Cytisinicline for Smoking Cessation
Final Policy Recommendations

FEBRUARY 12, 2026

Policy Recommendations

Introduction

The following policy recommendations reflect the main themes and points made during the Policy Roundtable discussion at the January 15th Midwest CEPAC public meeting on the use of cytisinicline for smoking cessation. At the meeting, ICER presented the findings of its revised report on this treatment and the Midwest CEPAC voting council deliberated on key questions related to their comparative clinical effectiveness, potential other benefits and contextual considerations, and long-term value for money at current prices. Following the votes, ICER convened a Policy Roundtable of two patient experts, two clinical experts, two payers, and one representative from a purchaser or large employer to discuss how best to apply the evidence and votes to real-world practice and policy. The discussion reflected multiple perspectives and opinions, and therefore, none of the statements below should be taken as a consensus view held by all participants.

A recording of the conversation can be accessed here, and a recording of the voting portion of the meeting can be accessed here. More information on Policy Roundtable participants, including conflict of interest disclosures, can be found in the appendix of this document. ICER's report on these treatments, which includes the same policy recommendations, can be found here.

The roundtable discussion was facilitated by Sarah Emond, President and Chief Executive Officer at ICER. The main themes and recommendations from the discussion are organized by audience and summarized below.

Health Equity

All Stakeholders

Recommendation 1

All stakeholders have a responsibility and an important role to play in ensuring that an effective new treatment for patients who smoke is introduced in a way that will help reduce health inequities and stigma.

Smoking remains the leading preventable cause of death in the United States. Individuals of lower socioeconomic status and those with serious psychological illness are over-represented among smokers. These two groups already suffer from reduced access to quality healthcare. In addition, smokers face significant stigma and shame. They are reminded of this daily, as they can no longer smoke in workplaces, schools, bars, and restaurants in much of the country. When diagnosed with smoking-related illnesses, many patients' reaction is that they brought this on themselves. Despite

nicotine being the most addictive legally available drug, they still blame themselves for a failure of will. And some in the broader community, including physicians, blame them as well.

We can all learn from the work of those engaged with patients who are struggling with obesity. Physicians and advocates have reframed the conception of obesity from personal failure to a complex health and social issue. We have shifted the narrative from moralizing "will power" stories to person-first language, with biological and environmental explanations. Guidelines now stress empathy, asking permission to talk about weight, providing privacy around weigh-ins, and recognizing weight bias as a quality-of-care issue rather than a motivational tool. Similar efforts for smokers offer the opportunity to engage them more deeply in their health care and to support them in their efforts to quit. As noted in the evidence report, seven out of ten smokers want to quit, and more than half try to quit each year.

To address health equity concerns:

<u>Manufacturers should take the following actions:</u>

- **Set the price of cytisinicline immediately to align with the value of added patient benefits.** The price for cytisinicline has not been set, but analyst estimates are as high as $5,000 for a 12-week treatment course, which may lead to significant access limitations. ICER's analysis suggested that treatment would achieve common thresholds for cost-effectiveness if priced between $1,900 to $2,700 for 12 weeks. For context, varenicline (brand name Chantix®) was priced at $250 for a 12-week course at launch and $1,300 just prior to losing patent exclusivity. In addition, the cost for an equivalent 12-week course in Poland would be about $150 dollars. The manufacturer should expect to charge more to account for the process of getting FDA approval, but a more than 30-fold price premium seems excessive.

  Unlike other drugs, the manufacturer was not taking on a high risk of failure to bring cytisinicline to market. Given the extensive clinical trial literature on cytisine elsewhere, the manufacturer could expect success with cytisinicline.

  Furthermore, the Affordable Care Act (ACA) may require that cytisinicline be offered without cost-sharing or prior authorization, as the US Preventive Services Task Force has given smoking cessation with a drug FDA-approved for smoking cessation an A rating. The manufacturer should not misuse this potential advantage in access to patients by setting an excessive price for cytisinicline. The manufacturer should price cytisinicline so that both individual patients and the health system will view the drug as fairly priced, leading to broader access and reducing disparities.

Payers should take the following actions:

- **Ensure that benefit designs developed in conjunction with employers and other plan sponsors do not impose out-of-pocket requirements that create major barriers to appropriate access for vulnerable patients.**

To address concerns about stigma:

Clinicians and Clinical Specialty Societies should take the following actions:

- **Work with patient advocacy organizations to ensure that guidelines and screening protocols on smoking assessment and cessation are patient-centered and sensitive to stigma directed at smokers.**
  Smoking should be referred to as an addiction resulting from biology, targeted marketing, and other social influences. Smoking should never be referred to as a moral failing or a failure of willpower. Patient-centered, empathic language should be used consistently when talking about people who smoke cigarettes. Shame can drive people away from help and toward covert use or alternative products rather than smoking cessation. Framing cessation as a shared problem solving process—acknowledging addiction, relapse risk, and emotional distress—helps maintain dignity while still clearly conveying the health benefits of quitting.

Payers

Recommendation 1

Payers should use the varenicline coverage policy as a guide for the cytisinicline coverage policy.

There is high certainty evidence that cytisinicline provides substantial net health benefits compared with behavioral therapy alone. Both cytisinicline and varenicline have the same mechanism of action. Indirect evidence supports likely equivalent efficacy with the potential for fewer side effects (nausea) with cytisinicline. There is more than 50 years of clinical experience with cytisinicline for smoking cessation in some European countries, which offers strong support for its efficacy and safety. Finally, the ACA requires that all FDA-approved drugs for smoking cessation be covered for patients because the USPSTF gives them an A rating.

Recommendation 2

Payers should cover telehealth for smoking cessation counseling and smoking cessation drug prescribing.

During the COVID pandemic, telehealth proved its efficacy in mental health care including counseling, psychiatric prescribing, and management of opioid use disorders. Telephone quit lines are readily available in most states and have a proven track record in providing behavioral support for smoking cessation. Adding telehealth as an option for prescribing smoking cessation medications will reduce barriers and increase access to these essential medications and may be particularly helpful in reaching younger patient populations. Additional tools, including text messaging programs and smart phone apps can also support patients in smoking cessation.

Coverage Criteria: General

ICER has previously described general criteria for fair coverage policies that should be considered as cornerstones of any drug coverage policy: https://icer.org/wp-content/uploads/2020/11/Cornerstones-of-Fair-Drug-Coverage--September-28-2020.pdf

Drug-Specific Coverage Criteria: Cytisinicline

As noted above, cytisinicline should be treated like varenicline.

Step Therapy

If cytisinicline's price does not align with its value, then step therapy with either varenicline and/or combined nicotine replacement would be reasonable. If it is fairly-priced, then immediate availability of the first FDA-approved drug in 20 years may encourage people who smoke to make another quit attempt, which would help to reduce the burden and cost of smoking-related illness in the United States.

Clinical Coverage Criteria

- **Age:** 18 years and older.
- **Clinical eligibility**: Patients who smoke cigarettes and are interested in quitting.
- **Exclusion criteria**: End-stage renal disease, pregnancy, breastfeeding. Cytisinicline is not contraindicated in patients with serious mental illness; this should not be an exclusion criterion.
- **Dose:** 3 mg by mouth three times daily for 12 weeks.
- **Provider restrictions**: There is no need for provider restrictions.

Purchasers

Recommendation 1

Purchasers should do more to promote smoking cessation among their covered lives.

Smoking cessation services are underutilized. Purchasers spend a tiny proportion of their pharmaceutical budget on smoking cessation, despite the large expenses due to smoking-related diseases. Greater promotion of smoking cessation services and drugs would be high yield with modest associated expenses.

Patient Advocacy Organizations

Recommendation 1

Patient advocacy organizations should promote peer support.

Peer support can play a significant role in smoking cessation by providing encouragement, shared experiences, practical advice, and accountability, which can improve the likelihood of quitting successfully. People who participate in peer support groups or engage with others who are also trying to quit smoking often feel less isolated and more motivated, which can help them manage cravings and setbacks. Patient advocacy organizations should continue to provide and promote peer support to enhance the success of smoking cessation efforts.

Researchers/Regulators

Recommendation 1

Pharmacists should be allowed to prescribe cytisinicline.

Cytisinicline has more than 50 years of clinical experience and has a good safety profile. It is available over the counter in some countries, such as Canada and those in Eastern Europe. Referrals to free smoking quit lines for behavioral therapy should be provided as part of the counseling provided by the pharmacist in writing the prescription.

Pharmacist-prescribing will expand access to this important therapy for the subset of patients with limited access to other health care providers in the US.

Recommendation 2

The FDA should provide an additional pathway for generic drug approval when the drug is approved elsewhere with extensive evidence of safety and efficacy outside the US.

The full FDA approval process from Phase I through two adequately powered Phase III studies, along with the regulatory process, is a time-consuming and expensive process. It represents a disincentive to bring such drugs to market in the US. Furthermore, given the expense of this process, manufacturers who bring a drug to market must charge high prices to recoup their investment. Offering a third path that requires fewer or no clinical trials could increase access to effective therapies in the United States and help limit the rise in health care costs.

Recommendation 3

The FDA should encourage moving safe drugs with important public health impacts, like cytisinicline, to over the counter status.

Nicotine replacement therapy is already available over the counter, which allows smokers to make a quit attempt using NRT without the intervention of a health care provider. Cytisinicline is already available over the counter in Canada, Portugal, Spain, Italy, and Poland. Quickly moving cytisinicline to over the counter status could improve uptake among hard to reach smokers and help sustain the steady decline in the percentage of Americans who smoke cigarettes.

Recommendation 4

Cytisinicline should be studied in populations excluded from the Phase III clinical trials.

This includes patients with psychiatric illness, recent heart attacks, and pregnant patients. Randomized trials are not needed. Observational data demonstrating safety and efficacy in these populations should be sufficient to extend the indication for cytisinicline to these populations.

Patients with psychiatric illness have particular difficulty with smoking cessation. The combination of cytisinicline with behavioral therapy tailored to this population could provide a real advance in smoking cessation.

Patients with a recent myocardial infarction (MI) were excluded from many smoking cessation trials, but experts told us that they did not think that this is necessary. On the contrary, these patients are often particularly motivated to quit, so additional data in this population on safety and efficacy could then be folded into existing cardiac rehabilitation programs, which have already been shown to prevent recurrent cardiovascular (CV) events and death for patients with recent heart attacks.

Pregnant women have new motivations for smoking cessation. Quitting smoking during pregnancy benefits both mother and baby by reducing risks of premature birth, low birth weight, sudden infant death syndrome, respiratory issues, and birth defects. Real-world evidence from other parts of the world may provide evidence on the risks and benefits of cytisinicline in pregnant women.

Preliminary evidence suggests that varenicline is not teratogenic, but it remains class C (risk cannot be ruled out).

Recommendation 5

There should be additional studies on the optimal duration of therapy for cytisinicline.

There is uncertainty about the optimal duration of therapy for cytisinicline. Studies found that 12 weeks of treatment was superior to six weeks. It is possible that longer therapy would be even more effective because it both decreases cravings and blunts the rewards of nicotine. Additionally, varenicline, which shares the same mechanism of action as cytisinicline, is often used for longer than 12 weeks. Long-term safety data submitted to the FDA apparently suggest no safety concerns when cytisinicline is taken for at least one year. There is a need for additional longer-term studies to evaluate the net benefits of cytisinicline for more than 12 weeks.

Recommendation 6

Perform a head-to-head trial of cytisinicline with varenicline.

There is indirect evidence from network meta-analyses that cytisinicline and varenicline have similar efficacy and adverse events (apart from nausea). Only data from a well-done randomized trial can clarify whether one of the therapies has important advantages, either in efficacy or safety. This would be an ideal study for PCORI to support as the manufacturers have minimal incentives to support such a study.

Recommendation 7

Complete the ORCA-V2 Study

There is limited evidence about the clinical benefits of cytisinicline in people who vape nicotine. While the preliminary data from the ORCA-V1 study are promising, further study is needed. We look forward to the results from the definitive ORCA-V2 trial on the efficacy of cytisinicline in helping patients using nicotine-containing e-cigarettes to quit using them. Additionally, the harms of vaping remain controversial, so the health benefits of quitting vaping are uncertain (recommendation 8).

Recommendation 8

Expand research on measuring the clinical impact of nicotine e-cigarettes (vaping).

Many people do not like feeling addicted to nicotine, whether through cigarettes, e-cigarettes, oral pouches or other delivery systems. Early evidence supports significant clinical harms from inhaling the components of e-cigarettes, but the literature is not mature. Additional evidence is needed to carefully describe the full range of potential harms from e-cigarette use. This is particularly

important as some people advocate the use of e-cigarettes as an aid to smoking cessation. In addition, e-cigarette use may be a gateway to cigarette smoking, which is unequivocally harmful.

Recommendation 9

Pursue research on the impact of financial compensation for smoking cessation.

Contingency management has been an approach that has shown promise in treating stimulant use disorders, a very challenging set of addictions. It involves giving small rewards (gift cards, vouchers) when specific goals are met, such as a negative test for the drug – in this case cotinine in the urine or carbon monoxide on breath testing. This could be a useful approach to smoking cessation in populations who have not successfully quit using other approaches.

Appendix

Appendix Tables 1 through 3 contain conflict of interest (COI) disclosures for all participants at the January 15th Public meeting of the Midwest CEPAC.

Appendix Table 1. ICER Staff and External Collaborators Conflict of Interest Disclosures

ICER Staff and External Collaborators	Conflict of Interest
Josh Carlson, PhD, MPH	No conflicts to disclose.
Hui-Hsuan Chan, MHS	No conflicts to disclose.
Anna Geiger, BS	No conflicts to disclose.
Kelsey Gosselin, MA	No conflicts to disclose.
Grace Ham, MSc	No conflicts to disclose.
Max Lee, PharmD	No conflicts to disclose.
Dmitriy Nikitin, MSPH	No conflicts to disclose.
Marie Phillips, BA	No conflicts to disclose.
Marina Richardson, PhD, MSc	No conflicts to disclose.
David M. Rind, MD, MSc	No conflicts to disclose.
Sol Sanchez, BA	No conflicts to disclose.
Temiwunmi Shobanke, MS	No conflicts to disclose.
Kangho Suh, PharmD, PhD	No conflicts to disclose.
Jeffrey A. Tice, MD	No conflicts to disclose.

Appendix Table 2. Midwest CEPAC Panel Member Participants Conflict of Interest Disclosures

Midwest CEPAC Member	Conflict of Interest
Eric Armbrecht, PhD Professor and Associate Provost, Saint Louis University Center for Health Outcomes Research, School of Medicine and College for Public Health & Social Justice	No conflicts to disclose.
Alan Balch, PhD Chief Executive Officer, Patient Advocate Foundation and the National Patient Advocate Foundation	No conflicts to disclose.
Bijan Borah, PhD Professor of Health Services Research, Mayo Clinic College of Medicine and Science Consultant, Division of Health Care Policy and Research, Department of Health Sciences Research, Mayo Clinic Joint Appointment as a Consultant, Department of Obstetrics and Gynecology, Mayo Clinic	No conflicts to disclose.
Kurt Vanden Bosch, PharmD System Formulary Manager, St. Luke's Health System, Idaho	No conflicts to disclose.
Donald Casey, MD, MPH, MBA, MACP, FAHA, DFACMQ, DFAAPL, CPE	No conflicts to disclose.

Midwest CEPAC Member	Conflict of Interest
Associate Professor of Internal Medicine, Rush Medical College Adjunct Professor of Healthcare Quality & Safety and Population Health, Thomas Jefferson University College of Population Health Affiliate Faculty, Institute for Healthcare Informatics, University of Minnesota Faculty, Artificial Intelligence in Cardiology Program (ATRIA)	
Yngve Falck-Ytter, MD, AGAF Professor of Medicine, Case Western Reserve University; Chief, Gastroenterology and Hepatology VA Northeast Ohio Healthcare System, Cleveland	No conflicts to disclose.
Heather Guidone, BCPA Program Director, Center for Endometriosis Care (CEC)	No conflicts to disclose.
Jayani Jayawardhana, PhD Associate Professor, Health Management & Policy, University of Kentucky's College of Public Health	No conflicts to disclose.
Jill Johnson, PharmD Professor, Department of Pharmacy Practice, University of Arkansas for Medical Sciences College of Pharmacy	As part of her income at the UAMS College of Pharmacy, she has support from one of their service divisions, the Evidence-based Prescription Drug Program. Through this, she has intellectual property income through UAMS Bioventures that exceeds $1000/year.
David Kim, PhD Assistant Professor of Medicine at the University of Chicago	No conflicts to disclose.
Timothy McBride, PhD Bernard Becker Professor, School of Public Health, Washington University in St. Louis Co-Director, Center for Advancing Health Services, Policy & Economics Research (CAHSPER) Co-Director, Policy and Structural Solutions (PS2) Innovation Research Network	No conflicts to disclose.
Reem Mustafa, MD, MPH, PhD Professor of Medicine, Division of Nephrology and Hypertension Director, Outcomes and Implementation Research, University of Kansas Medical Center	No conflicts to disclose.
Rachel Sachs, JD, MPH Professor of Law, Washington University in St. Louis Faculty Scholar, Washington University in St. Louis Institute for Public Health	No conflicts to disclose.
Timothy Wilt, MD, MPH Professor of Medicine, Core Investigator, and Staff Physician at the Minneapolis VA Center for Chronic Disease Outcomes Research, University of Minnesota School of Medicine	No conflicts to disclose.

Appendix Table 3. Policy Roundtable Participants and COI Disclosures

Policy Roundtable Participant	Conflict of Interest
Mike Hess Senior Director of Advocacy & Regulatory Affairs, COPD Foundation	80% of COPD Foundation's annual funding is from health care companies.
Hayden McRobbie, MB ChB, PhD Professor of Population Health, Queen Mary University of London	No conflicts to disclose.
Judy Nagy Patient Advocate	Judy Nagy volunteers with AiArthritis, Arthritis Foundation, and the Global Healthy Living Foundation and does not receive income from these organizations.
Nancy Rigotti, MD Professor of Medicine, Harvard Medical School; Director, Tobacco Research & Treatment Center, Massachusetts General Hospital	Dr. Nancy Rigotti has received research funding through Massachusetts General Hospital from Achieve Life Sciences, Inc. for conducting clinical trials of cytisinicline. She received consulting fees from Achieve Life Sciences through the end of 2022, but not since that time.
Benjamin Broder, MD, PhD Regional Assistant Medical Director of Quality and Clinical Analysis, Kaiser Permanente	Dr. Benjamin Broder is a full time employee of Kaiser Permanente.
Peter A. Glassman, MBBS, MSc, FACP Chair, Medical Advisory Panel, Veterans Affairs Pharmacy Benefits Management Services	Dr. Peter Glassman is a full time employee of the Department of Veterans Affairs.
Julia Logan, MD, MPH Chief Clinical Director, CalPERS	Dr. Julia Logan is a full time employee of CalPERS.