

REPORT AT A GLANCE: SMOKING CESSATION

KEY FINDINGS

Intervention	Comparators	Evidence Rating	US Price	Health-Benefit Price Benchmark
Cytisinicline 3 mg TID with behavioral support	Smoking Cessation (Indication)			
	No pharmacotherapy/behavioral support alone	A		
	Varenicline	C+		
	Combination NRT	C+		
	Varenicline plus combination NRT	I		
	Electronic cigarette with nicotine	I		
	Bupropion	B+		
	Vaping Cessation (Indication)			
	No pharmacotherapy/behavioral support	C++		
	Varenicline	P/I		

“Smoking cigarettes is the number one cause of preventable deaths in the US, and so any new therapy to assist with smoking cessation is extremely important. The drug we reviewed for this assessment, cytisinicline, has been used for decades in Europe and has similar efficacy to varenicline (Chantix®) but with less nausea. Manufacturer decisions on pricing are likely to have substantial effects on how easily smokers can access this medication.”

– ICER’s Chief Medical Officer, David Rind, MD, MSc

THEMES AND RECOMMENDATIONS

- Manufacturers should set the price of cytisinicline to align with the value of added patient benefits.
- Pharmacists should be allowed to prescribe cytisinicline.
- The FDA should provide a new pathway for generic drug approval when a drug has extensive evidence of safety and efficacy and is approved outside the US.

Clinical Analyses

KEY CLINICAL BENEFITS STUDIED IN CLINICAL TRIALS

Smoking cigarettes remains the number one cause of preventable deaths in the United States (US) with approximately half a million people dying each year from smoking-related illnesses. The main smoking-related causes of death are cardiovascular (strokes and heart attacks), cancer (lung, pancreatic, esophageal, bladder, colorectal, renal, and other cancers), and pulmonary (chronic obstructive lung disease [COPD], pneumonia). The economic costs of smoking in the US were estimated to be more than \$600 billion in 2018, including \$240 billion in direct health care costs and \$372 billion in lost productivity. These costs do not include the cost of tobacco products to consumers, which was estimated to be \$75.9 billion in 2021.

There are several treatment approaches that have been shown to help people quit smoking. The two most effective medical therapies for smoking cessation available in the US are varenicline (previously Chantix®) and combination nicotine replacement therapy (NRT), a long-acting patch combined with short-acting nicotine gum or lozenges.

Cytisinicline (cytisine) is derived from the seeds of an acacia bush; it has been used for smoking cessation for more than 50 years in Eastern Europe where it has historically been administered as a 1.5 mg tablet for 25 days using a downward titration schedule starting six times a day (100 tablets in total). Cytisine is a partial agonist of nicotinic acetylcholine receptors that helps to block the craving for cigarettes and blunts the short-term rewards that come from smoking a cigarette. This is essentially the same mechanism of action as varenicline. A new formulation from Achieve Life Sciences is a 3 mg pill given orally three times a day for 6 to 12 weeks. The Food and Drug Administration (FDA) Prescription Drug User Fee Act (PDUFA) date is June 20, 2026.

We performed a network meta-analysis (NMA) using two Phase III trials of the new formulation of cytisinicline to compare outcomes with varenicline. For other comparisons, we relied primarily on a 2023 Cochrane review. Cytisinicline is substantially more effective than behavioral support alone: approximately 16 more people out of 100 trying to quit would succeed for six months with cytisinicline. The efficacy of cytisinicline appears similar to varenicline for both smoking cessation and to quit vaping nicotine, but there is uncertainty in these estimates. The 2023 Cochrane review found no significant difference between the older formulation of cytisinicline and either combination NRT or electronic cigarettes used for smoking cessation.

Varenicline has gastrointestinal (GI) side effects that can limit its tolerability and can produce vivid dreams that some people find disturbing. Cytisinicline has GI effects similar to placebo; it is unclear whether it causes less sleep disturbances than varenicline. In clinical trials, rates of discontinuation for adverse events (AEs) were not different between varenicline and cytisinicline.

Because of the lower rate of GI side effects, we rated cytisinicline as “comparable or incremental” (C+) compared with varenicline for smoking cessation.

Economic Analyses

LONG-TERM COST EFFECTIVENESS

We developed an economic model focused on a hypothetical cohort of currently smoking patients who are interested in quitting cigarettes and who are being treated with one of three strategies at model entry: 1) cytisinicline with behavioral support, 2) varenicline with behavioral support, and 3) behavioral support alone. The model focused on the costs and harms of smoking.

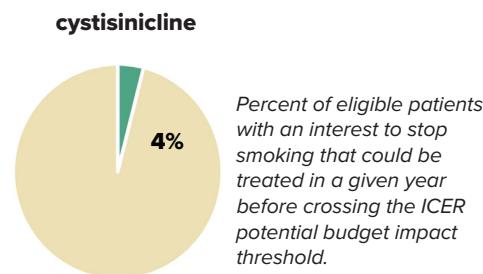
With an FDA PDUFA date of June 20, 2026, the price of cytisinicline is currently not known. Our cost-effectiveness analysis was based on a placeholder price of \$5,000 for a 12-week course. Under this assumption, cytisinicline meets commonly used thresholds for cost-effectiveness when compared with behavioral support alone but substantially exceeds these thresholds when compared with varenicline. Some analysts have suggested a lower estimated price for cytisinicline.

A potential additional benefit of cytisinicline not reflected in the comparative effectiveness or cost-effectiveness results is that some patients may be willing to try it for smoking cessation because it is a natural, plant-based product. Furthermore, any “new” therapy is likely to lead to some patients who previously were unable to quit smoking to make additional attempts. We also note that people living with serious psychiatric illness and those with low socioeconomic status are overrepresented in the population of current smokers in the US.

The Health Benefit Price Benchmark (HBPB) for cytisinicline is \$1,900 to \$2,700. For patients who have tried to quit smoking with varenicline and been unable to tolerate its gastrointestinal side effects, a somewhat higher price for cytisinicline might be appropriate.

POTENTIAL BUDGET IMPACT

At a placeholder price of \$5,000 per treatment course, and estimated eligibility and uptake assumptions, approximately 4% of patients expected to be eligible for treatment over five years could receive therapy without exceeding the potential budget impact threshold of \$880 million per year. At the lower end of ICER’s threshold prices for cytisinicline (\$1,300 per treatment course at \$50,000 per evLY), approximately 18% of patients could be treated. Given the uncertainty in the actual price of cytisinicline and anticipated uptake, ICER is not issuing an access and affordability alert for cytisinicline.



Public Meeting Deliberations

VOTING RESULTS

ICER's Virtual Public Meeting: Voting Results on Clinical Effectiveness and Contextual Considerations

ICER assessed, and the independent appraisal committee voted on the evidence for the net health benefit of cytisinicline. Some of the voting results on clinical effectiveness include the following:

- The panelists unanimously (14-0) voted that for people who smoke cigarettes the current evidence is **adequate** to demonstrate a net health benefit of cytisinicline is greater than that of behavioral support alone.
- The majority of panelists (13-1) voted that for people who smoke cigarettes, the current evidence is **not adequate** to demonstrate that the net health benefit of cytisinicline with behavioral support is greater than that of varenicline with behavioral support.

Panel members also weighed potential benefits and disadvantages beyond the direct health effects and weighed special ethical priorities. Voting highlighted the following as particularly important for payers and other policymakers to note: There is substantial unmet need despite currently available treatments.

- This condition is of substantial relevance for people from a racial/ethnic group that has not been equitably served by the healthcare system.

ICER's Virtual Public Meeting: Voting Results on Long-Term Value for Money

Cytisinicline is not yet approved, with a expected FDA action date in June 2026. The manufacturer has not yet announced a US price for the therapy if approved.

Consistent with ICER's process, because there is no firm estimate yet of a potential launch price for the treatment, the panel did not take a vote on the treatment's long-term value for money.

About ICER

The Institute for Clinical and Economic Review ([ICER](#)) is an independent, non-profit research institute that conducts evidence-based reviews of health care interventions, including prescription drugs, other treatments, and diagnostic tests. In collaboration with patients, clinical experts, and other key stakeholders, ICER analyzes the available evidence on the benefits and risks of these interventions to measure their value and suggest fair prices. ICER also regularly reports on the barriers to care for patients and recommends solutions to ensure fair access to prescription drugs. For more information about ICER, please visit www.icer.org.