

Analysis against factors for prohibited substances (Schedule 9)

1. The substance is included in either Schedule IV to the United Nations Single Convention on Narcotic Drugs, 1961 or in Schedule I to the United Nations Convention on Psychotropic Substances 1971.

Not relevant as alkyl nitrites are not included in these schedules.

2. The substance has no currently established therapeutic value and is likely to present a high risk of dependency, abuse, misuse or illicit use.

Several commonly used alkyl nitrites, like isopropyl nitrite, are currently not scheduled. There is a correlation of the use of poppers with illegal drug use. In addition, some alkyl nitrites that are currently in schedule 4 are obtained without a prescription, which is illegal.

Would a schedule 9, entry for all of these substances be appropriate? Should some remain in schedule 4 (such as amyl nitrite, where there is some clinical experience with the use of the substance), and all of the others be put into schedule 9?

If all alkyl nitrites were put into Schedule 9, then responsibility for enforcement of these regulatory controls would be given to state and territory law enforcement/police departments.

ACNP comment: Agree with the proposal to schedule 9 for all except one such as amyl nitrate, should there be a safe way to prescribe it under Schedule 4, with appropriate screening, counselling and dosage.

Analysis against factors for controlled drugs (Schedule 8)

1. The substance is included in Schedule I or II of the United Nations Single Convention on Narcotic Drugs 1961 or in Schedule II or III of the United Nations Convention on Psychotropic Substances 1971.

Alkyl nitrites are not included in these documents.

2. The substance has an established therapeutic value but its use, at established therapeutic dosage levels, is recognised to produce dependency and has a high propensity for misuse, abuse or illicit use.

Alkyl nitrites for inhalation to treat problems associated with receptive sexual intercourse do not produce dependency like other substances in schedule 8 such as cocaine, fentanyl, morphine or oxycodone¹.

ACNP Comment: Agree Schedule 8 not appropriate

¹ <https://adf.org.au/drug-facts/amyl-nitrite/>

Analysis against factors for prescription only medicines (Schedule 4)

1. The ailments or symptoms that the substance is used for require medical, veterinary or dental intervention².

Due to the mode of action of the alkyl nitrites and the resultant cardiovascular effects, medical review and assessment of the user may be beneficial before the substance is used. This would enable medical diagnosis of any underlying medical conditions such as cardiovascular disease, glaucoma or an enzyme deficiency (glucose-6-phosphate deficiency) that may be exacerbated by self-administration of alkyl nitrites.

2. The use of the substance requires adjunctive therapy or evaluation or specialised handling for administration.

The use of alkyl nitrites may require specialised handling for administration given that adverse effects are dependent on the amount used, how frequently they are used and how long they are used for, as well as the person's health and the other medications they may be taking. Since it is difficult to control how much is inhaled, people can accidentally overdose. Swallowing these products can lead to serious medical complications and may be fatal.

3. The use of the substance at established therapeutic dosage levels may produce dependency but has a moderate propensity for misuse, abuse or illicit use.

Alkyl nitrites for inhalation to treat problems associated with receptive sexual intercourse do not produce dependency³. However, products containing alkyl nitrites have been misused. Accidental swallowing by children and adults, and potentially deliberate swallowing by adults due to lack of information on how the drug should be taken could be minimised if made available as a prescription only medicine, and proper advice on use and possible adverse effects was provided.

4. The seriousness, severity and frequency of adverse effects are such that monitoring or intervention by a medical, veterinary or dental practitioner is required to minimise the risk of using the substance.

This factor appears to be particularly relevant due to the seriousness and severity of adverse events experienced by some alkyl nitrite users. Monitoring or intervention by a health care professional such as a medical practitioner may be beneficial in order to protect public health.

People with certain medical conditions and those taking certain medications (particularly drugs used to treat erectile dysfunction, and other drugs such as high blood pressure medications, certain migraine drugs, and high doses of aspirin) or illicit drugs are at particular risk of suffering adverse effects from use.

Amyl nitrite may increase intra-ocular and intracranial pressure and should be used with caution in patients with glaucoma, recent head trauma, or cerebral haemorrhage.

It is possible that medical advice about possible adverse events such as low blood pressure, tachycardia, dizziness, nausea and fainting, especially if the user is taking prescription medicines that lower blood pressure may assist to minimise the risks of using the substance.

Some people may be strongly encouraged by doctors or pharmacist not to try alkyl nitrites based on their medical history. It is unlikely that more serious and possibly permanent effects such as loss of vision (maculopathies or retinal damage) or methaemoglobinaemia could be minimised

² For the purposes of the document medical, veterinary or dental intervention is considered to include other authorised prescribers as described in relevant legislation of Australian states and territories.

³ <https://adf.org.au/drug-facts/amyl-nitrite/>

utilising medical monitoring or advice, since these are consequential following the use of the substance rather than associated with the problem being treated.

5. The margin of safety between the therapeutic and toxic dose of the substance is such that it requires medical, veterinary or dental intervention to minimise the risk of using the substance.

Presently, the risk profile of alkyl nitrites is not well defined. The risk factors for adverse effects, interactions and contraindications are known however the incidence of adverse events with the use of alkyl nitrites for inhalation to treat problems associated with receptive sexual intercourse is not well characterised in comparison with medicines that have been through the TGA's safety, quality and efficacy evaluation to become registered on the Australian Register of Therapeutic Goods.

Again, some people may be strongly encouraged by doctors not to try alkyl nitrites based on their medical history.

6. The seriousness or severity and frequency of the interactions of the substance (medicine-medicine, medicine-food, or medicine-disease) are such that monitoring or intervention is required by a medical, veterinary or dental practitioner.

Alkyl nitrites taken in combination with other vasodilators such as sildenafil are potentially life-threatening. The combination could lead to dangerously low blood pressure and heart rate, causing a person to faint, or even have a heart attack or stroke, therefore medical supervision of treatment could prevent harm and protect the public.

7. The use of the substance has contributed to, or is likely to contribute to, communal harm.

Not applicable

8. The experience of the use of the substance under normal clinical conditions is limited.

There is very little clinical experience with the use of alkyl nitrites. However, doctors can prescribe the following substances currently in Schedule 4: amyl nitrite; butyl nitrite; isoamyl nitrite; isobutyl nitrite and octyl nitrite. Patients may currently be able to access these substances through providing a prescription to a compounding pharmacy, or through access to unapproved medicines pathways.

ACNP Comment: It is clear that significant assessment and counselling is required to reduce risk, therefore Schedule 4 would be appropriate should there be a way to ensure safe and consistent dosage and administration.

Analysis against factors for pharmacist only medicines (Schedule 3)

1. The medicine is substantially safe with pharmacist intervention to ensure the quality use of the medicine. There may be potential for harm if used inappropriately.

If there was an available commercial product, perhaps it could be made available from a pharmacist in a pharmacy if guidance was provided on appropriate use.

Guidance could include counselling about the adverse event profile, including warnings about transient effects such as low blood pressure, tachycardia, dizziness, nausea and fainting, especially if the user is taking prescription medicines that lower blood pressure.

In addition, advice could be given about more serious and possibly permanent effects such as loss of vision (maculopathies or retinal damage). The risk of possible hospitalisation due to methaemoglobinaemia could be emphasised, particularly if the product were ingested or repeatedly inhaled.

It appears that consumers should be counselled about the adverse event profile and risk of more serious and possibly permanent effects such as loss of vision (maculopathies or retinal damage) and hospitalisation due to methaemoglobinaemia.

2. The use of the medicine is not expected to produce dependency at either the established therapeutic dose or at suprathreshold doses. Where risk of misuse, abuse or illicit use is identified, the risk can be minimised through pharmacist-consumer consultation.

Alkyl nitrites for inhalation to treat problems associated with receptive sexual intercourse do not produce dependency⁴. However, products containing alkyl nitrites have been misused. Accidental swallowing by children and adults, and potentially deliberate swallowing by adults due to lack of information on how the drug should be taken. Perhaps these risks could also be minimised if made available as a pharmacy-only medicine, and proper advice on use and possible adverse effects was provided by a pharmacist.

3. The risk profile of the medicine is well defined and the risk factors for adverse effects, interactions and contraindications are known, identifiable and manageable by a pharmacist.

Presently, the risk profile of alkyl nitrites is not well defined. The risk factors for adverse effects, interactions and contraindications are known however the incidence of adverse events with the use of alkyl nitrites for inhalation to treat problems associated with receptive sexual intercourse is not well characterised in comparison with medicines that have been through the TGA's safety, quality and efficacy evaluation to become registered on the Australian Register of Therapeutic Goods.

4. Where the medicine is intended for recurrent or subsequent treatment of a chronic condition, pharmacist intervention is required to monitor safe use of the medicine following recommendation by a medical practitioner or other authorised prescriber.

Problems associated with receptive sexual intercourse do not require medical diagnosis, however given the poorly characterised risk profile of alkyl nitrites the consumer may find it difficult to self-monitor the safe ongoing use of the medicine.

5. The use of the medicine at established therapeutic dosage levels may mask the symptoms or delay diagnosis of a serious condition.

The use of alkyl nitrites is unlikely to be safe to use in people with undiagnosed cardiovascular disease due to the mode of action being vascular dilatation and smooth muscle relaxation.

ACNP Comment: Given the risks associated, and the potential for misuse, the pharmacist is best placed to reinforce safety and counselling given by a Schedule 4 prescriber. Schedule 3 is not appropriate as extensive counselling and medical history is needed.

⁴ <https://adf.org.au/drug-facts/amyl-nitrite/>

Analysis against factors for pharmacy only medicines (Schedule 2)

1. The quality use of the medicine can be achieved by labelling, packaging, and/or provision of other information; however access to advice from a pharmacist should be available to maximise the safe use of the medicine.

There is currently no medicine containing alkyl nitrites for inhalation registered on the Australian Register of Therapeutic Goods. If there was, should it be available on the shelves in a pharmacy for consumers to access without first having to speak to a pharmacist for guidance on appropriate use?

2. The use of the medicine is substantially safe for short term treatment and the potential for harm from inappropriate use is low.

The potential for harm from inappropriate use does not appear to be low. If available, the use of medicines containing alkyl nitrites could lead to methaemoglobinaemia in users if the product was taken incorrectly and ingested. There could also be added risks for people with glaucoma or anaemia, and those with enzyme deficiencies that make them more prone to methaemoglobinaemia. Alkyl nitrites taken in combination with other vasodilators such as sildenafil could lead to dangerously low blood pressure and heart rate, causing a person to faint, or even have a heart attack or stroke.

3. The use of the medicine is very unlikely to produce dependency (at either the established therapeutic dose or suprathreshold doses) and the medicine is very unlikely to be misused, abused or illicitly used.

Alkyl nitrites for inhalation to treat problems associated with receptive sexual intercourse do not produce dependency⁵. However, products containing alkyl nitrites have been misused. Accidental swallowing by children and adults, and potentially deliberate swallowing by adults due to lack of information on how the drug should be taken. This risk is unlikely to be minimised if it was available on the shelves in a pharmacy for consumers to access without first having to speak to a pharmacist for guidance on appropriate use.

4. The risk profile of the medicine is well defined and the risks can be identified and managed by a consumer through appropriate packaging and labelling, including consultation with a health professional if directed by labelling.

Presently, the incidence of adverse events with the use of alkyl nitrites not well characterised in comparison with medicines that have been through the TGA's safety, quality and efficacy evaluation.

5. The use of the medicine at established therapeutic dosage levels is not likely to mask the symptoms or delay diagnosis of a serious condition.

The use of alkyl nitrites is unlikely to be safe to use in people with undiagnosed cardiovascular disease due to the mode of action being vascular dilatation and smooth muscle relaxation.

ACNP Comment: Not appropriate for Schedule 2

⁵ <https://adf.org.au/drug-facts/amyl-nitrite/>

What if alkyl nitrites were available for general sale?

There is currently no medicine containing alkyl nitrites for inhalation registered on the Australian Register of Therapeutic Goods. Despite this, people that use alkyl nitrites are buying bottles of isopropyl nitrite (currently an unscheduled substance) from adult shops or online.

There are several risks of allowing these products to remain unregulated. The main risk is that manufacturers are not compelled to ensure that the substance in the bottle matches what is on the label; provide any guidance on safe use; give warnings on possible adverse effects; directions in the case of overdose; present the product in packaging to minimise accidental or deliberate swallowing or even the identity of the manufacturer so that product complaints can be directed appropriately.

There has already been an increase in the number of hospitalisations over time, and use is becoming more widespread and not limited to use in the LGBTIQ community. Making alkyl nitrites available for general sale increases its general acceptance as a safe product, when current evidence of adverse events suggests otherwise.

Making alkyl nitrites available for general sale is unlikely to protect public health in line with the legislative requirements.

ACNP Comment: Agree, the risks are too great, and in the interest of protecting public health this needs to be regulated.

General Comments: Alkyl nitrates clearly pose a risk to public health. If it is not possible to ensure consistent and safe dosage and administration, along with appropriate counselling and assessment, and labelling of products, then all alkyl nitrates should be Schedule 9. We do support this medicine being available, subject to the above, for the purpose of use in the LGBTIQ community. ACNP has an interest as many of our members are working, and prescribing, within the specialty area of sexual health.