unclear. No deaths reported. Predicted to mirror ketamine overdose including sedation, hypertension, tachycardia, respiratory depression.¹⁵ Ketamine¹⁶ Moderate Iatrogenic overdoses of up to 50mg/kg IV are not usually fatal if prompt treatment is given. Mechanical ventilation may be required. Illicit overdose is rarely fatal unless

other drugs present.¹⁵ Sedation, respiratory depression, hypertension, tachycardia
 Lofepamine^{17,18} Low Unclear. Fatality unlikely if lofepramine taken alone. Sedation, coma, tachycardia, hypotension MAOIs^{17,19-21} (not moclobemide) High Phenzelzine - 400mg
 Tranylcypromine - 200mg Tremor, weakness, confusion, sweating, tachycardia, hypertension
 Mianserin²²⁻²⁴ Low Unclear but probably more than 1000mg. Fatality unlikely if mianserin taken alone. Sedation, coma, hypotension, hypertension, tachycardia, possible QT prolongation
 Mirtazapine^{4,25-28} Low Fatality unlikely in overdose of mirtazapine alone. One death reported following overdose with 990mg.²⁹ Sedation. Even large overdose may be asymptomatic. Tachycardia/ hypertension sometimes seen. Agitation. Moclobemide^{30,31} Low Unclear, but probably more than 8g. Fatality unlikely if moclobemide taken alone. Vomiting, sedation, disorientation Reboxetine^{4,32} Low Not known. Fatality unlikely in overdose of reboxetine alone. Sweating, tachycardia, changes in blood pressure SSRIs^{18,33-36} Low Unclear. Probably above 1-2g. Fatality unlikely if SSRI taken alone. Vomiting, tremor, drowsiness, tachycardia, ST depression. Seizures and QT prolongation possible. Citalopram most toxic of SSRIs in overdose^{28,37} (coma, seizures, arrhythmia); escitalopram is less toxic.^{38,39}

Psychotropic drugs in special conditions CHAPTER 13 Table 13.1 (Continued) Drug or drug group Toxicity in overdose* Smallest dose likely to cause death Signs and symptoms of overdose
 Trazodone^{11,40-43} Low Unclear but probably more than 10g. Fatality unlikely in overdose of trazodone alone. Mortality rate about 1 in 10,000 overdose exposures.²⁸ Drowsiness, nausea, hypotension, dizziness. Rarely QT prolongation, arrhythmia. Tricyclics^{17,19,20,44} (not lofepramine) High Around 500mg. Doses over 50mg/kg usually fatal. Sedation, coma, tachycardia, arrhythmia (QRS, QT prolongation), hypotension, seizures Venlafaxine^{4,45-48} (desvenlafaxine causes similar effects but may be less toxic⁴⁹) Moderate Probably above 5g, but seizures may occur after ingestion of 1g Vomiting, sedation, tachycardia, hypertension, seizures, acidosis, hypoglycaemia. Rarely QT prolongation, arrhythmia, rhabdomyolysis. Very rarely cardiac arrest/MI, heart failure.
 Vilazodone^{50,51} Low Doses below 300mg are not fatal. No fatalities recorded in 714 overdose exposures.²⁸ Drowsiness, agitation, vomiting, seizures Vortioxetine⁵² Low Unclear. An overdose of 250mg caused no symptoms. Nausea, somnolence, diarrhoea, pruritis Antipsychotics
 Amisulpride⁵³⁻⁵⁵ Moderate Around 16g QT prolongation, arrhythmia, cardiac arrest
 Aripiprazole⁵⁶⁻⁵⁸ Low Unclear. Fatality unlikely when taken alone. Sedation, lethargy, GI disturbance, drooling Asenapine⁵⁹ Probably low Unclear. No deaths from overdose reported. Oral absorption very limited. Sedation, confusion, facial dystonia, benign ECG changes Brexpiprazole³ Probably low No information available Presumably agitation and nausea Butyrophenones⁶⁰⁻⁶² (e.g. haloperidol) Moderate Haloperidol - probably above 500mg. Arrhythmia may occur at 300mg. Sedation, coma, dystonia, NMS, QT prolongation, arrhythmia Cariprazine⁶³ Low EU SPC reports one (non-fatal) overdose of 48mg Sedation, low blood pressure Clozapine^{64,65} Moderate Around 2g, but very much lower in those not tolerant to its effects⁶⁶ Lethargy, coma, tachycardia, hypotension, hypersalivation, pneumonia, seizures Iloperidone⁶⁷⁻⁶⁹ Probably moderate Unclear but probably more than 500mg. Potent effect on QT interval. Sedation, tachycardia, respiratory depression, hypotension likely Lumateperone⁷⁰ Probably low No overdoses reported Presumably sedation and dizziness (Continued)

916 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 13 Table 13.1 (Continued) Drug or drug group Toxicity in overdose* Smallest dose likely to cause death Signs and symptoms of overdose
 Lurasidone⁷¹ Low Unclear. An overdose of 1360mg was not fatal.⁷² One study reported

no deaths in 821 overdose exposures.²⁸ Very limited information. Minimal effect on QT interval. Olanzapine^{64,73-76} Moderate Unclear. Fatal outcomes have been reported for acute overdoses as low as 450mg. Lethargy, confusion, myoclonus, myopathy, hypotension, tachycardia, delirium. Possibly QT prolongation. Olanzapine and samidorphan³ Moderate Unclear. An overdose of 110mg/110mg was not fatal. Possible altered risk of fatality in opioid overdose due to opioid blockade. As for olanzapine Phenothiazines^{60,77-79} (e.g. chlorpromazine, fluphenazine) Moderate Chlorpromazine 5-10g Sedation, coma, tachycardia, arrhythmia, pulmonary oedema, hypotension, QT prolongation, seizures, dystonia, NMS Pimavanserin⁸⁰ Not known No overdoses reported but pimavanserin prolongs QT interval in clinical doses. Probably QT prolongation and arrhythmia. ?Nausea, vomiting, confusion.⁸¹ Quetiapine^{28,64,82,83} Moderate Unclear. Probably more than 5g. Fatalities can occur in single substance overdose. Lethargy, delirium, tachycardia, QT prolongation, respiratory depression, hypotension, rhabdomyolysis, NMS Risperidone^{64,84,85} (assume the same for paliperidone) Low Unclear. Fatality rare in those taking risperidone or paliperidone alone. Lethargy, dystonia, tachycardia, changes in blood pressure, QT prolongation. Renal failure with paliperidone. Ziprasidone⁸⁶⁻⁹¹ Low Around 10g. Fatality unlikely when taken alone. Drowsiness, lethargy, QT prolongation, Torsades de pointes Mood stabilisers Carbamazepine⁹²⁻⁹⁴ Moderate Around 20g, but seizures may occur at around 5g; an overdose of 44g was not fatal. Somnolence, coma, respiratory depression, ataxia, seizures, tachycardia, arrhythmia, electrolyte disturbance Lamotrigine^{95,96} Low At least 4g. Two deaths reported - one after 4g, the other after 7.5g, but overdoses of >40g have not proved fatal. Drowsiness, vomiting, ataxia, seizures, tachycardia, dyskinesia, QT prolongation Lithium⁹⁷⁻⁹⁹ Moderate Chronic toxicity probably more dangerous but single overdose is occasionally fatal. Six acute overdose deaths recorded in UK 2005-2012.¹⁰⁰ Nausea, diarrhoea, tremor, confusion, weakness, lethargy, seizures, coma, cardiovascular collapse, bradycardia, arrhythmia, heart block, renal failure Valproate¹⁰¹⁻¹⁰⁵ Moderate Unclear but probably more than 20g. Doses over 400mg/kg cause severe toxicity. Somnolence, coma, cerebral oedema, respiratory depression, blood dyscrasia, hypotension, hypothermia, seizures, electrolyte disturbance (hyperammonaemia)

Psychotropic drugs in special conditions CHAPTER 13 Table 13.1 (Continued) Drug or drug group Toxicity in overdose* Smallest dose likely to cause death Signs and symptoms of overdose Others Benzodiazepines¹⁰⁶⁻¹⁰⁸ Low Probably more than 100mg diazepam equivalents. Often involved in fatal mixed overdose but can be fatal when taken alone. Alprazolam is most toxic. Drowsiness, ataxia, nystagmus, respiratory dysarthria, depression, coma Buspirone²⁸ Low Limited data. Deaths not reported. Not known Daridorexant³ Not known No overdoses reported. In trials, 200mg was maximum dose. Not known. Likely increased somnolence, muscle weakness, cataplexy-like symptoms, headache. Lemborexant³ Not known No overdoses reported. In trials, 75mg was maximum dose. Not known. Likely increased somnolence. Methadone¹⁰⁹⁻¹¹¹ High 20-50mg may be fatal in non-users. Co-ingestion of benzodiazepines increases toxicity. Drowsiness, nausea, hypotension, respiratory depression, coma, pulmonary oedema, constricted pupils, rhabdomyolysis Modafinil¹¹²⁻¹¹⁴ Low Unclear, but no fatalities reported. Overdoses of >6g have not caused death. Tachycardia, insomnia, agitation, anxiety, nausea, hypertension, dystonia Pitolisant¹¹⁵ Not known No overdoses reported. In trials, 216mg was maximum dose. Probably QT prolongation, headache, insomnia, irritability, nausea, abdominal pain Pregabalin¹¹⁶⁻¹¹⁸ Low Often involved in fatal mixed overdose (e.g. with opiates) but can be fatal when taken alone. One overdose of 8.4g caused unconsciousness and coma. May be asymptomatic. Sedation and coma may occur Solriamfetol³ Not known No overdoses reported. In trials, 1200mg was maximum dose. Probably hypertension, tachycardia, QT prolongation Suvorexant^{114,119} Low Unclear. No deaths reported.

An overdose of 100mg caused enhanced sedation. Sedation, vomiting Zolpidem120-122 Low Unclear. Probably >200mg, but an overdose of 9g was not fatal. Fatality rare in those taking zolpidem alone. Drowsiness, agitation, respiratory depression, tachycardia, coma, absent brainstem reflexes Zopiclone106,123,124 Low Unclear. Probably >100mg. Fatality rare in those taking zopiclone alone. Ataxia, nausea, diplopia, drowsiness, coma * High = less than 1 week's supply likely to cause serious toxicity or death. Moderate = 1-4 weeks' supply likely to cause serious toxicity or death. Low = death or serious toxicity unlikely even if more than 1 month's supply taken. GI, gastrointestinal; IV, intravenous; MAOIs, monoamine oxidase inhibitors; MI, myocardial infarction; NMS, neuroleptic malignant syndrome; SPC, summary of product characteristics.

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