Clozapine: Benefits and Risks

To the Editor:

The National Institute of Mental Health and Dr. David Shore are to be thanked and congratulated for the very complete and informative issue of the Schizophrenia Bulletin entitled “Special Report: Schizophrenia 1993.”

Somehow the dangers of clozapine have been grossly exaggerated. Let us look at the facts. There are now over 60,000 patients being treated with clozapine in the United States. There have been seven deaths that arguably were due to agranulocytosis resulting from clozapine treatment. However, all of these deaths occurred in 1990 and 1991. There were no deaths in 1992 and so far there have been none in 1993. This is because of our greater experience with the medicine and the application of new drugs that cut the white blood cell count recovery time in half.

Also forgotten in evaluating the risks of clozapine is the known suicide rate of 10 percent for schizophrenia patients treated with standard neuroleptics. There have been no known suicides among those being treated with clozapine.

It might be rewarding to publish an entire issue of the Schizophrenia Bulletin examining the experiences of doctors, patients, and families in the use of clozapine and completely upgrading the statistics on its efficiency and risk. Such an issue might include some material from around the world on clozapine use; for example, the Chinese experience with making clozapine the medicine of choice in treating schizophrenia would be of great interest.

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Response to Fuchs

In his letter to the editor, Fuchs (1994, this issue) suggests that the dangers of clozapine are grossly exaggerated. We would agree with Mr. Fuchs that the current utilization levels of clozapine suggest that it is being markedly underutilized. Specifically, 60,000 patients have been exposed to the drug and 44,000 patients are currently receiving it (personal communication, Heidi Sykes-Gomez, Sandoz Pharmaceuticals, July 27, 1993); this number represents approximately 4 percent of patients with schizophrenia. Our experience, as well as estimates from the literature, regarding the prevalence of treatment-refractory or treatment-intolerant schizophrenia suggest that a trial of clozapine may be indicated in as many as 20 percent of the patients suffering from this illness. Clearly, utilization levels are far lower than one would expect.

We would not necessarily conclude, however, that the risks have been exaggerated. We now have a more precise estimate of the incidence of agranulocytosis (Alvir et al. 1993): 0.8 percent at 1 year, based on the first 11,555 patients treated in the United States between February 1990 and April 1991. Mr. Fuchs states that seven deaths have been attributed to clozapine-induced agranulocytosis, but that no deaths have occurred in 1992 or 1993. In fact, one of the seven deaths did occur in March 1992 and an eighth death occurred in July 1993 (personal communication, Heidi Sykes-Gomez, Sandoz Pharmaceuticals, July 27, 1993). Whether the risk of fatality has actually declined in recent years remains to be seen, since statistical analysis of the incidence of rare