

## Nitazenes: Synthetic opioids more deadly than fentanyl are starting to turn up in overdose cases

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The synthetic opioid fentanyl is well known for the many lives it has claimed—mainly <u>in the US</u>, but <u>elsewhere too</u>. Now, a less well-known



class of synthetic opioids called nitazenes is starting to crop up in overdose cases, on both sides of the Atlantic.

Nitazenes have recently been the subject of a <u>national patient safety alert</u> in the UK as a result of a spike in <u>opioid-related deaths</u> over the last two months, with several cases involving nitazenes.

Some drugs in the nitazene class are 100 times more potent than morphine—so about as potent as <u>fentanyl</u>. However, nitazenes may be more deadly.

A <u>recent study</u>, published in *Jama Network Open*, reported that people who overdosed on nitazenes typically needed two or more doses of the overdose-reversal <u>drug</u> naloxone, whereas those who overdosed on fentanyl typically only needed one dose.

Nitazenes were first developed by a Swiss company called Ciba Pharmaceuticals in the 1950s as a new type of potent painkiller (analgesic). But the drugs never made it to market.

It appears that chemists in clandestine labs have <u>pored over old research</u> <u>papers</u> looking for new synthetic opioids to make and stumbled across this class of deadly drugs.

These new synthetic opioids are illegal in the UK as they are covered under the <u>Psychoactive Substances Act 2016</u>, which bans all <u>chemical</u> <u>compounds</u> capable of producing a psychoactive effect in people.

## How do they work?

Opioids act at sites in the brain, and elsewhere in the body, called muopioid receptors. These brain receptors, when activated, can relieve pain, and at high doses evoke feelings of euphoria followed by drowsiness.



Morphine, heroin and fentanyl all activate these mu-opioid receptors. However, fentanyl can do so at much lower doses than morphine or heroin—and some nitazenes can relieve pain at even lower doses than fentanyl.

For example, a <u>study</u> in rats found that a nitazene called N-desethyl isotonitazene provided <u>pain relief</u> at a dose nearly ten times smaller than that needed for fentanyl, and around 1,400 times less than that for morphine, to see the same effect.

Not only do these drugs relieve pain and cause euphoria, they also suppress the respiratory system. That is, they reduce breathing, and this is the cause of death in opioid overdose.

N-desethyl isotonitazene causes <u>apnea</u> (where breathing stops) at about a third of the dose of fentanyl. It also takes much longer to recover normal breathing after N-desethyl isotonitazene (208 minutes) compared with fentanyl (67 minutes). One must assume, therefore, that some nitazenes may have the potential to be more deadly than fentanyl and heroin.

There are also issues with nitazenes being used as adulterants in other <u>illicit drugs</u>, such as <u>cocaine</u>, benzodiazepines and <u>synthetic cannabinoids</u> ("spice"). Illicit drug users may be unwittingly taking opioids and need to be aware of the risk of respiratory depression.

Several nitazenes have been found in overdose cases recently, and the number of new drugs in this class (called analogs) emerging on the streets appears to be growing. However, the true extent of this drug's penetration into the illicit market is <u>not known</u> as many testing facilities are not set up to test for nitazenes.

And it isn't just nitazenes that we need to be concerned about. There are also new non-nitazene synthetic opioids, such as the <u>brorphine-like</u>



<u>compounds</u>. As with nitazenes, these drugs have been found to be slightly more potent than fentanyl, and much more potent than heroin or morphine, in lab tests.

Mercifully, <u>opioid overdose</u> can be reversed with naloxone—which blocks the mu-<u>opioid</u> receptors and is very effective if given in time.

Public health agencies in the UK have highlighted the need to educate heroin users, and those who come into contact with them, about nitazenes and how to treat overdose with naloxone.

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