

# Cytisinicline

# Cytisinicline

**Authors:** Robert West, Magdalena Cedzyńska and Andy McEwen

**Contributors:** Julia Robson, Lou Ross

**Editor:** Andy McEwen

**Copy editor and proofing:** Jane Stevens

**Reviewers:** Hazel Cheeseman, Peter Hajek, Witold Zatonski

This document has been produced with the support  
of the Office for Health Improvement and Disparities

© 2026 National Centre for Smoking Cessation and Training (NCSCT)

Version 2. Date of last modification: March 2026

ISBN 978-1-915481-01-6

## Contents

<b>Summary</b>	4
<b>Background</b>	5
Existing stop smoking aids	5
History of cytisinicline	6
Cytisinicline overview	7
<b>Efficacy and effectiveness</b>	9
<b>Instructions for use</b>	11
<b>Safety, contraindications and side effects</b>	13
Contraindications	14
Cautions	15
Drug interactions	16
Side effects	16
Overdose	18
Reporting of suspected adverse reactions	18
<b>Health and social care professionals: recommendations for practice</b>	19
<b>Clinical issues</b>	21
<b>Conclusion</b>	24
<b>References</b>	25
<b>Annex 1</b>	27

## Summary

This briefing summarises what we know about the effectiveness and safety of tablets containing cytisinicline as a smoking cessation aid.

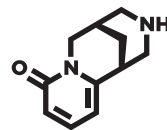
**Cytisiniclinee is a safe and effective treatment.** It works in a similar way to varenicline, reducing urges to smoke by attaching to some of the same neuronal receptors in the brain that nicotine does. Its side effects (gastric symptoms and sleep disturbance) are like those found with varenicline, but less common.

Cytisinicline is swallowed as a tablet or capsule. **The standard course of treatment is currently 25 days.** Using it for up to 12 weeks is probably more effective and it appears to be roughly as effective as varenicline when taken for the same duration (12 weeks). Even with 25 days' dosing, evidence suggests that it is as effective as nicotine replacement therapy (nicotine transdermal patch, gum, lozenge, nasal spray, inhalator and mouth spray).

Cytisinicline is available in many countries throughout the world, including Canada and Poland where it can be bought over the counter. It has been **used in parts of Europe for several decades as an effective smoking cessation aid with no apparent serious side effects.**

**Cytisinicline is now available in the UK as a prescription-only medication.**

**You may see cytisinicline sometimes referred to as cytisine – these names both refer to the same medication.** Two cytisinicline formulations, called Cytisinicline (formerly Cytisine) and Belnifrem, are licensed for sale in the UK. It has different brand names (e.g. Tabex, Desmoxan) in different countries.



cytisinicline

## Background

### Existing stop smoking aids

In the UK several stop smoking aids are widely used:

- nicotine replacement therapy (NRT)
- bupropion (Zyban)
- varenicline
- nicotine vapes (e-cigarettes)

These all significantly increase the chances of long-term success at stopping smoking.

**NRT** (nicotine transdermal patch, gum, lozenge, nasal spray, inhalator and mouth spray) is safe and raises the likelihood of achieving long-term abstinence.<sup>1,2</sup> Use of the nicotine transdermal patch plus a faster-acting product such as gum, lozenge or inhalator (combination NRT) is more effective than using a single product alone. The main side effects that can occur are irritation at the site of use, nausea and sleep disturbance. These NRT products are available on prescription and to buy directly from pharmacies and other kinds of retail outlet. They are used in approximately 15% of quit attempts in the UK.<sup>3</sup>

**Bupropion (Zyban)** is licensed for use in the US (under the brand name Wellbutrin) as an anti-depressant as well as a smoking cessation aid. It has similar effectiveness to NRT. It carries a slight risk of causing a seizure and of an allergic reaction.<sup>2</sup> A common side effect is insomnia. It is not to be used by people with a history of epilepsy, those with eating disorders or alcohol dependence, under 18s or women who are pregnant or breastfeeding. It is available only on prescription and is used in fewer than 1% of quit attempts in the UK.<sup>3</sup>

**Varenicline** is more effective than NRT or bupropion.<sup>2,4</sup> It received a marketing licence in the UK in 2007 and became widely used. There were concerns about the possibility that varenicline might increase the risk of serious neuropsychiatric and cardiac events but this is now considered very unlikely given the findings of a large safety randomised trial and several population-level studies.<sup>5</sup> It is not to be used by under 18s or by women who are pregnant or breastfeeding. It was withdrawn in 2020 in the UK over concerns about traces of carcinogens found in batches of the drug. It was reintroduced to the UK as a generic medication in 2024 and the proprietary formulation Champix was reintroduced by Pfizer in 2025.

**Nicotine vapes** are generally more effective than NRT in aiding smoking cessation with similar effectiveness to varenicline in clinical trials.<sup>6</sup> Concerns have been expressed about harms resulting from use but the available evidence supports the view that, whilst not risk-free, they are significantly less harmful than smoking cigarettes.<sup>7</sup> They are currently available on general sale and are the most popular stop smoking aid in the UK, being used in approximately 35% of quit attempts.<sup>3</sup> People who use them to stop smoking tend to continue to use them for months or years afterwards.

### History of cytisinicline

Cytisinicline was developed by two inspired Bulgarian pharmacologists, Professor Dymitar Paskov and Dr Hristo Dobrev, at the beginning of the 1950s but was not widely used.<sup>8</sup> Under the brand name Tabex, cytisinicline has been available as a smoking cessation medication in many countries in Central and Eastern Europe since the 1970s.<sup>9</sup> However, widespread use of cytisinicline only began during the late 1990s in Poland thanks to research by Professor Zatoński and his team, and in collaboration with Professor West and other British scientists.<sup>10,11,12</sup> Cytisinicline is available in several countries including Poland and Canada without prescription. Poland remains the only country with multiple companies producing affordable over-the-counter cytisinicline medicine, with sales approaching one million packages per year,<sup>13,14</sup> which contribute to cytisinicline being a key element of tobacco control globally.<sup>15,16</sup> Until recently, cytisinicline was not licensed for sale in the UK.

## Cytisinicline overview

**Cytisinicline is an alkaloid that can be extracted from parts of many plant species, most notably Laburnum seeds.**<sup>17</sup> There are now several formulations of cytisinicline available in a range of countries, including much of Europe, New Zealand and Canada.

**Cytisinicline acts as a selective partial agonist on the alpha-4 beta-2 nicotinic acetylcholine receptor, which plays an important role in nicotine dependence.**<sup>17</sup> In that respect its mode of action is very similar to varenicline. As a partial agonist it causes a limited amount of activation of neural pathways involving that receptor (enough to control urges to smoke) and blocks the receptor so that nicotine (e.g. from smoking a cigarette) cannot attach itself to it.

Formulations similar to Tabex, called Cytisinicline and Belnifrem, **have received marketing approval by the Medicines and Healthcare products Regulatory Agency (MHRA)**. These are the only formulations currently to have a marketing licence in the UK. Distribution of Cytisinicline (the first formulation to become available in the UK) by Consilient Health, whose UK office is based in London, began in early 2024.

Evidence suggests that 12 weeks of treatment is likely to be more effective than the prescribed 25 days of treatment.<sup>4</sup> **Consideration could be given to dosing for longer than 25 days and up to 12 weeks although this is outside the terms of the MHRA marketing approval** and the appropriate dosing for the extended period has not been determined.

**We would advise that patients access the forms of cytisinicline approved by the MHRA and prescribed by a GP rather than online versions whose provenance and authenticity are not certain.** Reviews on online marketplaces cast doubt on the quality of some products, and the lack of instructions in English is also an issue. The first two examples given below should be avoided; the third offers the future possibility of a dosing schedule that is easier for users to manage.

1. Tabex is the original brand of cytisinicline, manufactured in Bulgaria, and consists of tablets containing 1.5mg of cytisinicline which are taken orally. Starting with six tablets per day five days before stopping smoking, dosage reduces gradually to two tablets per day over 25 days. It is identical to the licensed version but it **does not** have marketing approval in the UK. Nonetheless, it is advertised on several retail websites, including Amazon, costing around £15 for a 25-day course.
2. Desmoxan is the brand name given to cytisinicline capsules manufactured in Poland by Alflofarm, who manufacture one of the licensed forms of cytisinicline available in the UK. Desmoxan has an identical formulation to the UK Cytisinicline brand. It consists of capsules containing 1.5mg to be taken under the same dosing schedule as Tabex. It **does not** have a marketing licence in the UK but is advertised on several retail websites, costing around £20 – 30 for a 25-day course.
3. Achieve Life Sciences, a US pharmaceutical company, is testing cytisinicline formulations and dosing regimens in clinical trials. A new formulation could become available in the UK within the next few years.<sup>18</sup> The likely formulation will involve a higher dose per tablet but fewer tablets per day.

## Efficacy and effectiveness

**A Cochrane systematic review found that cytisinicline significantly improved quit rates.**<sup>19</sup>

In 2011 a large randomised trial, carried out to modern standards, was published confirming previous findings that **cytisinicline was a safe and effective treatment to aid smoking cessation**.<sup>12</sup> Since then, several other trials have confirmed the safety and effectiveness of the approved 25-day cytisinicline reducing dose schedule.

One open label trial in New Zealand found it to be more effective than NRT.<sup>15</sup> Other stop smoking medications such as NRT, varenicline and bupropion, are typically licensed for 8–12 weeks or more, whereas cytisinicline treatment is licensed for 25 days, which makes direct comparison difficult. However, a trial in New Zealand found that 12 weeks of **cytisinicline had similar effectiveness to varenicline**,<sup>20</sup> while a trial in Australia found that 25 days (3.5 weeks) of cytisinicline dosing was probably less effective than 12 weeks (84 days) of varenicline.<sup>21</sup> A very large placebo-controlled trial of cytisinicline in tuberculosis patients in Bangladesh and Pakistan did not show clear evidence of benefit.<sup>22</sup>

Reviews of evidence from randomised controlled trials, including the trial in Bangladesh and Pakistan, estimated that on average **cytisinicline increased smoking cessation rates compared with a placebo by approximately 75%**.<sup>17</sup>

There have been no modern randomised trials of cytisinicline undertaken without any behavioural support and so its effectiveness in that context is unknown. The same is true of varenicline, nicotine vapes and bupropion. With NRT there have been some trials purportedly without behavioural support but by their nature randomised trials require a certain amount of involvement with clinical staff.

Observational data from England have shown that quit attempts involving the use of varenicline provided by prescription have higher success rates than quit attempts not using pharmacotherapy.<sup>23</sup> Quit attempts using NRT bought over the counter do not have higher success rates than those using no pharmacotherapy. Evidence on whether people that smoke in the general population who use nicotine vapes in quit attempts have higher success rates than those who try to quit without any pharmacotherapy is mixed.<sup>24</sup>

The head-to-head comparisons between cytisinicline and varenicline found **side effects to be less common for cytisinicline**.<sup>20,21</sup> Cytisinicline's main known side effects are gastric symptoms and sleep disturbance.<sup>17</sup>



**If patients use more cytisinicline than the recommended dose they might suffer from symptoms similar to nicotine overdose.** Based on data from people who have ingested large quantities of cytisinicline in a suicide attempt, the symptoms of cytisinicline overdose include malaise (general feeling of discomfort), nausea, vomiting, tachycardia (increased heart rate), fluctuations in blood pressure, breathing problems, blurred vision and convulsions. If patients develop any of these symptoms, they should **stop taking cytisinicline and contact their doctor or pharmacist.**

**If patients forget to use cytisinicline** they should **not** take a double dose to make up for the forgotten dose. They should just take their next dose as indicated.



## Safety, contraindications and side effects

Cytisinicline is licensed for smoking cessation and reduction of nicotine cravings in those who are willing to stop smoking.

The treatment goal of cytisinicline is the permanent cessation of the use of nicotine-containing products.

The use of cytisinicline allows for a gradual reduction of nicotine dependence by relieving craving and withdrawal symptoms.

In one form or another cytisinicline has been used in Europe by several million people who smoke, mostly without prescription, and to date there has been no evidence of any serious adverse events. Nevertheless, it is also wise to be cautious when prescribing medicines.

The following contraindications and cautions are from the original licence for cytisinicline when it was made available in Europe in the 1970s. They have been imported directly into the UK licence without modification. To modify them would require a lengthy and expensive process, and possibly additional clinical trials with specific patient groups.

A lack of clinical experience or safety data means that cytisinicline is **not recommended** for patients:

- with **renal** (kidney) **impairment**
- with **hepatic** (liver) **impairment**
- **over 65 years of age**
- **under 18 years of age**

The general safety profile of cytisinicline is likely to be similar to that of varenicline, but with fewer side effects.

## Contraindications

According to the Summaries of Product Characteristics for Cytisinicline and Belnifrem, cytisnicline should **not be used** if patients have:

- hypersensitivity to cytisnicline
- hypersensitivity to any of the excipients (non-active ingredients): mannitol, microcrystalline cellulose, magnesium stearate, glycerol dibehenate and hypromellose
- unstable angina (chest pain caused by reduced blood supply to the heart)
- had recent myocardial infarction (heart attack)
- clinically significant arrhythmias (irregular or abnormal heart rhythm)
- had a recent stroke

or are

- pregnant or breastfeeding

Women of childbearing age using hormonal contraception should **add a secondary barrier method whilst taking cytisnicline** as its impact on the effectiveness of oral contraceptives is not known.

## Cautions

According to the Summaries of Product Characteristics for Cytisinicline and Belnifrem, cytisinicline should be taken **with caution** if patients have:

- ischemic heart disease
- heart failure
- hypertension (high blood pressure)
- pheochromocytoma (tumor in the adrenal glands)
- atherosclerosis (thickening or hardening of the arteries) and other peripheral vascular diseases
- gastric and duodenal ulcer
- gastroesophageal reflux disease
- hyperthyroidism (overactive thyroid)
- diabetes
- schizophrenia
- **Belnifrem only:** phenylketonuria

This does not mean that cytisinicline should not be used. The caution should be discussed with the client, risks assessed and a close eye kept on any possible worsening of these conditions if cytisinicline is used.<sup>25</sup>

## Drug interactions

Cytisinicline should **not be used with anti-tuberculosis drugs**.

According to the approved product information for cytisinicline, clients are advised **not to combine it with nicotine-containing products** and health professionals always have to be cautious when prescribing a medicine in a way that is 'off label'. However, our understanding of the pharmacology of cytisinicline and nicotine, and the fact that the label allows for smoking and cytisinicline dosing during the first few days of treatment, suggests that it is safe. There may be situations such as hospital in-patient stays where patients could be started on NRT and cytisinicline from the first day of treatment. It should be stressed, however, that we do not have direct evidence of the safety and efficacy of this approach.

In some cases, as a result of stopping smoking, with or without cytisinicline, an adjustment of the dose of other medicines may be necessary. This is especially important for medicines which contain theophylline (to treat asthma), clozapine (for schizophrenia) and ropinirole (to treat Parkinson's disease). See here for information on monitoring and dose changes when individuals taking certain medicines stop, start or restart smoking: [www.sps.nhs.uk/articles/managing-specific-interactions-with-smoking](http://www.sps.nhs.uk/articles/managing-specific-interactions-with-smoking)

## Side effects

**Like all medicines, cytisinicline can cause side effects, although not everybody will experience them.**

Clinical studies and experience indicate **good tolerability of cytisinicline**. The proportion of patients in research studies who discontinued treatment because of adverse reactions was 6–15.5% and in controlled studies it was comparable to the proportion in the placebo group.

**Cytisinicline has no influence on the ability to drive and use machines.**

Mild to moderate side effects are the most likely to occur, and most frequently concern the gastrointestinal tract.

**Most adverse reactions occur when cytisinicline is started, and they usually resolve during treatment.** Some of these symptoms could also be the result of smoking cessation, rather than the use of cytisinicline.

The following information on side effects by frequency is from the Summary of Product Characteristics. These are symptoms that were observed in early trials of cytisinicline and were not necessarily more prevalent than in those receiving placebo or no treatment. In some cases (e.g. irritability, weight gain, change in appetite) they are likely to be the symptoms of nicotine withdrawal associated with stopping smoking.

### Side effects by frequency

**Very common** (may affect **more than 1 user in 10**): change in appetite (mainly increase), weight gain, dizziness, irritability, mood changes, anxiety, hypertension, dry mouth, diarrhoea, rash, fatigue, sleep disorders (insomnia, drowsiness, lethargy, abnormal dreams, nightmares), headaches, tachycardia, nausea, alters some flavours, heartburn, constipation, vomiting, abdominal pain (especially in the upper abdomen), muscle pain.

**Common** (may affect **1 to 10 users in 100**): difficulty in concentration, slow heart rate, abdominal distension, burning tongue, malaise.

**Uncommon** (affects **1 to 10 users in 1,000**): feeling of heaviness in the head, decreased libido, lacrimation (abnormal or excessive secretion of tears), dyspnea (shortness of breath), increased sputum (phlegm), excessive salivation, sweating, decreased elasticity of the skin, tiredness, increase in serum transaminase levels.

Side effects listed by system organ class can be found in Annex 1.

## Overdose

Symptoms that may be observed with an overdose of cytisinicline include:

- malaise
- nausea
- vomiting
- tachycardia
- blood pressure fluctuations
- breathing disorders
- visual disturbances
- clonic convulsions (seizures)

In all cases of overdose, action should be taken as in acute poisoning: gastric lavage (stomach wash) should be performed, and diuresis (production of extra urine) should be controlled with infusion fluids and diuretics. Anti-epileptic drugs may be used if necessary. Breathing, blood pressure and heart rate should be monitored.

## Reporting of suspected adverse reactions

Reporting of suspected side effects allows for continued monitoring of the risks and benefits of cytisinicline. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card scheme:

[www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard)

## Health and social care professionals: recommendations for practice

Stopping smoking is the most important health behaviour change that people who smoke can make. **The most successful way of stopping smoking is to use a combination of behavioural support and a stop smoking medicine or nicotine substitute.**

**Practitioners can recommend cytisinicline as a treatment medication with confidence**, provided they follow the manufacturer's instructions.

Cytisinicline is **not** recommended at this stage for people under 18, over 65 or for pregnant or breastfeeding women. Neither is it recommended for people with unstable angina, a recent myocardial infarction, clinically significant arrhythmias or who have had a recent stroke.

There are several **conditions for which cytisinicline should be used with caution** (see page 15). Here's what the British National Formulary says about Cautions:

"The information under Cautions can be used to assess the risks of using a drug in a patient who has co-morbidities that are also included in the Cautions for that drug – if a safer alternative cannot be found, the drug may be prescribed while monitoring the patient for adverse effects or deterioration in the co-morbidity."<sup>25</sup>

So, what this means is that in the absence of clinical experience it might be best to use other stop smoking aids with the patient groups listed. If cytisinicline is used, patients should be **closely monitored for side effects to make sure that it is not making their condition worse.**

**Incorporating cytisinicline into the Standard Treatment Programme for delivering behavioural support will maximise patients' chances of quitting successfully:**

[www.ncsct.co.uk/publications/ncsct-standard-treatment-programme](http://www.ncsct.co.uk/publications/ncsct-standard-treatment-programme)

Primary care colleagues should be notified that cytisinicline is now included in the treatment options for patients who smoke.

Outcomes should be recorded carefully, to assess effectiveness at both a local and national level. Cytisinicline is included as a treatment option by NHS Digital and can be recorded in stop smoking services' quarterly returns.

Adverse effects should be reported via the [MHRA Yellow Card scheme](#).

Several possible clinical issues are looked at in the next section, but further questions are welcomed by the NCSCT. You can get in touch with us at: [enquiries@ncsct.co.uk](mailto:enquiries@ncsct.co.uk)

## Clinical issues

**Q1. I've heard that varenicline should not be used by people with psychiatric problems. Is the same true for cytisinicline?**

*Cytisinicline is not contraindicated for people with psychiatric problems and neither is varenicline.*

**Q2. Is it OK to buy cytisinicline on the internet?**

*It is often unwise to buy medicine on the internet because of concerns over quality control, the lack of clinical supervision, inadequate patient information leaflets and the risk of being scammed. Health professionals should not recommend that patients do this, but it is ultimately the patient's choice.*

**Q3. When will cytisinicline become available to prescribe?**

*Cytisinicline became available in the UK in early 2024.*

**Q4. Can people use cytisinicline and NRT together?**

*This is probably best avoided though there have been studies of NRT and varenicline together which did not show evidence of serious adverse reactions. However, in theory, nicotine from NRT or nicotine vapes may lead to adverse reactions if they are used at the same time as cytisinicline (see page 16).*

**Q5. Laburnum seeds are poisonous so is cytisinicline really safe?**

*Like many medicines, cytisinicline is poisonous in high doses but safe at the doses used in the stop smoking medicines.*

**Q6. Does the quit date have to be on day 5 of the dosing schedule or can it be later?**

*Yes, as quitting on later dates has not been fully researched, so follow the instructions: "Smoking should be stopped no later than on the 5th day of treatment". This allows for an earlier quit date if desired, but a standardised approach will help us be clearer on how well cytisinicline works in practice.*

**Q7. What should patients do if they experience adverse side effects?**

*If patients are worried about side effects, it is best to consult with their doctor but if they are mild and tolerable there is no reason to stop taking the medicine. Most side effects get better or even disappear over time. Patients should be reminded that stopping smoking in itself causes a range of withdrawal symptoms and some of what they are experiencing will be among those. Also, the short-term discomfort will lead to long-term gains. Adverse events that give cause for concern should be reported to the MHRA via the [Yellow Card scheme](#).*

**Q8. What should patients do if they smoke after the quit date?**

*Ideally, they should continue with the quit attempt and keep taking the medicine. Having a cigarette after the quit date is not a reason for stopping cytisinicline and starting smoking. Given the similarity between cytisinicline and varenicline it is likely that cytisinicline will similarly help clients to resume abstinence after they have lapsed.*

**Q9. The drug label lists several contraindications that seem a bit odd. How strictly should these be adhered to?**

*The contraindications were developed several decades ago, and the reasons that they exist are not always clear. As a rule, it is generally best to stick to the medication recommendations.*

**Q10. Why can't cytisinicline be used in patients who are over 65 years of age?**

*All of the cytisinicline safety studies that informed the Summary of Product Characteristics were carried out on people under 65 years of age and data from more recent studies have not been taken into consideration. Although it is **highly unlikely that there will be any unwanted effects of cytisinicline because of age alone**, the lack of safety data means that cytisinicline is not licensed for this patient group.*

**Q11. Why are women of childbearing age using oral contraceptives (aka the pill) advised to also use a second, barrier contraceptive method (e.g. condoms) when using cytisinicline?**

*It is simply not known whether cytisinicline affects the effectiveness of oral contraceptives and so, as an extra precaution, additional contraceptives are recommended.*

**Q12. Why can pregnant women and those breastfeeding who want to give up smoking not use cytisinicline?**

*There have been no studies done on the effects of cytisinicline on pregnant women, nor on the unborn child or infants who are breastfeeding. Because of this lack of safety data, cytisinicline isn't recommended for this patient group.*

## Conclusion

People who smoke often search for something new, something that they haven't tried before – something that might mean that this time, finally, there might be a fix for their smoking. Cytisinicline holds this promise. It is not a magic wand, and it won't suit everyone, but as we work towards the goal of a Smokefree 2030, it is a new and important tool in our toolbox.

Cytisinicline is a safe, effective and cost-effective treatment to aid smoking cessation. It has a mode of action similar to varenicline. It has been used as a smoking cessation aid for several decades in many European countries. It is available over the counter in several countries, and it is now licensed in the UK.

Please let us know about how your clients get on with using cytisinicline at [enquiries@ncsct.co.uk](mailto:enquiries@ncsct.co.uk). The NCSCT will update this briefing and its online training and assessment programme as we learn more from you about your experience of using cytisinicline as a stop smoking aid.

## References

1. Stead, L. F. *et al.* Nicotine replacement therapy for smoking cessation. *Cochrane Database of Systematic Reviews* (2012) doi:10.1002/14651858.CD000146.pub4.
2. Anthenelli, R. M. *et al.* Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. *The Lancet* **387**, 2507–2520 (2016).
3. Monthly Tracking KPI – Graphs – Smoking in England. <https://smokinginengland.info/graphs/monthly-tracking-kpi>.
4. Cahill, K., Lindson-Hawley, N., Thomas, K. H., Fanshawe, T. R. & Lancaster, T. Nicotine receptor partial agonists for smoking cessation. *Cochrane Database of Systematic Reviews* (2016) doi:10.1002/14651858.CD006103.pub7.
5. Tonstad, S. *et al.* Varenicline: mode of action, efficacy, safety and accumulated experience salient for clinical populations. *Current Medical Research and Opinion* **36**, 713–730 (2020).
6. Livingstone-Banks, J., Lindson, N., Hartmann-Boyce, J. & Aveyard, P. Effects of interventions to combat tobacco addiction: Cochrane update of 2019 and 2020 reviews. *Addiction* **117**, 1573–1588 (2022).
7. Nicotine vaping in England: 2022 evidence update. GOV.UK [www.gov.uk/government/publications/nicotine-vaping-in-england-2022-evidence-update](http://www.gov.uk/government/publications/nicotine-vaping-in-england-2022-evidence-update).
8. Paskov V, Dobrev C. Pharmacological study of cytisine extracted in Bulgaria from *Cytisus laburnum*. *Izv Med Inst Bulgarian Academy of Science*, 1953, 1937, 54537
9. Granatowicz J. Smoking cessation through the use of cytisine and other chemotherapy. *World Smoking Health* 1976;1:8–11.
10. Zatoński W *et al.* An uncontrolled trial of cytisine (Tabex) for smoking cessation. *Tobacco Control* 2007;15(6):481–4.
11. Tutka P, Zatoński W. Cytisine for the treatment of nicotine addiction: from a molecule to therapeutic efficacy. *Pharmacological Reports* 2006;58(6):777–98.
12. West R *et al.* Placebo-controlled trial of cytisine for smoking cessation. *New England Journal of Medicine*. 2011;365:1193–1200.
13. Zatoński W, Zatoński M. Cytisine versus nicotine for smoking cessation. *New England Journal of Medicine*. 2015; 372(11): 1072.
14. Zatoński WZ, Janik-Koncewicz K, Stępnicka Z. History of smoking cessation treatment in Poland – the strengthening role of cytisine as the most effective and safe pharmacotherapy. *Journal of Health Inequalities*. 2020; 6 (2): 116–123.
15. Walker N *et al.* Cytisine versus nicotine for smoking cessation. *New England Journal of Medicine*. 2014; 371(25): 2353–2362
16. Rigotti NA *et al.* Cytisineline for smoking cessation: A randomized clinical trial. *Journal of the American Medical Association*. 2023; 330(2): 152–160
17. Tutka, P., Vinnikov, D., Courtney, R. J. & Benowitz, N. L. Cytisine for nicotine addiction treatment: a review of pharmacology, therapeutics and an update of clinical trial evidence for smoking cessation. *Addiction* **114**, 1951–1969 (2019).

18. Nides, M., Rigotti, N. A., Benowitz, N., Clarke, A. & Jacobs, C. A Multicenter, Double-Blind, Randomized, Placebo-Controlled Phase 2b Trial of Cytisine in Adult Smokers (The ORCA-1 Trial). *Nicotine & Tobacco Research* **23**, 1656–1663 (2021).
19. Lindson N *et al.* Pharmacological and electronic cigarette interventions for smoking cessation in adults: component network meta-analyses. *Cochrane Database of Systematic Reviews*. 2023;9. Available from: <https://doi.org/10.1002/14651858.CD015226.pub2>
20. Walker, N. *et al.* Cytisine versus varenicline for smoking cessation in New Zealand indigenous Māori: a randomized controlled trial. *Addiction* **116**, 2847–2858 (2021).
21. Courtney, R. J. *et al.* Effect of Cytisine vs Varenicline on Smoking Cessation: A Randomized Clinical Trial. *JAMA* **326**, 56–64 (2021).
22. Dogar, O. *et al.* Cytisine for smoking cessation in patients with tuberculosis: a multicentre, randomised, double-blind, placebo-controlled phase 3 trial. *The Lancet Global Health* **8**, e1408–e1417 (2020).
23. Kotz, D., Brown, J. & West, R. 'Real-world' effectiveness of smoking cessation treatments: a population study. *Addiction* **109**, 491–499 (2014).
24. Brown, J., Beard, E., Kotz, D., Michie, S. & West, R. Real-world effectiveness of e-cigarettes when used to aid smoking cessation: a cross-sectional population study. *Addiction* **109**, 1531–1540 (2014).
25. National Institute for Health and Care Excellence. How to use BNF publications online. [bnf.nice.org.uk/about/how-to-use-bnf-publications-online/#:~:text=The%20information%20under%20Cautions%20can,deterioration%20in%20the%20co%2Dmorbidity](https://bnf.nice.org.uk/about/how-to-use-bnf-publications-online/#:~:text=The%20information%20under%20Cautions%20can,deterioration%20in%20the%20co%2Dmorbidity)

# Annex 1

## Side effects by system organ class

### Metabolism and nutrition disorders

---

Very common: change in appetite (mainly increase), weight gain

---

### Nervous system disorders

---

Very common: dizziness, irritability, mood changes, anxiety,  
sleep disorders, headaches

---

Common: difficulty in concentration

---

Uncommon: feeling of heaviness in the head, decreased libido

---

### Eye disorders

---

Uncommon: lacrimation

---

### Cardiac disorders

---

Very common: tachycardia

---

Common: slow heart rate

---

### Vascular disorders

---

Very common: hypertension

---

### Respiratory, thoracic, and mediastinal disorders

---

Uncommon: dyspnoea, increased sputum

---

**Gastrointestinal disorders**

---

Very common: dry mouth, diarrhoea, nausea, alters some flavours, heartburn, constipation, vomiting, abdominal pain (especially in the upper abdomen)

---

Common: abdominal distension, burning tongue

---

Uncommon: excessive salivation

---

**Skin and subcutaneous tissue disorders**

---

Very common: rash

---

Uncommon: sweating, decreased elasticity of the skin

---

**Musculoskeletal and connective tissue disorders**

---

Very common: myalgia (muscle aches and pains)

---

**General disorders and administration site conditions**

---

Very common: fatigue

---

Common: malaise

---

Uncommon: tiredness

---

**Investigations**

---

Uncommon: increase in serum transaminase levels

---



