Drug Costs Need Not Limit Options

BY DENISE NAPOLI

As debate continues over whether to enact a public health plan in the United States, researchers from Canada and Australia assert that "the use of cost- effectiveness in coverage decisions need not be an undue barrier to drug funding" by a national plan.

That goes "even for expensive medications, when there is robust evidence of effectiveness, at least in some patient subgroups," Fiona M. Clement, Ph.D., of the University of Calgary (Alta.) and her colleagues reported (JAMA 2009;302:1437-43).

Comparative effectiveness and cost-effectiveness research need not result in only either-or decisions, according to Dr. Clement and her colleagues. "Medications can be reimbursed in specific subgroups where they are felt to be cost effective or can be listed with a higher co-payment if choice and access to therapy are valued highly."

The Food and Drug Administration does not take cost-effectiveness into consideration when approving medications, nor does Medicare when making coverage decisions.

The investigators looked at a total of 602 decisions by governmental agencies tasked with determining whether new drugs should be listed in public formularies in their respective countries: the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom, the Pharmaceutical Benefits Advisory Committee (PBAC) in Australia, and the Common Drug Review (CDR) in Canada.

The investigators made case studies of three high-cost drugs that were considered by all three agencies: ranibizumab (marketed as Lucentis in the United States); insulin glargine (Lantus), and teriparatide (Forteo).

Ranibizumab, which clinical studies showed to be highly effective for wet age-related macular degeneration, was approved by all three agencies, despite a high cost per monthly injection.

In the case of insulin glargine, which is three times more expensive than the already approved intermediate-acting insulin NPH, "although each of the committees agreed that insulin glargine offered small incremental benefits over insulin NPH, all felt that unrestricted use at the price submitted was not cost-effective," the authors wrote.

Nevertheless, out of the three agencies studied, only Canada's CDR denied coverage of the drug. Australia's PBAC negotiated an unrestricted benefit for Lantus in that country at a "confidential," cheaper price after five resubmissions by the maker.

And in the United Kingdom, the drug was still recommended for all type 1 diabetes patients, as well as for a subset of type 2 patients without restriction.

When it came to teriparatide, "each of the committees agreed that [the drug] had been shown to reduce the incidence of vertebral and nonvertebral fractures in comparison with placebo, but felt that bisphosphonates would have been a more appropriate comparator within randomized trials," wrote the authors.

The CDR and PBAC denied coverage, but NICE "felt that the use of this agent might be cost-effective in a small subgroup of patients with severe osteoporosis for whom bisphosphonates had failed, and listed it for this small subset of patients."

The investigators concluded that "perhaps the main lesson from the experience of the three countries is that systematic, durable, and widely accepted decisions can be made using comparative effectiveness and cost-effectiveness, although it is evident that other information beyond these two criteria can be incorporated into decision making."

The study was funded by a grant from the Canadian Agency for Drugs and Technologies in Health.

No individual financial disclosures were reported. ■

EVIDENCE-BASED PSYCHIATRIC MEDICINE

Treating Peginterferon-Induced Depression

The Problem

You work in a state prison and are consulted on cases for evaluation and treatment of hepatitis C patients with a history of depression who are about to undergo peginterferon therapy.

The Question

Which treatments are effective for peginterferon-induced depression?

The Analysis

We first searched the Cochrane Database of Systematic Reviews (www.cochrane.org/reviews) and found no reviews. We then searched Medline combining "depression" and "interferon."

BY JAN LEARD-HANSSON, M.D.

BY LAURENCE GUTTMACHER, M.D.

The Evidence

We were able to locate a recent review article, from which our evidence is gleaned (Can. J. Psychiatry 2009;54: 614-25).

Hepatitis C virus (HCV) is transmitted mainly through IV drug use (65%). Of those with acute HCV, 85% will develop chronic HCV, of which 20% will develop liver cirrhosis. Genotypes 1, 2, and 3 account for most infections in North America (with genotypes 4, 5, and 6 occurring in Egypt, South Africa, and Southeast Asia). Genotype 1 is treated with a 48-week course of weekly IM peginterferon and daily oral ribavirin. Genotypes 2 and 3 are treated with a 24-week course. Response to treatment (undetectable HCV at 6 months post therapy) is about 50% for genotype 1 and 80% for genotypes 2 and 3.

Depression occurs in about 25% of patients with untreated HCV. About 33% of patients undergoing peginterferon treatment for HCV become depressed. Of this latter group, 75% of them develop depression (plus or minus suicidal ideation) within the first 8 weeks of peginterferon treatment.

For this review, the authors looked at more than 170 studies but narrowed these down to 4 (3 prophylactic trials and 1 symptomatic trials), based on including only randomized controlled trials.

Dr. Charles L. Raison conducted a double-blind, placebo-controlled study examining the efficacy of paroxetine pretreatment to prevent peginterferon-induced depression (Aliment. Pharmacol. Ther. 2007;25:1163-74). A total of 15 patients with a prior history of major depression and 46 patients with no history of mood disorder were randomized to receive paroxetine 10-40 mg/day or placebo. Treatment started 2 weeks before peginterferon therapy and continued for the 24-week regimen. Patients in the paroxetine group experienced significantly lower depressive symptoms.

Benjamin Morasco, Ph.D., conducted a double-blind, placebo-controlled study examining the efficacy of paroxetine pretreatment (J .Affect. Disord. 2007;103:83-90). A total of 33 patients were included, and participants were excluded if they showed any psychiatric symptoms for 6 months prior to study start.

Treatment started 4 weeks before peginterferon therapy and continued for the 48-week regimen. Prophylactic treatment with paroxetine did not decrease the likelihood of peginterferon-induced depression, but, in 10 of 11 patients who developed peginterferon-induced depression and entered the rescue arm of the study, open-label treatment with paroxetine reduced symptoms of depression.

Dr. Martin Schaefer conducted an open-label prospective study examining the efficacy of citalopram pretreatment (J. Hepatol. 2005;42:793-8). In that study, a group of 14 patients, primarily with affective disorders, were prescribed 20 mg/day citalopram starting 2 weeks before peginterferon treatment. The incidence of depression was compared with 11 patients with psychiatric disorders and 11 patients without psychiatric disorders who received no pre-citalopram treatment. The incidence of major depression during the first 6 months of peginterferon treatment was 14%, 64%, and 55%, respectively. Patients who developed major depression in the latter two groups improved with citalopram rescue treatment.

Dr. Martin R. Kraus conducted a randomized, double-blind, placebo-controlled study examining the efficacy of citalopram in treating peginterferon-induced depression (Gut 2008;57:531-6). A total of 100 patients with HCV were included in the study. During peginterferon therapy, they were monitored using a standardized scale for depression. Fourteen patients with clinically significant depression were then randomly assigned to placebo and 14 were assigned to citalopram 20 mg/day. Patients in the citalopram group showed significant improvement within 4 weeks of citalopram treatment. Patients in the placebo group showed no improvement. In five placebo patients, rescue citalopram was given and led to significant deceases in the depression scores.

The authors of the Canadian review article cautioned against rare risks of bone marrow suppression with mirtazapine, selective serotonin reuptake inhibitor–induced mania during peginterferon treatment, and risk of spontaneous bleeds with SSRIs in HCV patients.

The Conclusion

Best available evidence suggests that paroxetine and citalopram prophylactic or symptomatic treatment are effective for peginterferon-induced depression. Conclusions should be tempered by the small sample sizes.

DR. LEARD-HANSSON is a forensic psychiatrist who practices in San Diego. DR. GUTTMACHER is chief of psychiatry at the Rochester (N.Y.) Psychiatric Center. They have no financial interest in any product or service discussed in this column.

INDEX OF ADVERTISERS