# Alprazolam (Xanax)



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**Drug overview:** *Alprazolam* is a benzodiazepine with an intermediate onset of action. It is best known by the brand name **Xanax** (*pronounced zan~ax*). It was introduced as a treatment for anxiety and panic disorders in the US in 1981 and became a popular recreational drug.<sup>1</sup>

**Background:** Although reports of alprazolam use and adulteration date back a decade or more<sup>2</sup> the recreational use of benzodiazepines in the UK has typically involved those prescribed by the NHS, in particular diazepam diverted from regulated supplies or imported.<sup>3</sup>



2mg Xanax bar

A number of unlicensed benzodiazepines, such as *phenazepam* and *etizolam* have emerged on the new psychoactive substance (NPS) market in the last decade.<sup>4</sup> The availability and popularity of alprazolam in the UK appears relatively recent.

The current size of the illicit UK benzodiazepine market is unknown, but a 2018 parliamentary debate reported that over 130 million benzodiazepines and other hypnotics were diverted from the regulated supply chain in the last three years.<sup>5</sup> Alprazolam accounted for over 3% of total UK dark-web trades in a 2017 study.<sup>6</sup>

There are no accurate UK estimates of alprazolam prevalence but there are numerous indications that the drug has become more widely available and popular for both self medication and as a recreational drug.<sup>5,6,7,8,9,10,11,12,13,14</sup>

**Availability:** Alprazolam is not available on the NHS, but is available in 0.25mg (250mcg) and 0.5mg (500mcg) tablets with a private/online prescription. Other websites offer alprazolam in 1mg and 2mg doses without a prescription (see 'Legal Status' page 6).

User forums and local intelligence suggest alprazolam is readily available in 1mg tablets and 2mg bars from street deals and from foreign and crypto (dark-web) markets.<sup>6,7,8</sup> It is believed that counterfeit Xanax can be more potent than the stated dose and/or may also be sold in more potent 'pressed high dose' form.<sup>7,8,9,17</sup>

**Chemical name:** 8-chloro-1-methyl-6-phenyl-4H-[1,2,4]triazolo[4,3-a] [1,4]benzodiazepine.<sup>18</sup>

**Brain chemistry:** Alprazolam, like other benzodiazepines, binds to benzodiazepine receptors (BZR) which in turn change how GABA-A receptors function. Benzodiazepines effectively "enhance" the effect of GABA at GABA receptors, reducing electrical charge within neurons.<sup>18</sup>

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**Brand names:** Xanax is by far the most well known brand name for alprazolam, but there are numerous other brand names such as *Alprazolan, Alprox, Alpraz, Cassadan, Ralozam, Tafil, Trankimazin* etc.<sup>19</sup>

**Classification:** Alprazolam belongs to a class of benzodiazepines called *triazolobenzodiazepines* and is classed as a depressant drug.

**Appearance:** Legitimate pharmaceutical Xanax comes in doses of:



**0.25mg:** white, oval, scored, imprinted 'XANAX 0.25'





**0.5mg:** peach, oval, scored, imprinted 'XANAX 0.5'





**1mg:** blue, oval, scored, imprinted 'XANAX 1.0'



**2mg:** white, oblong, multiscored, imprinted 'XANAX' on one side and '2' on the reverse side.

Yellow and green Xanax bars are 2mg. Red/Pink Xanax bars either generic or fake have been thought to be up to 5mg. Pharmaceutical Xanax comes in controlled release form (up to 12 hours) and instant release form (3-6 hours) and is also available as an oral solution.

Alprazolam in the UK recreational drug market usually comes in two main forms: blister packed generic brands and pressed Xanax bars. Generic brands and fakes come in both white and various shades of blue, violet, purple and pink. Alprazolam is also sold in powder form<sup>20</sup> and there have been unconfirmed reports of alprazolam powder\* in UK prisons.<sup>8,9</sup>

**Potency:** Alprazolam is 20 times the potency of diazepam i.e. 0.5mg of Alprazolam is equal to 10mg of diazepam.<sup>21</sup> Alprazolam is approximately twice as potent as etizolam.

**Cost:** The price for the legitimate Pharmacia product is  $60 \times 0.5$ mg Xanax tablets for £6.09. Online pharmacies offer 1mg tablets for under £1 each in quantities of 100 or more, while bulk dark-web prices are as low as 40p a tablet. UK street prices are thought to be around £1.50 for 1mg and £3-5 for a 2mg Xanax bar, but like all street prices these vary considerably and are cheaper the more are purchased.

<sup>\*</sup>When in powdered form estimating dosage becomes far more problematic. The powder is often dissolved into a liquid to more accurately estimate dose, known as volumetric liquid dosing.

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#### Route of administration:

Oral	Snorting	Smoking & Injecting
Swallowing alprazolam tablets is the safest route of use. Some online forums suggest a more rapid onset of effects if the tablets are chewed or ground to a powder and swallowed in a cigarette paper (bombed/parachuted) as powder may be absorbed more quickly. <sup>22</sup>	A recent UK report describe a 'ketamine-like' effect when alprazolam is snorted.8 Some websites claim snorting increases potency23 but most user forum discussions maintain snorting is ineffective. The effects felt are due to powder slipping down the throat after snorting and are more rapid due to the drug being in powdered	Smoking & Injecting  Smoking alprazolam is thought ineffective.  Alprazolam is non water soluble. Injecting any sort of crushed tablet may cause serious vascular and tissue damage due to the filler content and overdose is also more likely. Alprazolam has been reported as an adulterant in UK heroin and in a recent Scottish incident was sold as heroin. 9,26
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**Therapeutic dose:** Short-term use in anxiety; adult 0.25mg-0.5mg 3 times a day; elderly 0.25mg 2-3 times a day. Doses may be increased up to 3mg daily.<sup>27,28</sup>

**Recreational dose:** Online forums generally suggest the following oral doses:

Light	0.25mg	Common	0.5mg to 1.5mg
Strong	2mg	Heavy	3mg

**Onset and duration of effects:** Effects start within 20-40 minutes. The main effects peak within 1-2 hours.<sup>29,30</sup> User reports claim the effects of the drug last from 2-6 hours with lingering after-effects for up to 12 hours.<sup>31</sup> Alprazolam is eliminated from the body (half-life) in 6-12 hours as opposed to the 20-100 hours for diazepam.

**Subjective effects:** Alprazolam has been described as less 'buzzy' (stimulating) but more euphoric than etizolam, but more 'buzzy' and just as euphoric as diazepam<sup>32</sup> as well as being shorter acting and more sedating than both of them. There are reported strong physical feelings of pleasure, relaxation and bodily comfort, disinhibition and reduction in anxiety. Sedation/lethargy is dose-related and has been described as feeling "stoned/lobotomised' and in higher doses forcing sleep and unconsciousness.

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Physical effects may include: 31,32,33	Psychological effects may include: 31,32,33
Sedation Dizziness Muscle relaxation Motor control loss Respiratory depression Seizure suppression Decreased heart rate Perception of bodily heaviness Physical euphoria Visual effects Blurred vision Slurred speech	Amnesia Anxiety suppression Confusion and slowing of thoughts Euphoria Disinhibition Compulsive redosing Dampening of emotions Lethargy

**After-effects:** A paradoxical increase in hostility and aggression may be reported by patients taking any benzodiazepine.<sup>27,28</sup> After-effects such as rebound anxiety, vivid dreams,<sup>34</sup> irritability and grogginess are commonly reported by recreational users the following day.

**Prescribed drug interactions/contraindications:** Interactions leading to an increase in availability (the amount of alprazolam required to produce its pharmacological effects) are known to occur with a number of prescribed drugs.<sup>27,28</sup> A similar effect may be caused by grapefruit.<sup>35</sup> Prescribing alprazolam is contraindicated for a number of conditions\*. Avoidance when driving, during pregnancy and while breast feeding are recomended.<sup>27,28,36</sup>

**Hepatotoxicity:** A small number of case reports of acute liver injury have been reported.<sup>37</sup>

**Tolerance and dependence:** If taken over an extended period alprazolam causes physical and psychological dependence. In particular there is evidence of rapid tolerance, dependence and withdrawal among opioid users.<sup>38</sup> Tolerance will develop to the sedative-hypnotic effects within a short period of continuous use.<sup>39</sup> Sudden withdrawal for dependent individuals is potentially dangerous, sometimes resulting in seizures or death.<sup>40</sup>

**Withdrawal:** Effects can include increased anxiety, agitation, confusion and panic attacks, and can lead to acute psychosis in vulnerable people. Withdrawal should be medically supervised, usually by substituting with a longer acting benzodiazepine such as diazepam and tapering the dose over an extended period.<sup>21</sup> There is evidence that benzodiazepines with a short elimination half-life cause a more severe withdrawal than those with a long elimination half-life. Alprazolam withdrawal syndrome is reported to be especially intense and/or long lasting.<sup>41</sup>

<sup>\*</sup>Acute pulmonary insufficiency, marked neuromuscular respiratory weakness, sleep apnoea syndrome, unstable myasthenia gravis, chronic psychosis, hyperkinesis, obsessional states, phobic states and respiratory depression.

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**Poly drug use:** Benzodiazepines are used on their own but commonly also with alcohol and a wide range of other drugs, for example: enhancing the relaxing/sedative effects of cannabis, taking the edge off stimulant drug come-down, bringing people out of a psychedelic drug trip and in cases reported from UK festivals in 2017, used to enhance the dissociative effects of other drugs such as ketamine.<sup>3,12</sup> Benzodiazepines are commonly used by opioid users in combination with heroin or methadone, causing severe drowsiness and clumsiness and an increased risk of accidents or overdose.<sup>3</sup>

**Overdose:** Signs of an overdose include confusion, impaired coordination, diminished reflexes and coma. Overdose death has been reported with alprazolam alone and with a single alprazolam tablet and alcohol. <sup>42</sup> Fatalities from taking alprazolam alone are thought rare, <sup>36,42</sup> however simultaneous use of alprazolam with any other benzodiazepines or depressant drugs such as heroin, methadone, buprenorphine (Subutex/Suboxone), gabapentinoids (Pregabalin and Gabapentin) and alcohol greatly increases the risk of non-fatal and fatal overdose through respiratory depression. <sup>43,44</sup>

Benzodiazepine use is often a factor in drug related deaths in opioid users, with benzodiazepines a contributing factor in 28% and present in 72% of Scottish drug related deaths. Figures for alprazolam deaths alone are not available, but between 2012 to 2016 the number of deaths where benzodiazepines were mentioned rose from 284 to 406 in England and Wales.

**Emergency situations:** In the event of any serious adverse reactions or illness go to A&E or ring for an ambulance. As unconsciousness or overdose is possible try to make sure a friend is around who is not using the drug. If a user becomes unconscious place them in the recovery position to prevent choking, then call an ambulance (see images below).



Start by placing their arm as if they are waving.



Place the other arm across their chest and hold their hand against their cheek.



Lift up the knee that is furthest from you. Continue to hold their hand in place.



Turn them on their side by pulling the knee towards you and down.

For further information on Overdose & Emergencies see UK and Ireland DrugWatch Information Sheet.

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**Legal Status:** Alprazolam is controlled by the Misuse of Drugs Act as a Class C schedule 4 drug. Possession is legal if the drug was obtained with a prescription. Possession without a prescription could lead to a charge (maximum sentence up to 2 years). Supplying or attempting to supply alprazolam carries penalties of up to 14 years and/or a fine.<sup>47</sup>

**Drug screening:** Alprazolam will cross react with most benzodiazepine immunoassays but it will be present in urine at much lower amounts than diazepam because the effective dose is 20 times lower. It is detectable after high doses. Not all immunoassays use the same antibodies so their sensitivity to alprazolam may vary.<sup>48</sup>

#### Harm reduction advice for clients:

- Wherever possible, do not use on your own.
- Look after your friends.
- Alprazolam is 20 times the potency of diazepam. Try a small test amount (e.g. 0.25mg) and wait at least 1 hour before taking any more.
- Do not drive or operate machinery as accidents can occur from everyday activities...
   like trying to stand up.
- Place sleeping people in the recovery position (see diagram page 5).
- Injecting crushed tablets in a solution is very dangerous as the tablets contain high amounts of filler which can lead to collapsed veins and cause serious vascular and tissue damage.
- Be aware that tolerance and dependency can develop quickly.
- It is best not to take alprazolam on a regular basis and for more than 4 weeks due to the tolerance and dependence that can develop.
- If you have been using on a regular basis alprazolam should not be stopped suddenly. Always reduce use gradually with your doctor's supervision.
- The risk of overdose is much higher when alprazolam is taken together with alcohol, opioids or any other depressant drugs.
- Naloxone will not reverse the effects of benzodiazepine drugs like alprazolam, but it will reverse the effects of any opioid drugs that have also been taken. If unsure what has been taken naloxone should still be administered.

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Where to get help: We would advise anyone experiencing issues from alprazolam or other substances to seek medical support via their GP or the NHS. There are a wide range of local drug services throughout the UK, to find out what is available in your area please use the links:

England: Find Support | Frank Scotland: Scottish Drug Services

Wales: **Dan 24/7** Northern Ireland: **Public Health Agency** ROI: **DRUGS.ie** 

For further advice, medical professionals can use the National Poisons Information Service 24-hour telephone service on 0344 892 0111 or its online database, TOXBASE. Any health professional encountering an unusual or unexpected adverse reaction to the use of alprazolam (or any other drug) should report the reaction to **RIDR**.

#### **References:**

- National Survey on Drug Use and Health (NSDUH-2016). https://www.datafiles.samhsa.gov/study/national-surveydrug-use-and-health-nsduh-2016-nid17184 (accessed February 2018).
- Ramsey J, Scott J. Contaminants and routes of drug administration - key points for Harm Reduction practitioners. Presentation at National Conference on Injecting Drug Use. Nov 19th-24th 2008.
- 3. Newcombe R. Wobbled Up: The illicit use of diazepam in Redcar. Lifeline 2010. <a href="http://michaellinnell.org.uk/michaellinnellinnellinnellinnellinn
- UK and Ireland DrugWatch/Scottish Drugs Forum. Etizolam information Sheet, 2014. <a href="http://www.thedrugswheel.com/resources/Etizolam\_Infosheet\_SDF\_DrugWatch1\_2.pdf">http://www.thedrugswheel.com/resources/Etizolam\_Infosheet\_SDF\_DrugWatch1\_2.pdf</a> (accessed February 2018).
- Misuse of Xanax. Public Administration and Constitutional Affairs Committee – in the House of Commons on 15th January 2018. <a href="https://www.theyworkforyou.com/debates/?id=2018-01-15b.696.13&s=drugs#g701.0">https://www.theyworkforyou.com/debates/?id=2018-01-15b.696.13&s=drugs#g701.0</a> (accessed February 2018).
- Analysis of data reported in Guardian. 5.2.2018. <a href="https://www.theguardian.com/society/2018/feb/05/xanax-misuse-uk-dark-web-sales-health?CMP=Share\_iOSApp\_Other.">https://cmp-Share\_iOSApp\_Other.</a>

   Taken from Dittus M, Wright J, Graham M. Platform Criminalism: The 'Last-Mile' Geography of the Darknet Market Supply Chain. <a href="https://arxiv.org/abs/1712.10068">https://arxiv.org/abs/1712.10068</a>
   (accessed February 2018).
- Flemen K, Drink and Drugs News, April 2017. <a href="https://drinkanddrugsnews.com/wp-content/uploads/2017/04/DDN-April-2017-web.pdf">https://drinkanddrugsnews.com/wp-content/uploads/2017/04/DDN-April-2017-web.pdf</a> (accessed February 2018).
- Greater Manchester Drugs Early Warning System. Professional Information Network posts 2016/2017. Not in the Public Domain.
- 9. UK and Ireland DrugWatch Forum posts 2016/2017. Not in the Public Domain.
- BBC News report May 2017. 20 teenagers hospitalized in Wiltshire.http://www.bbc.co.uk/news/uk-englandwiltshire-39855184 (accessed February 2018).

- North Wales Police. Gottwood Festival Test Results of Amnesty bin seizures. 8-9th June 2017. Not in the Public Domain.
- 12. Chill Welfare/Scottish Drugs Forum. Welfare briefing/key drug trends, Summer 2017. Not in the Public Domain.
- Public Health England. Drug health harms national intelligence briefing December 2017. Not in the Public Domain.
- 14. Police Scotland. Drug Trend Bulletin Issue 17 December 2017. Not in the Public Domain
- 15. For example: UK online pharmacy offering alprazolam. <a href="http://www.lloydspharmacy.com/">http://www.lloydspharmacy.com/</a>
- For example: Website offering 1mg and 2mg alprazolam without prescription. <a href="http://www.uksleeping-pills.com/">http://www.uksleeping-pills.com/</a> (accessed February 2018).
- 17. UK Chemical Research discussion forum. <a href="https://www.ukchemicalresearch.org/Thread-Alprazolam-Xanax-harm-reduction-and-comparison-to-diazepam-and-etizolam">https://www.ukchemical Research discussion forum. <a href="https://www.ukchemicalresearch.org/Thread-Alprazolam-Xanax-harm-reduction-and-comparison-to-diazepam-and-etizolam">https://www.ukchemical Research discussion forum. <a href="https://www.ukchemicalresearch.org/Thread-Alprazolam-Xanax-harm-reduction-and-comparison-to-diazepam-and-etizolam">https://www.ukchemicalresearch.org/Thread-Alprazolam-Xanax-harm-reduction-and-comparison-to-diazepam-and-etizolam</a> (accessed February 2018).
- Haefely W. Benzodiazepine interactions with GABA receptors. Neurosci Lett. 1984 Jun 29;47(3):201-6. <a href="http://www.ncbi.nlm.nih.gov/pubmed/6147796">http://www.ncbi.nlm.nih.gov/pubmed/6147796</a> (accessed February 2018).
- PubChem, US National Library of Medicine. <a href="https://pubchem.ncbi.nlm.nih.gov/compound/alprazolam#">https://pubchem.ncbi.nlm.nih.gov/compound/alprazolam#</a> (accessed February 2018).
- 20. Online vendor selling alprazolam powder. <a href="https://www.kamuddrugs.com/product/alprazolam-powder/">https://www.kamuddrugs.com/product/alprazolam-powder/</a> (accessed February 2018).
- Ashton C H, Benzodiazepines how they work and how to withdraw, (aka The Ashton Manual) 2002. <a href="https://www.benzo.org.uk/manual/index.htm">https://www.benzo.org.uk/manual/index.htm</a> (accessed February 2018).
- Drugs Forum: discussion of swallowing/chewing 'parachuting' alprazolam. <a href="https://drugs-forum.com/threads/alprazolam-chewing-vs-swallowing.69037/">https://drugs-forum.com/threads/alprazolam-chewing-vs-swallowing.69037/</a> (accessed February 2018).
- Example of website claiming alprazolam snorting is more potent. <a href="http://prescription-drug.addictionblog.org/snorting-xanax/">http://prescription-drug.addictionblog.org/snorting-xanax/</a> (accessed February 2018).
- Reddit forum: arguments against snorting alprazolam. https://www.reddit.com/r/Drugs/comments/5njqpm/ snorting\_xanax/ (accessed February 2018).

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- 25. Drugs Forum: arguments against snorting alprazolam. https://drugs-forum.com/threads/got-some-xannies-what-does-snorting-them-do.184230/ (accessed February 2018).
- Scottish drug alert. <a href="http://www.sdf.org.uk/news\_drug-alert-issued-grampian-increasing-illicit-xanax-uses/">http://www.sdf.org.uk/news\_drug-alert-issued-grampian-increasing-illicit-xanax-uses/</a> (accessed February 2018).
- 27. Summaries of Product Characteristics, The electronic Medicines Compendium. <a href="https://www.medicines.org.uk/emc/medicine/9658">https://www.medicines.org.uk/emc/medicine/9658</a> (accessed February 2018).
- 28. NICE/BNF guidance. https://bnf.nice.org.uk/drug/alprazolam.html (accessed February 2018).
- 29. Smith RB, Kroboth PD, Vanderlugt JT, Phillips JP, Juhl RP. Psychopharmacology (Berl). 1984;84(4):452-6. Pharmacokinetics and pharmacodynamics of alprazolam after oral and IV administration. <a href="https://www.ncbi.nlm.nih.gov/pubmed/6152055">https://www.ncbi.nlm.nih.gov/pubmed/6152055</a> (accessed February 2018).
- Sheehan DV, Sheehan KH, Raj BA. Psychopharmacol Bull. 2007;40(2):63-81. The speed of onset of action of alprazolam-XR compared to alprazolam-CT in panic disorder. <a href="https://www.ncbi.nlm.nih.gov/pubmed/17514187">www.ncbi.nlm.nih.gov/pubmed/17514187</a> (accessed February 2018).
- 31. Erowid: alprazolam basics. <a href="https://erowid.org/pharms/alprazolam/alprazolam\_basics.shtml">https://erowid.org/pharms/alprazolam/alprazolam\_basics.shtml</a> (accessed February 2018).
- 32. UK Chemical Research: forum thread. <a href="https://www.ukchemicalresearch.org/Thread-Alprazolam-Xanax-harm-reduction-and-comparison-to-diazepam-and-etizolam">https://www.ukchemicalresearch.org/Thread-Alprazolam-Xanax-harm-reduction-and-comparison-to-diazepam-and-etizolam</a> (accessed February 2018).
- 33. Psychonautwiki. Alprazolam. <a href="https://psychonautwiki.org/wiki/Alprazolam#cite\_note-tripsit-1">https://psychonautwiki.org/wiki/Alprazolam#cite\_note-tripsit-1</a> (accessed February 2018).
- 34. Goyal S, Kaushal J, Gupta MC, Verma S "Drugs and Dreams." Indian Journal of Clinical Practice. <a href="http://medind.nic.in/iaa/t13/i3/iaat13i3p624.pdf">http://medind.nic.in/iaa/t13/i3/iaat13i3p624.pdf</a> (accessed February 2018).
- 35. Bailey DG, Dresser GR, Kreeft JH, Munoz C, Freeman DJ, Bend JR "Grapefruit-felodipine interaction: Effect of unprocessed fruit and probable active ingredients." Clin Pharmacol Ther 68 (2000): 468-77. https://www.ncbi.nlm.nih.gov/pubmed/11103749 (accessed February 2018).
- American Society of Health-System Pharmacists 2016;
   Drug Information 2016. Bethesda, MD. 2016, p. 2665 from HSDB. Source: HSDB Record Name: ALPRAZOLAM. URL: https://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+hsdb:@term+@rn+@rel+28981-97-7 (accessed February 2018).
- Source: LiverTox. Record Name: Alprazolam URL: <a href="https://livertox.nlm.nih.gov//Alprazolam.htm">https://livertox.nlm.nih.gov//Alprazolam.htm</a> (accessed February 2018).

- 38. Jones, J. D., Mogali, S. and Comer, S. D. (2012), 'Polydrug abuse: a review of opioids and benzodiazepine combination use', Drug and Alcohol Dependence 125, p. 14. <a href="https://www.ncbi.nlm.nih.gov/pubmed/22857878">https://www.ncbi.nlm.nih.gov/pubmed/22857878</a> (accessed February 2018).
- 39. Principles and Practice of Psychopharmacotherapy. <a href="http://books.google.com/books?id="ePK9wwcQUMC&pg=PA535">http://books.google.com/books?id="ePK9wwcQUMC&pg=PA535">ePK9wwcQUMC&pg=PA535</a>. (accessed February 2018).
- Lann MA, Molina DK. Am J Forensic Med Pathol. 2009 Jun;30(2):177-9. A fatal case of benzodiazepine withdrawal. https://www.ncbi.nlm.nih.gov/pubmed/19465812 (accessed February 2018).
- 41. Wolf B, Griffiths RR Drug Alcohol Depend. 1991 Dec 31;29(2):153-6. Physical dependence on benzodiazepines: differences within the class. <a href="https://www.ncbi.nlm.nih.gov/pubmed/1686752">https://www.ncbi.nlm.nih.gov/pubmed/1686752</a> (accessed February 2018).
- 42. NIH; DailyMed. Current Medication Information for Xanax (Alprazolam) Tablet (Updated: October 2016). https://dailymed.nlm.nih.gov/dailymed/druglnfo.cfm?setid=388e249d-b9b6-44c3-9f8f-880eced0239f (accessed February 2018).
- 43. I White, J. M. and Irvine, R. J. (1999), 'Mechanisms of fatal opioid overdose', Addiction 94(7), pp. 961–72. <a href="https://www.ncbi.nlm.nih.gov/pubmed/10707430">https://www.ncbi.nlm.nih.gov/pubmed/10707430</a> (accessed February 2018).
- 44. I Lintzeris, N., Mitchell, T. B., Bond, A. J., Nestor, L. and Strang, J. (2007), 'Pharmacodynamics of diazepam coadministered with methadone or buprenorphine under high dose conditions in opioid dependent patients', Drug and Alcohol Dependence 91(2–3), pp. 187–94. https://www.ncbi. nlm.nih.gov/pubmed/17624687 (accessed February 2018).
- 45. Drug-related deaths in Scotland 2013', published by National Records Scotland. <a href="https://www.nrscotland.gov.uk/statistics-and-data/statistics/statistics-by-theme/vital-events/deaths/drug-related-deaths-in-scotland/2013">https://www.nrscotland.gov.uk/statistics-and-data/statistics/statistics-by-theme/vital-events/deaths/drug-related-deaths-in-scotland/2013</a>. (accessed February 2018).
- 46. Number of drug-related deaths where selected substances were mentioned on the death certificate, deaths registered in England and Wales, 2012 to 2016. <a href="https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsrelatedtodrugpoisoninginenglandandwales/2016registrations#deaths-involving-selected-substances">https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsrelatedtodrugpoisoninginenglandandwales/2016registrations#deaths-involving-selected-substances</a> (accessed February 2018).
- 47. Misuse of Drugs Act 1971.https://www.legislation.gov.uk/ ukpga/1971/38 (accessed February 2018).
- 48. Fraser AD1, Meatherall R . J Anal Toxicol. 1996 Jul-Aug;20(4):217-23. Comparative evaluation of five immunoassays for the analysis of alprazolam and triazolam metabolites in urine: effect of lowering the screening and GC-MS cut-off values. <a href="https://www.ncbi.nlm.nih.gov/pubmed/8835658">https://www.ncbi.nlm.nih.gov/pubmed/8835658</a> (accessed February 2018).

Written by Michael Linnell in association with **UK and Ireland DrugWatch**: an informal online professional information network established by a group of professionals working in the UK and Irish drugs sector. The aim of the group is to raise/establish standards for drug information, alerts and warnings. It is currently an unfunded, bottomup initiative that works in the spirit of mutual co-operation. Details of current members can be found <a href="https://example.com/here/beta-based-approximation-network-networks-network