Four countries shed light on drug-review policies

Drug policy is a mix of scientific evidence, judgment, altruism, self-interest, and politics that are superimposed on a complex, semirational, constantly changing, overburdened system, said Andreas Laupacis, chair of the Canadian Expert Drug Advisory Committee (CEDAC).

Or at least, he said, that is what it feels like in Canada.

But, Laupacis added, he takes comfort in knowing that other nations are also struggling with the same complex issues of how best to evaluate the effectiveness and safety of prescription drugs and determine which medications should be publicly funded.

Laupacis joined representatives from the United Kingdom, Germany, the United States, and the pharmaceutical industry at an April 22 forum in Washington, D.C., to discuss methods used in conducting systematic reviews of prescription drugs, what other information is used in determining coverage, and the public’s and other stakeholders’ roles in the process.

The Capitol Hill briefing was sponsored by two nonpartisan groups: the Commonwealth Fund and the Alliance for Health Reform.

In Canada, Laupacis said, the federal government has drug-approval authority, but provincial and territorial governments have the last word on determining which medications will be publicly funded.

CEDAC, an 11-member panel consisting of 8 physicians and 3 pharmacists, makes national recommendations about drug coverage based on systematic reviews of clinical evidence and pharmacoeconomic data, known as the Common Drug Review, he added.

But the ultimate decision about whether a drug will be funded is left to the ministers of health for each of the 10 provinces and 3 territories, Laupacis said.

One controversy surrounding CEDAC, he said, is that there are no public members or economists on the committee.

Inpatient drugs in Canada are covered by the nation’s “hospital global budget,” Laupacis said, while outpatient medications for patients who are 65 years or older are publicly reimbursed as long as those products are on an approved formulary.

However, about 34% of Canada’s population relies on private health plans for prescription drug coverage, he noted.

Unlike in the United States, Laupacis said, health plans in Canada cannot negotiate drug prices with manufacturers because the law sets prices based on the median price charged in seven countries, one of which is the United States.

Aside from Australia, he claimed, Canada has had the most experience using cost-effectiveness evaluations to make decisions about drug reimbursement.

“I would remind you that there are two words in cost-effectiveness, and in my opinion the most important one is effectiveness,” Laupacis said. “A drug cannot be cost-effective if it isn’t clearly effective. And in many instances, an extremely expensive drug, if it is extremely effective, is actually cost-effective.”

The average evaluation time for a drug undergoing the Common Drug Review process, he said, is about five months, unless a pharmaceutical company appeals a negative decision by CEDAC.

Drug companies have a one-time-only appeal available for each medication, Laupacis said, unless a future clinical trial shows new evidence of a product’s safety and efficacy.

While CEDAC tries to make the drug-evaluation process as transparent as possible, he said, one drawback is that pharmaceutical firms have an option to submit unpublished data that can be kept from the public’s view.

“So in some of our recommendations you’ll see this slightly bizarre thing that says, ‘We reviewed three randomized trials, and this is the result of the one, and by the way, we can’t tell you about the others,’” Laupacis said.

He noted that while there are some drawbacks to restricted formularies, he pointed to a decision a few years ago by the provincial government in British Columbia, which decided not to include rofecoxib on its formulary.
They were never convinced that the drug was cost-effective and always had concerns about its overall risk–benefit ratio, and they are now sort of pointing to the fact that they believe that having a restrictive formulary actually saved the lives of some British Columbians in terms of avoiding cardiovascular disease,” Laupacis said.

Canadian province health ministries are also using reviews from the Drug Effectiveness Review Project (DERP)—a consortium of 15 U.S. states, the California HealthCare Foundation, and the California Public Employees Retirement System—to help inform their decisions about drug coverage, said Mark Gibson, deputy director of the Center for Evidence-Based Policy of the Oregon Health and Science University, which maintains DERP.

The project obtains and synthesizes global evidence on the relative effectiveness, safety, and effect on subpopulations of 25 classes of drugs, Gibson said.

DERP states use the reviews to guide policy for Medicaid preferred-drug lists, and several states use the reviews in determining public employees’ pharmaceutical coverage, he said.

Research for DERP is done by organizations designated by the Agency for Healthcare Research and Quality as evidence-based practice centers, he added.

The DERP review process is thorough and transparent, Gibson insisted.

Draft questions and reports are placed on the Web where the public, pharmaceutical industry, and advocacy organizations have an opportunity to read and comment on the material. Final reports can also be accessed by anyone on the Internet.

However, Gibson warned, “we believe that our reports are really tough for an individual consumer to use. They’re not consumer-friendly.”

The Consumers Union, publishers of Consumer Reports, and AARP recently have started translating the DERP reports into more consumer-friendly formats and have placed completed information on their respective Web sites, he noted.

In evaluating data, Gibson said, reviewers first search for head-to-head, randomized, controlled trials comparing effectiveness, safety, and effect on subpopulations of the medications.

However, he said, those types of studies often do not exist. Reviewers next consider randomized, controlled trials that compare a medication to placebo.

Researchers also evaluate observational studies, Gibson said, because most clinical trials tend to be fairly short.

“Observational studies have a longer timeline that allows us to catch complications and side effects that may show up after general use of the drug,” he said.

Reviewers must also evaluate the quality of the studies, Gibson said.

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“Not all studies are created equal,” he said. “Some are good and some are not very good. We carefully read those studies, and we determine which are high quality. Those that are of high quality are synthesized into a cumulative look at what the research available tells us about the drugs that we have under consideration.”

The major problem for agencies that are charged with conducting drug reviews, said Peter T. Sawicki, director of the newly formed German Institute for Quality and Economic Efficacy in Health Care, is that “the available evidence is not always sufficient evidence.”

The larger the gap between the sufficient and the available evidence, he said, the stronger the need is going to be for an “extensive explanation” about a government’s decision to make the public pay for a drug.

“So the gap between available and sufficient evidence must be put into a relation, for example, nature and severity of the disease,” he said.

Germany, Sawicki said, has a “solidarity system” of health care in which “everybody’s insured” because all citizens pay for a so-called statutory health insurance fund.

Although the prescribing rate of unnecessary medications has decreased in recent years because physicians are using a more evidence-based approach to prescribing, he said, the nation, nonetheless, continues to struggle with rising prescription drug costs.

Peter Littlejohns, clinical and public health director of the United Kingdom’s National Institute for Health and Clinical Excellence, said one issue his organization is mulling over is how to assess the cost-effectiveness of medications, such as orphan drugs, that affect a small population.

“What we have is a probability of accepting or rejecting a drug based on cost-effectiveness, but also on other issues of fairness, equity, the quality of data and, indeed, how can you assess one drug where it is the only intervention that is life saving against drugs where there may be 10 other drugs?” he said.

Marc L. Berger, vice president of outcomes research and management at Merck & Co., said that while his company supports comparative effectiveness to inform best practice guidances and coverage policies, “We believe that population-based, evidence-based medicine should not preclude access to nonpreferred interventions that are medically necessary.”

“There are always some people who may not benefit or be able to tolerate a preferred drug,” he said. “They should also, as appropriate, have access to those nonpreferred drugs.”

What makes sense on average for the whole population, Berger argued, may not make sense for an individual patient.

—Donna Young

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