

Interactions between prescribed medications and novel psychoactive substances (NPS)

In the absence of hard evidence of interactions between prescribed medications and NPS, it isn't currently possible to give precise and specific advice about whether to withhold prescribed medication when NPS has been used.

Key Messages

- Little is known about the risks of poly-drug use either of NPS together or NPS with classical recreational drugs, alcohol, over the counter (OTC) medicines, or prescription medicines. **Any drug combinations should be considered potentially dangerous. [1,2]**
- Due to the lack of clear information, decisions about continuity of prescribed medicines should be made on a case by case basis.
- Clear, written protocols are needed that include who may make a decision to omit a dose of medication or to discontinue a medicine altogether, as these decisions will frequently need to be made in the absence of a prescriber. A prescriber should review these decisions as soon as possible.

In general, the nature of the presenting symptoms and signs should be considered alongside the possible effects of an individual's prescribed medication on those symptoms and signs. This is important for medicines that cause drowsiness or affect the central nervous system e.g. hypnotics, anxiolytics, antipsychotics, antidepressants, antiepileptic drugs, drugs for ADHD, analgesics, antihistamines.

Possible side effects of medicines are available in the -

British National Formulary (BNF) <http://www.evidence.nhs.uk/formulary/bnf/current>

Summary of Product Characteristics (SPC) <http://www.medicines.org.uk/emc/>.

Factors to consider when deciding whether to withhold or continue medication include:

- Whether or not the facility has an in-patient unit for closer healthcare supervision.
- The healthcare workforce availability and capability to assess and follow-up the care of the patient.

Examples of when treatment might be withheld include:

- If an affected prisoner was showing signs of significant drowsiness it might be necessary to withhold opioid analgesics, opiate substitute treatment or hypnotics.
- If an individual presented with a lowered pulse and blood pressure, antihypertensives might need to be reduced or discontinued for a period of time.

Examples where continuation of critical medicines is more likely to be needed to avoid harm include:

- Continuing essential medication, such as insulin or warfarin. Close therapeutic monitoring of the effect of these doses is advised.
- Given the association between synthetic cannabis [SC] use (the more common type of NPS) and convulsions, it would be advisable to continue antiepileptic drugs.

Potential interactions

NPS	Interacting medicine (list not exhaustive)	Potential effect
Ketamine [3]	Ritonavir, cobicistat Efavirenz and nevirapine	Decrease the rate of ketamine clearance and potentiate its toxicity. Decrease in ketamine effects.
Ecstasy, MDPV, PMA, mephedrone, methamphetamine, cocaine, butylone, methylone, phenethylamines, methamphetamine [3]	Monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), opiate analgesics, tramadol, OTC cough medicines, antibiotics, weight-loss agents, antiemetics, antimigraine agents.	Increased risk of serotonin syndrome. Some MAOIs have a long half life (e.g. phenelzine, tranylcypromine), interactions may still be possible up to 2 weeks after the drug is stopped.
Methamphetamine [3]	Amiodarone, citalopram, codeine, fluoxetine, haloperidol, methadone, paroxetine and valproic acid, cobicistat	Increase the toxicity of methamphetamine.
Mephedrone [3]	Ritonavir, cobicistat	Increase the toxicity of mephedrone.
Ecstasy [3]	Ritonavir, dextromethorphan, fluoxetine, paroxetine, moclobemide, haloperidol, thioridazine, quinidine, cobicistat, elvitegravir, atazanavir, darunavir	Increase the toxicity of Ecstasy.
Synthetic cannabis [4-6]	Antifungals: itraconazole, ketoconazole, fluconazole Macrolide antibiotics: clarithromycin, telithromycin, erythromycin Anti-HIV drugs: indinavir, nelfinavir, ritonavir, saquinavir Antipsychotics: clozapine, quetiapine	These medicines inhibit the liver enzyme CYP3A4 this leads to an increase in plasma level of synthetic cannabis and decreased rate of clearance which potentiates its toxicity. Concomitant use may cause brain, kidney, liver or heart injury.

References

1. Bonnici KS, Dargan PI, Wood DM. Novel psychoactive substances or 'legal highs'. British Journal of Hospital Medicine 2015; 76 (9): c130-134.
2. Baumeister D, Tojo LM, Tracy DK. Legal highs: staying on top of the flood of novel psychoactive substances. Therapeutic Advances in psychopharmacology 2015; 5 (2): 97-132.
3. Abdulrahim D, Bowden-Jones O, on behalf of the NEPTUNE Expert Group. Guidance on the Management of Acute and Chronic Harms of Club Drugs and Novel Psychoactive Substances. Novel Psychoactive Treatment UK Network (NEPTUNE). London, 2015.
4. Schifano F, Orsolini L, Papanti DG et al. Novel psychoactive substances of interest for psychiatry. World Psychiatry 2015; 14: 15-26.
5. Zawilska JB, Andrzejczak D. Next generation of novel psychoactive substances on the horizon – A complex problem to face. Drug and Alcohol Dependence 2015; 157: 1-17.
6. Smith CD, Robert S. 'Designer drugs': update on the management of novel psychoactive substance misuse in the acute care setting. Clinical Medicine 2014; 14 (4): 409-15.