Cytisine 1.5mg Tablets from Consilient Health

Product Summary

Please refer to the Cytisine Summary of Product Characteristics (SPC) for full prescribing information, available at: https://www.consilienthealth.co.uk/products/ or https://www.medicines.org.uk/emc/product/15789/

For more information, please contact Consilient Health on infouk@consilienthealth.com or visit the Consilient Health Cytisine website: www.quitsmokingsupport.co.uk

- Cytisine 1.5 mg Tablets are approved for smoking cessation and reduction of nicotine cravings in smokers who are willing to stop smoking. The treatment goal of Cytisine is the permanent cessation of the nicotine containing products use.
- Cytisine (also known as cytisinicline) is a plant alkaloid that is a nicotine receptor partial agonist that allows for a gradual reduction of nicotine dependence by relieving withdrawal symptoms.
- Cytisine is a Prescription Only Medicine (POM) with a duration of therapy of just 25 days
- Cytisine has been added to NICE guidelines NG209 as a first line treatment option for smoking cessation (https://www.nice.org.uk/guidance/ng209) and is recommended for use by AWMSG
- A national PGD template for cytisine has been issued by the Specialist Pharmacy Service. See https://www.sps.nhs.uk/articles/cytisinicline-for-smoking-cessation/
- One pack of Cytisine (100 tablets) is sufficient for a complete 25-day treatment course
- The price of a treatment course (1 pack) is £115.00.
- Stock is available to order now via all mainline and selected short-line wholesalers

About Cytisine (Consilient Health) 1.5mg Tablets

- The active ingredient, Cytisine, is a plant alkaloid, found in seeds of golden chain, genus *Laburnum*, with a chemical structure similar to nicotine.
- Cytisine is a nicotine receptor partial agonist that allows for a gradual reduction of nicotine dependence by relieving withdrawal symptoms.
- Cytisine is also known as cytisinicline

Licensed indication

- Smoking cessation and reduction of nicotine cravings in smokers who are willing to stop smoking. The treatment goal of Cytisine is the permanent cessation of the nicotine containing products use.

Dosage and administration:

- The duration of therapy is 25 days.
- One package of Cytisine (100 tablets) is sufficient for a complete treatment course.
- Cytisine should be taken according to the following 25-day reducing schedule:

Days of treatment	Recommended dosing	Maximum daily dose
From the 1st to the 3rd day	1 tablet every 2 hours	6 tablets
From the 4th to the 12th day	1 tablet every 2.5 hours	5 tablets
From the 13th to the 16th day	1 tablet every 3 hours	4 tablets
From the 17th to the 20th day	1 tablet every 5 hours	3 tablets
From the 21st to the 25th day	1-2 tablets a day	to 2 tablets

- Take orally with a suitable amount of water
- Smoking should be stopped no later than on the 5th day of treatment. Smoking or use of products containing nicotine should not be continued during treatment as this may aggravate adverse reactions.
- In case of treatment failure, the treatment should be discontinued and may be resumed after 2 to 3 months.
- Patient Dosing Leaflets are available from Consilient Health. These include a chart that allows patients to track their dose over the 25-day course. Copies available on request or visit https://www.quitsmokingsupport.co.uk/cytisine/#how-to-use-cytisine

Special populations:

- There is no clinical experience of Cytisine in patients with renal or hepatic impairment, therefore it is not recommended for use in this population.
- Due to limited clinical experience, Cytisine is not recommended for use in patients over 65 years of age.
- The safety and efficacy of Cytisine in persons under 18 years of age have not been established. Cytisine is not recommended for use in persons under 18 years of age.

Contraindications:

- Cytisine is contraindicated in patients with: hypersensitivity to active substance or excipients (see page 4); unstable angina; recent myocardial infarction or stroke; clinically significant arrhythmias; pregnancy and breastfeeding.

Warnings and precautions

- Cytisine should be used only for patients with serious intention of weaning off nicotine.
- Use with caution in: ischemic heart disease, heart failure, hypertension, pheochromocytoma, atherosclerosis and other peripheral vascular diseases, gastric and duodenal ulcer, gastroesophageal reflux disease, hyperthyroidism, diabetes and schizophrenia.
- Depressed mood, rarely including suicidal ideation and suicide attempt, may be a symptom of nicotine withdrawal. Smoking cessation, with or without pharmacotherapy, has been associated with exacerbation of underlying psychiatric illness (e.g. depression). Care should be taken with patients with a history of psychiatric illness and patients should be advised accordingly.

- Polycyclic aromatic hydrocarbons in tobacco smoke induce metabolism of drugs metabolised by CYP 1A2 (and possibly by CYP 1A1). Stopping smoking may result in slower metabolism and a rise in blood levels of such drugs. Potentially clinically important if narrow therapeutic window, e.g. theophylline, tacrine, clozapine and ropinirole. Plasma concentration of products metabolised in part by CYP1A2 e.g. imipramine, olanzapine, clomipramine and fluvoxamine may also increase on smoking cessation; data are lacking and clinical significance unknown. Limited data indicate the metabolism of flecainide and pentazocine may also be induced by smoking
- Women of childbearing potential: Must use highly effective contraception while taking cytisine. It is currently unknown whether cytisine may reduce the effectiveness of systemically acting hormonal contraceptives, and therefore women using systemically acting hormonal contraceptives should add a second barrier method
- Drug interactions: Should not be used with anti-tuberculosis drugs

Tolerability:

- Cytisine has been used in Eastern Europe for smoking cessation for over 50 years (Tutka et al 2005).
- Clinical studies and previous experience with use of cytisine-containing product indicate a good tolerability of cytisine (Cytisine SPC).
- The proportion of patients who discontinued treatment because adverse reactions was 6-15.5% and in controlled studies it was comparable to the proportion of patients who discontinued treatment in the placebo group (Cytisine SPC).
- Mild to moderate adverse reactions have usually been observed, most frequently concerning the gastrointestinal tract. The majority of adverse reactions occurred at the beginning of the therapy and resolved during treatment. These symptoms could also be the result of smoking cessation, rather than the use of drug product (Cytisine SPC).

Frequency in clinical trials	**Undesirable effect (Cytisine SPC)**
Very common: (≥ 1/10)	• change in appetite (mainly increase), weight gain • dizziness, irritability, mood changes, anxiety, sleep disorders (insomnia, drowsiness, lethargy, abnormal dreams, nightmares), headaches • tachycardia • hypertension • dry mouth, diarrhea, nausea, changes flavour, heartburn, constipation, vomiting, abdominal pain (especially in the upper abdomen) • rash • myalgia • fatigue
Common: (≥ 1/100 to < 1/10)	• difficulty in concentration • slow heart rate • abdominal distension, burning tongue • malaise
Uncommon: (≥ 1/1,000 to < 1/100)	• dyspnea • See Summary of Product Characteristics for full list of “Uncommon” undesirable effects

Mode of Action

- Cytisine is a nicotine receptor partial agonist.
- Cytisine affects acetylcholine nicotinic receptors; its action is similar but generally weaker than nicotine. Cytisine competes and binds stronger to these receptors, displacing nicotine. It stimulates specific nicotinic receptors less than nicotine and doesn't pass into the central nervous system as much as nicotine.
- It is believed to act on mechanisms related to nicotine dependence in the central nervous system, preventing full activation of the mesolimbic dopamine system, increasing dopamine levels in the brain, reducing nicotine withdrawal symptoms. In the peripheral nervous system, it influences breathing, catecholamine secretion, and blood pressure and helps mitigate peripheral symptoms of nicotine withdrawal.

Pharmaceutical form, packaging and storage

- Each tablet contains 1.5 mg of cytisine; tablets are white, round, biconvex with diameter 6 mm.
- Excipients are: mannitol, microcrystalline cellulose, magnesium stearate, glycerol dibehenate, hypromellose
- Shelf life is 2 years from date of manufacture
- Store at temperatures below 25°C. Store in the original package in order to protect from moisture and light.
- PVC/PCTFE/Aluminium blisters placed into cardboard box containing 100 tablets

Price and availability

- Cytisine is a Prescription Only Medicine (POM).
- One pack of Cytisine (100 tablets) is sufficient for a complete, 25-day treatment course; the price of a pack (1 treatment course) is £115.00.
- Stock is available now via all three mainline wholesalers: AAH, Alliance and Phoenix, and selected short-line wholesalers.
- Cytisine is listed in the **Drug Tariff** (June 2024) and the **BNF** (see under “cytisinicline”)

NICE & AWMSG and other guidance

National Institute for Health and Care Excellence (NICE)

- Cytisine (cytisinicline) has been added to NICE guideline [NG209] Tobacco: preventing uptake, promoting quitting and treating dependence, updated 4 February 2025, as a first line option for smoking cessation.
- Cytisine has been included in section 1.12.8 as an option that, when combined with behavioural support, are more likely to result in them successfully stopping smoking.
- See full NICE guideline here https://www.nice.org.uk/guidance/ng209 for more information
- A national Patient Group Direction (PGD) template for the supply of cytisinicline (cytisine) tablets as part of a local tobacco dependence treatment service has been issued by the Specialist Pharmacy Service. See https://www.sps.nhs.uk/articles/cytisinicline-for-smoking-cessation/

All Wales Medicines Strategy Group (AWMSG)

- Cytisine has been recommended by AWMSG for use within NHS Wales for smoking cessation and reduction of nicotine cravings in smokers willing to stop smoking and has been included in the All Wales Guide: Pharmacotherapy for smoking cessation, updated November 2024.
- See full AWMSG guidance here: https://awttc.nhs.wales/medicines-optimisation-and-safety/medicines-optimisation-guidance-resources-and-data/prescribing-guidance/pharmacotherapy-for-smoking-cessation/

British Thoracic Society (BTS)

- The British Thoracic Society (BTS) included Cytisine as an effective nicotine analogue medication for tobacco dependency in its framework for clinicians to help patients address their tobacco dependence during a hospital stay.
- It notes that Cytisine is an important part of hospital-based tobacco dependency treatment particularly with the benefits of providing the full 25-day course supply to inpatients without the need for further prescriptions.
- See full clinical statement at https://www.brit-thoracic.org.uk/document-library/clinical-statements/medical-management-of-inpatients-with-tobacco-dependency/medical-management-of-inpatients-with-tobacco-dependency-main-document/

National Centre for Smoking Cessation and Training (NCSCT)

- Cytisine has been recommended as a first choice stop smoking aid by the National Centre for Smoking Cessation and Training (NCSCT) in the latest version of 'Local Stop Smoking Services and support: commissioning, delivery and monitoring guidance', updated April 2024.
- See full guidance at: https://www.ncsct.co.uk/publications/commissioning-delivery-monitoring

Cytisine 1.5mg Tablets from Consilient Health

Clinical Evidence Summary

- Cytisine (also known as cytisinicline) has been used in Eastern Europe for smoking cessation for over 50 years (Tutka & Zatonski 2005).
- Cytisine was approved for use in the UK in 2019 as a Prescription Only Medicine as a treatment for smoking cessation (Cytisine SPC).
- The efficacy of Cytisine has been demonstrated in randomized, placebo-controlled clinical trials (West et al 2011, Vinnikov et al 2008, Hajek et al 2013) and real world use (Zatonski et al 2006, Jiminez-Ruiz et al 2023).
- Cytisine was compared favourably to combination nicotine-replacement therapy (NRT) in an open-label trial in daily smokers (Walker et al 2014)
- In trials comparing Cytisine, given for 25 days, when compared with varenicline, given for 84 days, Cytisine did not achieve non-inferiority; however, it was associated with higher adherence and lower adverse event rates (Courtney et al 2021, Oreskovic et al 2023)
- Clinical studies and previous experience with use of cytisine-containing product indicate a good tolerability of cytisine. The proportion of patients who discontinued treatment because adverse reactions was 6-15.5% and in controlled studies it was comparable to the proportion of patients who discontinued treatment in the placebo group (Cytisine SPC).

- There are a number of published clinical trials for Cytisine for when used for smoking cessation dating back to the late 1960's (Hajek et al 2013)
- The key clinical evidence relevant for UK clinicians, i.e. have been conducted using the dosing regime and smoker populations consistent with the UK SPC, are:
    - Cytisine vs placebo: Vinnikov et al 2008; West et al 2011; Phusahat et al 2022; Hajek et al 2013
    - Cytisine observational / uncontrolled studies: Zatonski et al 2006; Jiménez-Ruiz et al 2023
    - Cytisine vs Nicotine Replacement Therapy: Walker et al 2014
    - Cytisine vs varenicline: Courtney 2021; Oreskovic et al 2023
- A summary of these trials is provided below. Links to the full papers can be found in the References section.

Cytisine vs Placebo

- The efficacy of Cytisine has been shown in randomized, placebo-controlled clinical trials (West et al 2011, Vinnikov et al 2008, Hajek et al 2013) and real world use (Zatonski et al 2006, Jiminez-Ruiz et al 2023).
- There are 2 main trials showing the efficacy of Cytisine vs placebo: Vinnikov et al 2008 and West et al 2011.

- Summary of Vinnikov et al 2008
    - Randomized, double-blind, placebo-controlled trial in n=171 smokers age 20+, smoked ≥ 15 cigarettes/day, with a high motivation to quit and no prior cytisine use, followed up over 6 months.
    - All patients were from the staff of the mining company in Kyrgyzstan, mainly men.
    - Exclusion criteria:
        - Serious or unstable disorders based on annual screening data including chest X-ray, electrocardiogram, cardiac ultrasonography upon indications, lung function testing, blood cell count, and blood biochemical assay.
        - Contra-indications for cytisine
    - Primary endpoint was continuous abstinence (defined as no cigarettes at all) verified by exhaled CO from day 5 to weeks 8 and 26. Patients that reported continuous abstinence but had exhaled CO level 9 ppm or more along with those who missed at least one visit were considered smokers.Week 8 Abstinence was Cytisine 10.6% vs. Placebo 5.7% (p = 0.38);
    - Week 26 Abstinence was Cytisine 10.6% vs. Placebo 1.2% (p = 0.01)
    - Side effects leading to discontinuation: 4 patients (4.7%) in each group; common adverse effects: dyspepsia, nausea, and headache (not conclusively linked to study medication)
- Summary of West et al 2011
    - Randomized, single-centre, double-blind, placebo-controlled trial (conducted in Poland) in n=740 adult smokers, 10+ cigarettes/day, willing to quit. Minimal behavioral support. Follow-up at 4 weeks, 6 months, 12 months.
    - Primary outcome was 12 months of abstinence after the end of treatment, defined according to the Russell Standard criteria i.e. Participants reporting:
        - Fewer than five cigarettes in each of the previous 6 months at the 6-month and 12-month follow-up visits
        - Not smoked any cigarettes in the week before the follow-up visit, and
        - Carbon monoxide concentration in exhaled breath of less than 10 ppm at the 12-month follow-up visit
    - Other inclusion criteria: not pregnant or breast-feeding or planning to become pregnant; willing to attend all study sessions; able to read and write Polish and provide informed consent; and could be contacted by telephone
    - Exclusion criteria: diagnosis of a current psychiatric disorder or a medical condition that was a cytisine contraindication
    - Secondary outcomes included: 6-month sustained abstinence, 12-month point prevalence.
    - Cytisine group: 8.4% 12-month abstinence vs. 2.4% in placebo. Percentage point difference: 6.0% (p<0.001) Relative rate of abstinence: 3.4.
    - 6-month abstinence: 10.0% cytisine vs. 3.5% placebo (6.5% difference; p<0.001). 12-month point prevalence: 13.2% cytisine vs. 7.3% placebo (5.9% difference; p=0.01).
    - Serious events: 7 total (4 in the cytisine group, 3 in the placebo group). Non-serious events: 203 (120 cytisine, 83 placebo). Gastrointestinal issues more common with cytisine (13.8% vs 8.1%, p=0.02)

- A meta-analysis of trials of Cytisine vs placebo was published by Hajek et al in 2013. It included Vinnikov et al 2008 and West et al 2011 plus 5 other trials: Paun et al 1968; Scharfenberg et al 1971; Schmidt et al 1974; Marakulin et al 1984; Monova et al 2004.

  - From the 7 trials, Cytisine was significantly more effective than the comparators (RR=1.59; 95% CI 1.43 to 1.75).
  - Using data from the two trials with the highest quality ratings (Vinnikov 2008 and West 2011), which validated smoking status and provided follow-up for at least 6 months, Cytisine was significantly more effective than placebo, increasing the chance of successful quitting more than threefold (RR=3.29; 95% CI 1.84 to 5.90).
  - Patients on Cytisine reported more gastrointestinal symptoms than patients on placebo (RR=1.76, 95% CI 1.28 to 2.42). However, there was no difference in overall reports of adverse events and no specific safety concerns emerged.

- A fourth trial, Phusahat et al 2022, conducted in Thailand compared Cytisine with placebo, plus counselling. Although the results with Cytisine are consistent with the findings in other trials, there was a higher than expected quit rate in the placebo group, so the difference at 48 weeks was no significant.
  - Randomized, single-center, double-blind, parallel design; 5 counselling sessions by pharmacists; n=132 ages 18–65, smoking >10 cigarettes/day, willing to quit.
  - Exclusion criteria: cardiac arrhythmia, cardiovascular disease, cancer, chronic renal disease (eGFR ≤ 30 mL/min/1.73 m^2), psychiatric disorders (depression, schizophrenia, or using other drugs, such as marijuana and amphetamines), pregnancy, breast-feeding, or treatment with other smoking cessation medications. Female participants of reproductive age were required to have a contraception before and during the study.
  - Primary endpoint: Continuous Abstinence Rate (CAR; self-reported continuous abstinence confirmed by exhaled carbon monoxide <7 ppm) at week 48.
  - CAR at week 48: Cytisine group: 10 (14.93%), Placebo group: 4 (6.15%). Risk Ratio (RR) for CAR at week 48: 2.41 (95% CI; 0.80, 7.35; p = 0.10).
  - In addition, the CARs at week 2, week 4, and week 12 were significantly higher in the cytisine group, but it was not significant at week 24 (Cytisine: 16.42%, Placebo: 9.23%. P=0.219)
  - Adverse events: Cytisine: 55%, Placebo: 40%. Most adverse events were common and non-serious and included gastrointestinal events, insomnia, dizziness and drowsiness.

- The efficacy of Cytisine seen in these placebo-controlled studies is supported by real-world evidence from observational studies (Zatonski et al 2006, Jiminez Ruiz et al 2023)
  - Zatonski et al (2006) evaluated the effectiveness of 25 days of Cytisine in aiding smoking cessation at the Warsaw clinic. This open, uncontrolled trial as a clinical audit of 436 smokers found CO verified abstinence rate of 13.8% at 12 months. 15.5% stopped medication due to adverse effects; there were no serious adverse events recorded.
  - Jiménez-Ruiz et al (2023) assessed patient satisfaction with a 25-day treatment course of Cytisine in an observational study conducted in Spain in 105 primary and secondary care patients. 76% of patients were abstinent at post-treatment visit while

37.1% experienced an adverse event; most were mild or moderate (most common being sleeping disorders, nausea (12.4%), and vomiting (3.8%)). Overall patient satisfaction was high: 39.0% very satisfied, 38.1% satisfied.

Cytisine vs Nicotine Replacement Therapy (NRT)

- Walker et al 2014, compared Cytisine given as a 25-day treatment course with combination Nicotine Replacement Therapy in an open-label trial of daily smokers in New Zealand (NRT).
- In this trial, Cytisine was superior to combination NRT for smoking cessation in dependent smokers
- Summary of Walker et al 2014
    - Pragmatic, open-label, randomized, controlled, non-inferiority trial comparing Cytisine (25-day course) and NRT patches and gum and/or lozenges over 8 weeks.
    - N=1310 adults (18+), daily smokers, motivated to quit, contacting New Zealand's national Quitline.
    - Exclusion criteria: pregnant or breast-feeding, taking smoking cessation medication, enrolled in another cessation program or study; self-reported pheochromocytoma; systolic blood pressure above 150 mm Hg, a diastolic blood pressure above 100 mm Hg, or both; schizophrenia, or self-reported cardiovascular event in the 2 weeks before study enrolment.
    - The type and strength of NRT were determined by Quitline advisors in accordance with participant preference and New Zealand Smoking Cessation Guidelines (Ministry of Health 2007), which recommends combination NRT.
    - NRT was supplied via pharmacy vouchers for patches (in doses of 7 mg, 14 mg, or 21 mg) and for gum (2 mg or 4 mg) or lozenges (1 mg or 2 mg) or both gum and lozenges for 8 weeks.
    - Cytisine 25-day course (100 tablets) was posted to subjects. Subjects were offered vouchers for NRT for use after the 25 day treatment course if they still had not stopped smoking or required ongoing support.
    - Additional support was provided as low-intensity telephone behavioural support for both groups.
    - Primary outcome was continuous abstinence from smoking (self-reported abstinence since quit day, with an allowance for smoking a total of five cigarettes or less, including during the previous 7 days) 1 month after quit day. Self-reported continuous abstinence was also assessed at 6 months. Secondary Outcomes were assessed at 1 week and at 1, 2 and 6 months.
    - Results: Higher continuous abstinence rate at 1 month in cytisine group (40%) compared to NRT group (31%, $p<0.001$).
    - Higher continuous quit rates at 2 and 6 months (31% vs 22%, $p<0.001$; 22% vs 15%, $p=0.002$) and longer time to relapse

- Adverse effects were more frequent in cytisine group (288 events in 204 participants) than NRT group (174 events in 134 participants; incidence rate ratio: 1.7 (95% CI, 1.4 to 2.0; P<0.001); however, the majority were non-serious and mild to moderate severity. The most frequent in cytisine group: nausea, vomiting, sleep disorders. Serious Adverse Events were Cytisine: 45 participants (7%). NRT: 39 participants (6%).
- Overall, Cytisine was found superior to nicotine-replacement therapy (NRT) for smoking cessation in dependent smokers

Cytisine vs varenicline

- Varenicline was withdrawn from the UK market in July 2021 due to presence of the nitrosamine, N-nitroso-varenicline, a potential carcinogen, above the acceptable daily intake limit (EMA 2021). However, generic varenicline is now available (https://dmd-browser.nhsbsa.nhs.uk/).
- There are two trials comparing Cytisine (using a 25-day treatment course) with varenicline (using a 3-month course): Courtney et al 2021, Oreskovic et al 2023
- These trials show that Cytisine, given for 25 days, was not as effective as varenicline, given for 84 days:
  - 6-Month Continuous Abstinence Rates 11.7% vs 13.3%; p=0.03 (Courtney et al 2021);
  - Self-reported 7-day abstinence at 24 weeks: 32.46% in Varenicline, 23.12% in Cytisine. OR: 0.63, RR: 0.71 (Oreskovic et al 2023).
  - However, the 25-day course of Cytisine was associated with higher adherence and lower adverse event rates (Courtney et al 2021, Oreskovic et al 2023).
- Summary of Courtney et al 2021
  - Non-inferiority, open-label randomized, controlled trial comparing Cytisine 1.5mg for 25 days (quit on day 5) vs varenicline, starting with 0.5-mg tablets, increasing to 1-mg twice daily for 84 days (quit on day 8). Additional telephone-based behavioral support and informational kit was offered.
  - N= 1452, Adults ≥18 years, daily smokers, willing to quit, with telephone access
  - Exclusion criteria: pregnancy, breastfeeding, or planning to get pregnant within the next 7 months; current use of smoking cessation medications or in another smoking cessation program; hypersensitivity to active substances or excipients; hospitalization in previous 3 months for arrhythmia, myocardial infarction, stroke, or severe angina; or pheochromocytoma or hyperthyroidism
  - Primary outcome was continuous abstinence from smoking (self-report of not having smoked >5 cigarettes during the 6-month period preceding the 7-month follow-up) verified carbon monoxide breath test (expired CO ≤9 ppm).
  - Primary end point: Cytisine 11.7%, Varenicline 13.3%; noninferiority was not confirmed (risk difference -1.62%, P = 0.03).
  - There was lower discontinuation due to adverse events in Cytisine group (16.5% vs. 34.3%, P < .001) and adverse events were less frequent (997 events reported by 71.4% of participants vs. 1206 events in 76.9% participants, IRR 0.88, P = 0.002); there was no significant difference in serious adverse events.
  - Overall, cytisine treatment for 25 days did not demonstrate non-inferiority in smoking cessation compared to 84 days of varenicline treatment

- Summary of Oreskovic 2023
    - Compared Varenicline for 12 weeks; Cytisine for 25 days in n= 377 adult smokers, interested in quitting, in primary care in Croatia and Slovenia
    - Inclusion criteria: primary care MD at a participating practice; aged 18 or older; smoking at least one cigarette per day; a desire to quit; did not have contraindications (per SPCs); and indicated an interest in pharmacotherapy.
    - Exclusion criteria: cognitive impairment; a mental disorder; considered be insufficiently collaborative; considered by MDs to have frequent adverse reactions to multiple drugs in the previous treatment of acute and chronic diseases; pregnant or breastfeeding; and in another smoking-cessation program
    - The primary outcome (self-reported 7-day abstinence at 24 weeks) was: 32.46% in Varenicline, 23.12% in Cytisine. OR: 0.63, RR: 0.71.
    - There was higher adherence in Cytisine group and also fewer adverse events (Cytisine: 326 total adverse events reported by 53.8% of participants, vs varenicline 677 events reported by 72.8% of participants; (IRR: 0.59; 95% CI: 0.43 to 0.81). There were also fewer severe adverse events reported in the cytisine group (18 vs. 25; IRR: 0.72; 95% CI: 0.35 to 1.47).
    - Overall, 25 day Cytisine treatment was less effective than 84 day treatment with varenicline for smoking cessation, but has higher adherence and lower adverse event rates.
- *Note: there is a third head-to-head trial of Cytisine vs varenicline (Walker et al 2021); however, as this used a Cytisine dosage regime inconsistent with the SPC, it is not relevant for UK healthcare professionals.*

Cytisine vs bupropion

- There are no head-to-head data of Cytisine vs bupropion.

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Cytisine Summary of Product Characteristics

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Zatonski W, Cedzynska M, Tutka P et al. An uncontrolled trial of cytisine (Tabex) for smoking cessation. Tobacco Control 2006;15:481–484. doi: 10.1136/tc.2006.016097 https://tobaccocontrol.bmj.com/content/15/6/481

Cytisine 1.5mg tablets Prescribing Information. Please refer to the Summary of Product Characteristics for full details.

Product name: Cytisine 1.5mg tablets Composition: 1.5mg of cytisine **Indication:** Smoking cessation and reduction of nicotine cravings in smokers willing to stop. Treatment goal is the permanent cessation of use of nicotine-containing products. **Posology and administration: Adults:** One pack (100 tablets) is sufficient for a complete treatment course of 25 days: Day 1-3: 1 tablet every 2 hours (maximum 6 per day); Day 4-12: 1 tablet every 2.5 hours (maximum 5 per day); Day 13-16: 1 tablet every 3 hours (maximum 4 per day); Day 17-20: 1 tablet every 5 hours (maximum 3 per day); Day 21-25: 1-2 tablets a day (maximum 2 per day). Stop smoking no later than 5th day of treatment; continuing smoking may aggravate adverse reactions. In case of treatment failure, discontinue; may be resumed after 2 to 3 months. **Special populations:** *Renal or hepatic impairment:* no clinical experience; not recommended. *Elderly (over 65 years):* limited clinical experience; not recommended. *Paediatric population (under 18 years):* Safety and efficacy not established; not recommended. **Method of administration:** Orally with water. **Contraindications:** Hypersensitivity to active substance or excipients; unstable angina; recent myocardial infarction or stroke; clinically significant arrhythmias; pregnancy and breastfeeding. **Warnings and precautions (see SPC for full details):** Only for patients with serious intention of weaning off nicotine. Patient should be aware that simultaneous smoking or use of nicotine-containing products could lead to aggravated adverse reactions of nicotine. Use with caution in: ischemic heart disease, heart failure, hypertension, pheochromocytoma, atherosclerosis and other peripheral vascular diseases, gastric and duodenal ulcer, gastroesophageal reflux disease, hyperthyroidism, diabetes and schizophrenia. Polycyclic aromatic hydrocarbons in tobacco smoke induce metabolism by CYP 1A2 (and possibly CYP 1A1). Stopping smoking may slow metabolism and raise blood levels of such drugs. Potentially clinically important if narrow therapeutic window, e.g. theophylline, tacrine, clozapine, ropinirole. Levels of products partly metabolised CYP1A2 e.g. imipramine, olanzapine, clomipramine, fluvoxamine, may also increase; data are lacking, clinical significance unknown. Limited data indicate metabolism of flecainide and pentazocine may be induced by smoking. Be aware of serious neuropsychiatric symptoms in patients attempting to quit smoking, with or without treatment, including: depressed mood, rarely including suicidal ideation and suicide attempt; exacerbation of underlying psychiatric illness (e.g. depression) - take care in these patients and advise accordingly. (See Pregnancy). **Pregnancy**: Contraindicated. Women of childbearing potential must use highly effective contraception. If on systemically acting hormonal contraceptives, add a second barrier method. **Breast-feeding:** Contraindicated. **Fertility:** No data available. **Undesirable effects: Very Common (≥ 1/10):** change in appetite (mainly increase), weight gain, dizziness, irritability, mood changes, anxiety, sleep disorders (insomnia, drowsiness, lethargy, abnormal dreams, nightmares), headaches, tachycardia, hypertension, dry mouth, diarrhea, nausea, changes flavour, heartburn, constipation, vomiting, abdominal pain (especially in the upper abdomen), rash, myalgia, fatigue **Common (≥1/100 to <1/10):** difficulty in concentration, slow heart rate, abdominal distension, burning tongue, malaise. **Uncommon (≥1/1000 to <1/100):** dyspnea. See SPC for full list of Uncommon undesirable effects. **NHS Price:** £115.00 per box of 100 tablets. **Legal Classification:** POM **MA numbers:** PL 51228/0001 **Marketing Authorisation Holder:** Bonteque Consulting Ltd, 29 Westcott Crescent, Hanwell, W7 1PL, United Kingdom. **Further information is available on request from:** Consilient Health (UK) Ltd, No.1 Church Road, Richmond upon Thames, Surrey TW9 2QE or drugsafety@consilienthealth.com. **Job Code:** UK-CYT-162 **Date of preparation of PI:** July 2024

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/.

Adverse events should also be reported to Consilient Health (UK) Ltd, No. 1 Church Road, Richmond upon Thames, Surrey TW9 2QE UK or drugsafety@consilienthealth.com