REPORT OF THE DEPARTMENT OF
MENTAL HEALTH, MENTAL RETARDATION
AND SUBSTANCE ABUSE SERVICES

A Study of Private Pay for Expensive Medications

TO THE GOVERNOR AND
THE GENERAL ASSEMBLY OF VIRGINIA

HOUSE DOCUMENT NO. 3

COMMONWEALTH OF VIRGINIA
RICHMOND
1994

COMMONWEALTH of VIRGINIA
DEPARTMENT OF
Mental Health, Mental Retardation and Substance Abuse Services

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TO: The Honorable Lawrence Douglas Wilder, Governor of Virginia
Members of the General Assembly

House Joint Resolution 175, adopted by the 1992 General Assembly, directed the Department of Mental Health, Mental Retardation and Substance Abuse Services (DMHMRSAS) with the assistance and cooperation of the Department of Medical Assistance Services (DMAS) and the Office of the Attorney General to "evaluate the advisability, efficiency, efficacy, and potential cost savings which may be realized through the implementation of a system in state mental health institutions which allows for private payment for all or part of the cost of medications." It was requested that recommendations regarding such a system be submitted to the 1993 session of the General Assembly. Our agency held a series of meetings with staff of DMAS, the Department of Social Services (DSS), and the Office of the Attorney General as well as with physicians and other professional staff of DMHMRSAS facilities and community services boards. A national meeting was hosted by DMHMRSAS to facilitate expert input from across the country. We have the honor of submitting herewith the report on "A Study of Private Pay for Expensive Medications."

Respectfully submitted,

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HJR 175

EXECUTIVE SUMMARY

House Joint Resolution 175 (Appendix A) called for a study of mechanisms for the delivery of expensive medications to patients in facilities operated by the Department of Mental Health, Mental Retardation and Substance Abuse Services. This study was stimulated by the desire to effectively respond to constituents who wanted improved access to clozapine, an antipsychotic medication (Clozaril, manufactured by Sandoz Pharmaceuticals), for consumers in state mental hospitals. The question of private payment for this expensive medication raised a number of clinical, legal, and ethical questions, some of which often arise as attempts are made to deliver new services in Virginia and other state public mental health systems. This is a summary of the findings and recommendations of the study.

The study was focused in the DMHMRSAS Office of Medical Affairs. The department's Clozapine Background Paper (1990) was utilized as a reference and guide for the study. Discussions were held with other state agencies including the Department of Medical Assistance Services (DMAS), the Department of Social Services (DSS), and the Office of the Attorney General. Meetings were held with Chief Medical Officers of the DMHMRSAS inpatient facilities, and with staff members of a large number of Community Services Boards across the Commonwealth. A national meeting was hosted by DMHMRSAS for the purpose of gaining the insights and experiences of leaders and experts from across the country in public mental health, health economics, medical ethics, mental health advocacy, and psychopharmacology.

Recommendations

1. DMHMRSAS should continue to make clozapine available for the treatment of severely ill schizophrenic patients who have failed to respond adequately to standard antipsychotic drug treatment.

2. Priority for clozapine trials should continue to be based on lack of availability of other treatment options, patient and staff safety concerns, severity of illness, potential for rehabilitation and/or discharge, maximum potential for benefit and, importantly, patient preference.

3. Selection of patients for trials on clozapine should not be made based solely on the patient's ability to pay for the drug and the necessary laboratory and case management services. At the same time, patients should not be limited from contributing financially to their own care.

facilities. Appropriately selected residents of mental retardation training centers who fulfil criteria for clozapine trials can also be covered by this fund.

5. Each of these facilities will appoint a clozapine oversight committee responsible for selection of patients for clozapine trials and assessment of the success of these trials based upon objective measures.

6. DMHMRSAS should continue to utilize its recently appointed Pharmacy Committee which has begun to provide guidance and oversight for pharmacy activities throughout the department. This committee, staffed and supported by the DMHMRSAS pharmacy consultant, will consider options to improve the quality of services provided while limiting the growth of the overall pharmacy budget. This committee will also oversee the further development of mechanisms to improve the delivery of clozapine to patients in community settings.

7. DMHMRSAS will begin a formal analysis of the cost effectiveness of clozapine. This study will provide a more detailed analysis of the impact of clozapine on facility census and cost projections, and community tenure of patients with schizophrenia.

8. The DMHMRSAS Office of Medical Affairs will continue to meet with staff of the Department of Medical Assistance Services and the Department of Social Services to ensure administrative case management for those patients that are in danger of returning to or remaining in state facilities as a result of lack of funding for clozapine.

Clozapine and Schizophrenia

Clozapine is an atypical antipsychotic medication that is distributed by the Sandoz Pharmaceuticals Corporation and marketed under the trade name Clozaril for the treatment of schizophrenia. Its introduction received much attention due to the therapeutic superiority of this agent in the treatment of schizophrenia, an illness that affects nearly 40,000 people each year in the Commonwealth of Virginia. Clozapine's major advantages over previous antipsychotic drugs used for the treatment of schizophrenia are that it has demonstrated:

- o superior efficacy in the treatment of the estimated 10% of patients with schizophrenia who fail to response adequately to standard antipsychotic treatment
- o apparent absence of the movement-disorder side effects that often limit patients' ability to take anti-psychotic medication
- o lack of an association with tardive dyskinesia, which is an often persistent and sometimes irreversible movement disorder affecting as many as 20% of patients who take antipsychotic medication for any prolonged period of time.

Unfortunately clozapine is associated with a 1-2% incidence of a serious blood disorder, agranulocytosis. For the group of patients with this side effect, clozapine is toxic to the cells in the bone marrow that produce the white blood cells (granulocytes) that fight infections. This side effect, although relatively rare, can be fatal if not rapidly detected and clozapine discontinued. For this reason, the introduction of clozapine into the United States was delayed for approximately ten years until a system could be developed to severely limit the possibility of serious agranulocytosis or deaths.

Large multicenter studies were conducted during the 1980's that demonstrated clearly the superiority of clozapine in patients with schizophrenia who had failed to respond to adequate trials of conventional antipsychotic medications. It was demonstrated that in a large group of patients with schizophrenia who showed no improvement with the standard antipsychotic drugs, Thorazine and Haloperidol (even at significant doses) 30% of these patients showed significant improvement within six weeks on clozapine and approximately 50% showed significant improvement at the end of six months. In addition, clozapine was not associated with the severe movement disorders that sometimes prevents patients from being able to take antipsychotic medications. Clozapine also was not associated with tardive dyskinesia. A program of weekly blood monitoring enabled all cases of blood disorders to be promptly detected and the medication stopped. In all such cases, the blood disorder was reversed and no fatalities were encountered.

Based on the information from these studies, the FDA approved

clozapine for patients with schizophrenia who had not adequately responded to other appropriate antipsychotic treatments and/or who could not receive conventional antipsychotic treatments because of unacceptable adverse side effects. The Sandoz Pharmaceutical Corporation developed the "Clozaril Patient Management System" that included weekly blood testing through Roche Laboratories and case management administered by Caremark Homecare. Clozapine was available only through the "Clozaril Patient Management System." With this system, clozapine was dispensed only one week at a time and only after the case manager made sure the patient had the necessary blood test. If a patient either demonstrated a drop in their blood count, below a predetermined level or did not take the blood test, no further clozapine was dispensed. The price of clozapine through the "Clozaril Patient Management System" (CPMS) was $172 per week, or approximately $8944 per year for the "package" including medication, laboratory testing, and case management services, regardless of the dosage of medication. Sandoz did not offer discounts to federal or state systems that were able to utilize their own case management and laboratory systems. Participation in the CPMS was required for obtaining the drug.

Because the pricing and restrictions on distribution limited access to the drug for most public sector patients, a number of legal cases developed across the country. The Virginia Office of the Attorney General participated in a multi-state antitrust suit against Sandoz Pharmaceuticals in which complaints were made of illegal "tying" of the purchase of the drug to the exclusive use of Sandoz-approved laboratory and case management services (CPMS). Prior to the completion of this suit, the manufacturer announced the "unbundling" of Clozaril and the Clozaril Patient Management System (CPMS). This allowed DMHMRSAS to develop its own system of purchase, distribution, and monitoring of Clozaril.

The DMHMRSAS Guidelines for Clozapine Use (Appendix B) defined requirements for inpatient facilities and community services boards wishing to prescribe Clozaril for treatment resistant schizophrenia. The population eligible for Clozaril trials was outlined, as were mechanisms for funding the purchase of Clozaril and related laboratory services. Medicaid funding was identified as the primary financial support for patients in outpatient settings. During the period of piloting of Clozaril distribution, facility budgets were to be supplemented by the Office of Medical Affairs for the purchase price of Clozaril for selected patients.

Interest was initially very high in the mental health community regarding the availability of clozapine for patients with schizophrenia, particularly patients who had not responded significantly to previous treatments, and for patients who have developed tardive dyskinesia. Many members of both the National and Virginia Alliance for the Mentally Ill and other consumer and family groups expressed great interest in obtaining this medication

for family members suffering from schizophrenia. Staff at state hospitals and community mental health centers similarly expressed interest in obtaining the medication for identified patients. There has also been considerable interest in the use of clozapine expressed by state mental health program directors and commissioners.

Due to the continued high cost of the drug, even after "unbundling", several important issues remained to be discussed as Clozaril began to be used in DMHMRSAS facilities and CSB clinics. The wholesale purchase price of $2.84 per 100 mg tablet, along with the cost of the still required weekly laboratory testing and case management results in a cost of approximately $20 per day for outpatients ($7300/year), and drug costs alone of $5000 per year for inpatients. As a result, a limited number of slots were made available for inpatients in DMHMRSAS facilities. Questions discussed in "Clozaril Roundtables" held in each region of the state included:

- Who should occupy a Clozaril "slot"?
- Should patients' personal or family sources of funds be utilized for Clozaril if slots are not available?
- How long should a patient remain in a "drug trial"?
- How is outcome best measured?

Patient Selection

The population of patients appropriate for referral for a possible trial of clozapine was initially defined by Sandoz Pharmaceuticals Corporation in the labelling information for Clozaril as follows:

> "Clozaril is indicated for the management of severely ill schizophrenic patients who fail to respond adequately to standard antipsychotic drug treatment. Because of the significant risk of agranulocytosis and seizure associated with its use, Clozaril should be used only in patients who have failed to respond adequately to treatment with appropriate courses of standard antipsychotic drugs, either because of insufficient effectiveness or the inability to achieve an effective dose due to intolerable adverse effects from those drugs."

DMHMRSAS operational criteria to determine a "severely ill schizophrenic patient" are that the patient meets DSM-III R diagnostic criteria for schizophrenia, and shows persistent symptoms of psychosis with significant mental status abnormalities related to either conceptual disorganization, suspiciousness, hallucinations, or unusual thought content. "Appropriate courses of standard antipsychotic drugs" was defined to include at least two antipsychotic drugs of different chemical classes, given for a duration of at least six weeks each at the maximum dosage recommended in standard pharmacology texts.

Treatment Priority Strategies

The departmental concept paper developed in 1990 discussed prioritization for clozapine trials for patients who have failed to respond to standard antipsychotic drugs because of insufficient effectiveness of those drugs. That paper listed the principles that were to be used to make decisions about Clozaril trials:

- No other treatment options remain to be tried.
- Safe management requires high levels of system resources.
- The potential for discharge to the community exists if treatment is successful.
- The potential for vocational rehabiliatation exists if treatment is successful.
- Treatment of the patient may benefit the greatest number of people.
- Severity of illness may indicate potential for response.
- **Patient preference for clozapine must be considered.**

As discussed in that paper, factors considered in the prioritization of patients for clozapine trials will necessarily change as we gain experience with atypical antipsychotics and other innovative interventions.

It is clear that a number of these prioritization principles would support a system in which individuals and/or their families might contribute financially to the cost of Clozaril treatment. It is therefore a recommendation of this study that the Department consider loosening its restrictions on such contributions.

This more liberal practice has been utilized in some CSB operated programs where patients and their families are expected to play a major role as members of the "team" responsible for the care that is delivered. Clozapine has become more available to patients in a variety of settings with several different payment mechanisms. Some patients now use their own funds to purchase the medication and laboratory work. For some of them, private funds have been used when Medicaid or other reimbursement has been temporarily unavailable.

Facility clozapine committees have been instructed to consider current and potential payment mechanisms when selecting patients for drug trials. Of the patients currently treated with clozapine, all were started without regard to their financial status. It should not be seen, therefore, as discriminatory if a patient is allowed to contribute personal funds to some parts of his own care.

Legal, Ethical and Human Rights Issues

The nature of the potential risks and benefits of clozapine treatment and the intense emotions that they have evoked require special considerations regarding informed consent. Given that clozapine is targeted at those patients who have poorly controlled chronic schizophrenia, special attention must be given to the process of obtaining consent for this treatment. Informed consent

for administration of clozapine needs to be based not only upon information about the potential risks and benefits of the drug as compared to other treatment alternatives, but also upon the criteria for continuing or discontinuing the medication at the various decision points outlined in this document, and the process by which these decisions will be made. Patients and/or authorized substitute decision makers (when patients are determined to lack the capacity to make an informed decision about whether or not to try clozapine) must be informed about the process of approval for a clozapine trial and the mechanisms for monitoring and evaluating the effectiveness of that trial. Because the decision to discontinue a clozapine trial may have a significant and negative emotional effect on a patient and his/her family, this prospect and the decision process involved need to be explicitly outlined in the initial consent process.

The length of time a patient should be tried on clozapine raises another ethical issue. As funding will continue to be limited in coming years, it is clear that continuing treatment for a patient that is demonstrating minimal or no improvement will keep another patient from receiving a trial. There is not yet a consensus as to the length of time that a clozaril trial should continue. Presentations made at the department-sponsored national conference supported the possibility of late response for some patients, even after the first six months of treatment. This will therefore have to be a clinical decision to be made by the physician and treatment team in consultation with the facility Clozaril Committee.

It was the consensus of discussion groups that all patients should have equal access to clozapine if all selection criteria and prioritization principles are satisfied or considered. While initially there were major fiscal barriers (lack of departmental funds, early unavailability of Medicaid funding, expense of bundled Clozaril/CPMS, departmental policy of disallowing private payment for facility services), by the time of the completion of this study, treatment decisions were being made for inpatients without primary attention to ability to pay. (Some facility Clozaril Committees did continue to include the availability or potential for community funding as one of several selection criteria.)

Fiscal Impact of Clozapine on DMHMRSAS

The potential scope of clozapine use for the DMHMRSAS was discussed in the Clozapine Background Paper. The number of potential clozapine patients can be determined from the total number of public-sector patients with schizophrenia who may meet the criteria for a trial of the drug and do not have a medical contra-indication to its use. This needs to be considered together with the likely percentage of patients who will show significant improvement and be recommended to continue on the drug, and the corresponding percentage of patients who do not continue on the drug.

According to Sandoz representatives, their marketing research indicated that over 4000 patients in Virginia may meet the criteria for a clozapine trial. This figure is consistent with data on the prevalence of schizophrenia and the rates of response and non-response to standard antipsychotic treatments, but does not address the issue of medical contra-indications. The rate of such contra-indications is probably between 5 and 15 percent, however, still yielding a range of between 3400 and 4000 patients who should be eligible for a clozapine trial. Approximately 80% of these patients are cared for by the public sector, including state systems (hospitals and community programs) and the Veterans Administration. The Veterans Administration accounts for around 15 - 20 % of the nation's total public sector inpatient beds and a comparable percentage of outpatient care. The state system is thus responsible for about 2/3 of the patients who are potential clozapine candidates, calculated in this manner to be between 2200 and 2600 people in Virginia.

Virginia Adult Population	
Total Adults	6,000,000
Adults with Schizophrenia	40,000
Treatment Resistant Patients	4,000
DMHMRSAS Facilities and CSB's	2,400
Private Sector and VA System	1,600
DMHMRSAS Inpatients with Schizophrenia	1,400
DMHMRSAS Inpatients on Clozapine[a]	122
Potential Inpatients in Need of Clozapine[a]	204

[a] Survey of DMHMRSAS Facilities, January, 1993

An unresolved financial issue is the extent to which Medicaid will be a potential funding source for clozapine and the other laboratory and case management services. Medicaid reimbursement was estimated to be potentially available to 50% of patients who would be discharged into the community and who would otherwise be eligible for Medicaid coverage of psychiatric services such as drugs and case management. This estimate is based on previous DMHMRSAS estimates of the percentage of patients with schizophrenia in the community who meet Medicaid eligibility criteria, and upon Department of Medical Assistance Services (DMAS) estimates of the number of Medicaid recipients who have schizophrenia.

Unfortunately, many patients who are otherwise eligible for Medicaid reimbursement enter a financial condition of "spend down" during which time the patient must assume financial responsibility for medical care until a certain percentage of his income and other resources has been contributed. Medicaid eligible patients who also receive Social Security Disability Income or who inherit property have had problems with outpatient treatment with clozapine because

of this episodic problem. Some patients have only been able to continue their medication by assuming responsibility for the drug during "spend down". Community services boards and the Aftercare Pharmacy will examine options for maintaining these patients so that needless hospitalizations can be avoided.

If the estimated 2,400 public sector patients with treatment resistant schizophrenia were to be prescribed clozapine at this time, state expenditures would be as high as 12-14 million dollars per year. The cost of serving the estimated 300 current inpatients selected for clozapine, and an equal number of outpatients in CSB operated clinics would total approximately 3 million dollars per year.

The issue of potential "savings" from clozapine use in facilities remains speculative. It is very difficult to predict the extent of possible cost savings resulting from the successful treatment and return to the community of patients who have previously required continued hospitalization. There is no cost offset in our system when a patient is discharged to the community and the bed is then taken by a new patient. Cost offset will only occur when a sufficient number of patients can be discharged to allow the closing of wards in facilities. Several DMHMRSAS facilities are currently operating in excess of 100% capacity on their admission units. It is therefore uncertain whether discharge of patients who are successfully treated with clozapine would result in more than "decompression" of currently overutilized hospital programs, at least in the short term. In addition, the availability of appropriate housing alternatives for discharged patients will need thorough review. However, Virginia's continuing population growth creates a situation in which the usage of clozapine and discharge of patients to the community may reduce the need to establish additional institutional beds in the future, thus reducing the demand for new money.

These issues will be studied during the next year as we examine the cost effectiveness of clozapine. In addition, DMHMRSAS will develop a Clozapine Patient Data Base in which all facility and CSB data realted to clozapine will be included. This data base will include patient demographic data and data regarding duration of illness and duration and severity of functional impairment. We will be able to examine the clinical efficacy of the drug for the population as a whole using statewide outcome data.

Staff Education

Education regarding the use and monitoring of clozapine spans all DMHMRSAS professional groups. In addition to psychiatrists learning about the drug, its indications, dosage strategies, side effects, and interactions, they will need to become familiar with objective outcome measures. Nursing staff will need to learn about the drug's side effect profile and special monitoring requirements. The greatest educational challenge, however, applies to all

facility and community staff who will work with patients who are "emerging" from psychosis for the first time in many years. These patients have multiple needs for rehabilitation as they grapple with learning the psychosocial skills necessary for living in the community. In addition, some of these patients undergo significant emotional turmoil as they realize how severely ill they have been, and how much they have lost to their illness. Educational resources for hospital and community staff will be developed around the existing expertise in these areas at Central State Hospital, Western State Hospital, the Medical College of Virginia Schizophrenia Program, and the University of Virginia School of Medicine.

Recommendations

1. DMHMRSAS should continue to make clozapine available for the treatment of severely ill schizophrenic patients who have failed to respond adequately to standard antipsychotic drug treatment.

2. Priority for clozapine trials should continue to be based on lack of availability of other treatment options, patient and staff safety concerns, severity of illness, potential for rehabilitation and/or discharge, maximum potential for benefit and, importantly, patient preference.

3. Selection of patients for trials on clozapine should not be based solely on the patient's ability to pay for the drug and the necessary laboratory and case management services. At the same time, patients should not be limited from contributing financially to their own care.

4. DMHMRSAS should continue to provide funding for clozapine for up to 150 patients at state mental health inpatient facilities. Appropriately selected residents of mental retardation training centers who fulfil criteria for clozapine trials can also be covered by this fund.

5. Each of these facilities will appoint a clozapine oversight committee responsible for selection of patients for clozapine trials and assessment of the success of these trials based upon objective measures.

6. DMHMRSAS should appoint a Pharmacy Committee which will provide guidance and oversight for pharmacy activities throughout the department. This committee, supported by the DMHMRSAS pharmacy consultant, will consider options to improve the quality of services provided while limiting the growth of the overall pharmacy budget. This committee will also oversee the further development of mechanisms to improve the delivery of clozapine to patients in community settings.

7. DMHMRSAS will begin a formal analysis of the cost effectiveness of clozapine. This study will provide a more detailed analysis of the impact of clozapine on facility census and cost projections, and community tenure of patients with schizophrenia.

8. The DMHMRSAS Office of Medical Affairs will continue to meet with staff of the Department of Medical Assistance Services and the Department of Social Services to ensure administrative case management for those patients that are in danger of returning to or remaining in state facilities as a result of lack of funding for outpatient clozapine.

APPENDIX A

GENERAL ASSEMBLY OF VIRGINIA--1992 SESSION

HOUSE JOINT RESOLUTION NO. 175

Requesting the Departments of Mental Health, Mental Retardation and Substance Abuse Services and Medical Assistance Services, in conjunction with the Office of the Attorney General, to study the advisability of a system in which private payment for costly medications can be utilized in state mental health facilities.

Agreed to by the House of Delegates, February 9, 1992
Agreed to by the Senate, March 4, 1992

WHEREAS, so-called "miracle" drugs usually do not live up to their name, but occasionally drugs do evolve which can dramatically affect the course of disease and the eventual ability of mental patients to live a relatively normal life outside of institutions; and

WHEREAS, because of the costs of developing such drugs and the patent life for any drug, many of these medications are sole source drugs and can be very expensive especially when the drugs are "bundled" with other services which are required to be provided as a protection both to the patient and the legal liability of the pharmaceutical company; and

WHEREAS, average cost for institutionalization for a patient in a mental facility is $55,000 per year and the cost of human suffering for the patient and family is immeasurable; and

WHEREAS, the cost of many of these drugs is prohibitive within many state budgets, and therein lies the quandary when the pharmaceutical company refuses to lower the price of the drug until sales increase and sales do not increase because of the prohibitive cost; and

WHEREAS, the Code of Virginia requires that any medication to be covered by Virginia Medicaid must not be restricted and must be freely available, and most third-party payors do not cover pharmaceutical costs for that drug generally unless the federal government has approved Medicaid coverage for that drug; and

WHEREAS, the state does not generally allow private pay for medications because it is seen to be discriminatory in that it provides services based on ability to pay, and the state does not generally allow outside financing of certain projects; and

WHEREAS, many parents or other involved individuals are willing to sacrifice to help pay for certain medications which are not generally available for mental health clients; now, therefore, be it

RESOLVED by the House of Delegates, the Senate concurring, That the Departments of Mental Health, Mental Retardation and Substance Abuse Services and Medical Assistance Services, in conjunction with the Office of the Attorney General, evaluate the advisability, efficiency, efficacy, and potential cost savings which may be realized through the implementation of a system in state mental health institutions which allows for private payment for all or part of the cost of medications which could not otherwise be made available to patients and where the general distribution drugs would not be otherwise affected.

The Departments shall complete their study in time to submit their findings and recommendations to the 1993 Session of the General Assembly as provided in the procedures of the Division of Legislative Automated Systems for the processing of legislative documents.

APPENDIX B

COMMONWEALTH of VIRGINIA

DEPARTMENT OF

Mental Health, Mental Retardation and Substance Abuse Services

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M E M O R A N D U M

November 15, 1991

TO: Commissioner's Staff
Facility Directors
Facility Medical Directors
Community Service Boards' Executive Directors
Community Service Boards' Medical and
Mental Health Directors

FROM: King E. Davis, Ph.D.
Commissioner

SUBJECT: Policy Guidance on Clozapine

This memorandum and attachments are being distributed to provide DMHMRSAS facilities and mental health clinics with current guidelines for the use of the antipsychotic drug clozapine (Clozaril, Sandoz Pharmaceuticals). As of this date, clozapine is approved for limited use for the treatment of schizophrenia in those patients in our system who have been judged unresponsive to conventional pharmacological treatment. Since its approval by the Food and Drug Administration last year, the distribution and use of clozapine has been delayed because of multiple medical, administrative, legal, and fiscal issues surrounding its use. While clozapine has been shown to be clearly efficacious for some neuroleptic non-responders, and offers hope for significant improvement for treatment-resistant schizophrenic patients, its potentially serious side effects and continued high cost limit its widespread use.

As a result of continued limited fiscal resources across the Commonwealth and within the Department, facilities and clinics will need to develop local protocols to make selections of those patients who may be candidates for clozapine, to screen them for eligibility for a trial on the drug, and to monitor them closely for both dangerous side effects as well as for progress and

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improvement. Efforts must be made on a local basis to develop a fair and nondiscriminatory patient selection process to prioritize this treatment for those patients with the best chances of gaining benefit from such a trial. At the same time, the responsibility and decision making for the prescribing, monitoring, and continuing of clozapine must be maintained at the level of the physician-patient relationship, with appropriate and necessary input from the interdisciplinary treatment team as well as from patients' families and advocates.

Questions regarding Clozaril and its use in DMHMRSAS facilities and CSB clinics can be referred to Ronald O.Forbes, M.D.,Director, Office of Medical Affairs.

GUIDELINES FOR CLOZAPINE USE

Clozapine Use at DMHMRSAS Facilities

In order for clozapine to be used at a mental health or mental retardation facility operated by the Department, a "Clozaril Treatment System" should be registered with Sandoz Pharmaceutical Corporation. The facility director or medical director must co-sign a "Patient Safety Understanding Form" along with the facility pharmacy director, acknowledging their understanding and acceptance of the information in the Clozaril package insert, and their agreement to adhere to its requirements. As you probably know, these requirements are primarily intended to insure that pharmacies will only dispense a one week supply of medication after receiving documentation of a current white blood cell examination within the acceptable safe range. Information on treatment system registration is included in this package in the attachment "Treatment Systems Requirements".

Each facility must develop a written plan to oversee and insure the appropriate management of the local Clozaril Treatment System. Responsibility for this institutional oversight process may be assigned to the Pharmacy and Therapeutics, Quality Assurance, or other appropriate medical staff committee. A facility may choose to use a specially appointed multidisciplinary Clozaril Committee to provide this oversight function. Copies of the facility plans, with the names of the assigned oversight committees and responsible contact persons should be sent to our Office of Medical Affairs. That office will provide feedback and other assistance, and will periodically monitor the facility management of the local Clozaril Treatment System.

Criteria for patient eligibility for a trial on Clozaril are attached. From those who meet these criteria, further selection and prioritization should be based on consideration of the following:

- Severity of the illness, including the status of non-psychiatric medical conditions that would negatively affect or be affected by the use of Clozaril.

- Treatment of patients which would impact the greatest number of people (other patients, staff, family).

- Realistic potential for successful discharge to the community. Community Services Boards and family members must be included in assessing the readiness of communities to provide support for these patients after successful treatment.

- Patient and family's informed and active cooperation including acceptance of their responsibility to follow through with treatment requirements on a long-term basis.

Informed consent must be obtained prior to the initiation of Clozaril treatment. This consent must be obtained from the patient or legally responsible representative, and must be fully documented in the patient medical record. Family members should participate in the discussions concerning Clozaril treatment, and should be invited to provide support for the patient as he or she considers the decision to accept the treatment offered. Consent forms should be developed in consultation with and risk management advisors, and should be sent to the Office of the Attorney General for approval.

Patients already taking Clozaril who are admitted to DMHMRSAS facilities must also provide informed consent if they are to be continued on the medication. An assessment must be done to determine the patient's best course of treatment which may include continuing the Clozaril, tapering and discontinuing the medication, seeking outside consultation, or referring the patient to another facility. Any patient not clearly meeting the facility's diagnostic and clinical selection criteria should be referred to the oversight committee for review.

Facility pharmacies will be responsible for making arrangements to purchase or otherwise acquire Clozaril from the manufacturer or wholesalers. Inventory records must be maintained according to facility pharmacy and administrative guidelines. Information as to patients on Clozaril, amount of medication dispensed, and cost of the medication dispensed should be forwarded to the Office of Medical Affairs on a monthly basis. During this first year of the Clozaril pilot program, facility budgets will be supplemented on a quarterly basis to cover the cost of Clozaril that has been dispensed.

Laboratory services required by Clozaril Treatment Systems will be provided by facility laboratories or through contract arrangements with private clinical laboratories. Consistent reliability and timely reporting of white blood cell counts must be assured by the laboratory providing the service. Funding for laboratory services must come from existing facility budgets as will any other non-pharmacy costs related to the utilization of Clozaril in DMHMRSAS facilities.

Clozapine Use at Community Services Board Clinics

In order for Clozaril to be used at mental health clinics in the communities, individual Clozaril Treatment Systems must be registered with Sandoz Pharmaceuticals Corporation. These systems must include a signed agreement between the clinic medical director or chief administrative officer and a designated pharmacy services provider who agree to follow the package insert requirements which ensure weekly distribution of Clozaril being linked to the pharmacy's receipt of a current white blood cell count.

CSB clinics wishing to use Clozaril should develop a written policy concerning the use of the medication. This policy must follow the requirements of Sandoz Pharmaceuticals "Treatment Systems Requirements" which is attached. In the development of this policy, close attention should be given to the availability of psychiatric and non-psychiatric medical staff with knowledge and experience necessary to manage clinical problems that may arise in patients started on Clozaril. A single clinician should be identified as the responsible contact person to handle problems and issues related to patients on Clozaril.

Patient eligibility and selection criteria are attached, and are the same as those for patients in DMHMRSAS facilities. Given limited resources at this time, we must look closely at the selection process to ensure that those patients with the greatest potential for significant benefits will be initiated on Clozaril.

Plans are being developed for the continuation of Clozaril for those patients initiated in DMHMRSAS facilities and who are discharged to the community. The medication is not yet available through the State Aftercare Pharmacy. Included with this package is a copy of a Special Medicaid Memo describing coverage for Clozaril under Virginia Medicaid. Case administration (such as is currently provided by Caremark or other commercial home health care agencies) is not a covered service and must be provided by the Community Services Board.

The Department does not pay for Clozaril for outpatients at this time. Patients should not be referred for admission to state hospitals solely for the purpose of initiation of Clozaril treatment.

Informed consent is required of all patients receiving Clozaril. Patients, their families, and/or their authorized representatives should be supplied with written information clearly stating the risks and possible benefits of Clozaril. The informed consent form should be approved by your risk management advisors. A signed copy of the form should be maintained in the medical record and a copy should be given to the patient.

Patients should be seen by the clinic psychiatrist on a regular

basis prior to and after starting Clozaril. Arrangements must be made for the weekly white blood cell test at the clinic or through a contract laboratory in the community. Assurances must be given that the laboratory results will be reliable and will be forwarded to the clinic in a timely fashion. A prescription for a one week supply of Clozaril along with the laboratory results will be sent to the community pharmacist. If the results of the current white blood cell count are within an acceptable range, the medication is dispensed. Details of this operating protocol must be included in the clinic's written Clozaril plan, and must be agreed upon by all parties involved.

Staff Education

The DMHMRSAS Office of Medical Affairs will assist in arranging necessary continuing education to provide knowledge, and to facilitate the sharing of early clinical and administrative experiences with Clozaril. The office will also develop a Clozaril Resource Center which will serve as a source of recent medical literature, model facility and clinic Clozaril plans, consent and other reporting forms, psychiatric symptom rating scales, and other information needed for the development and safe operation of Clozaril treatment programs.

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APPENDIX C

C L O Z A R I L F A C T S H E E T

CLOZAPINE (Clozaril - Sandoz Pharmaceuticals) is one of a group of novel antipsychotic medications useful in the treatment of patients with schizophrenia. Clozapine has been released specifically for management of treatment resistant schizophrenic patients, those who have not shown an adequate response to traditional neuroleptics.

Controlled studies of the efficacy of clozapine in this treatment resistant population have demonstrated significant improvement in one third of those given the medication. Clozapine has been shown to be clearly superior to traditional neuroleptic medications in this population.

CLOZAPINE was released by the Food and Drug Administration in spite of a significant 1-2% incidence of agranulocytosis, a serious side effect that can been fatal if not recognized and treated early in its course. Patients taking clozapine have reported a number of additional serious side effects while taking the drug, including seizures, rapid heartbeat, respiratory difficulties, low blood pressure, sedation, drooling, weight gain, and urinary problems.

CLOZAPINE can only be prescribed if the physician and pharmacist agree to strictly follow the package insert which requires a weekly test of the white blood cell count (WBC) prior to releasing the weekly supply of the medication to the patient.

By closely monitoring the WBCs of patients on clozapine, the incidence of agranulocytosis has been kept to a minimum, and deaths have been largely avoided.

Sandoz Pharmaceuticals has exclusive rights to manufacture and distribute clozapine (Clozaril) in this country. Currently, the wholesale cost of the drug is $2.85 per 100 mg tablet. For a patient stabilized on an average dose of 400 mg daily, the annual wholesale cost is approximately $4200. With markup and the cost of the required laboratory work, the estimated cost for a year of clozapine treatment is approximately $5000 per patient.

Current DMHMRSAS plans included a pilot program in 1991-92 in our mental health facilities, treating 150 treatment resistant schizophrenic individuals with clozapine. Efforts are being made to expand the availability of the drug through our Community Services Board operated mental health clinics for those treatment resistant schizophrenics in outpatient settings.

It is anticipated that some of the patients successfully treated with clozapine will be able to move to less restrictive and/or less intensive levels of care as their conditions improve. We do not expect major shifts of clozapine patients from inpatient to outpatient settings during this current year. We do expect some patients to be more able to participate in psychosocial and vocational rehabilitative programming, possibly requiring additional treatment resources in facilities and clinics.

As additional fiscal resources are identified and clozapine is made more available to our hospital and clinic populations, we will see an increasingly significant dampening effect on the rate of readmissions to our facilities, leading to some reduction of census and/or increased ability to provide services to a broader patient population across the Commonwealth.

Current per diem rates in our facilities range from $183 to $371. The median length of stay for a schizophrenic patient admitted to one of our hospitals is 7-8 weeks. The current rate of readmissions to our facilities, while seeming to indicate inadequate or unsuccessful treatment in communities, may as well be interpreted as a sign of our committment to the rights of our chronically ill patients to be placed in community settings, and our repeated efforts to effect a successful discharge.

We are equally committed to providing state of the art interventions, typified by medications such as clozapine, the best care available, and the best staff possible for our patients throughout our system.

APPENDIX D

CLOZARIL ELIGIBILITY CRITERIA

Patients being considered for a trial on Clozaril should meet the following criteria:

1. **DIAGNOSIS.** The patient has a current DSM-III-R diagnosis of schizophrenia or schizoaffective disorder as documented in the clinical record.

2. **AGE.** The patient is age 16 years or older.

3. **TREATMENT HISTORY.** (A. and B., or C.)

A. The patient has had an inadequate response to at least two previous trials on different neuroleptics at an adequate dosage and for adequate duration. The trials should have been with neuroleptics of different pharmacological classes, at least one of which being a non-phenothiazine. "Adequate" is defined as doses equivalent to 1000 mg per day of chlorpromazine for at least six weeks. "Inadequate response" implies continued prominent positive and/or negative symptoms of schizophrenia, or continuing unacceptable or intolerable side effects, including tardive dyskinesia.

B. The patient has exhibited consistently poor psychosocial functioning for the preceding 24 months.

C. The patient has severe intolerable extrapyramidal symptoms while taking neuroleptic medication that are unresponsive to standard antiparkinson treatment or reduction in dose of the neuroleptic medication.

4. **PROGNOSIS.** As a result of taking Clozaril, the patient has a reasonable chance for significant improvement such as decrease in intensity of required care, ability to be maintained in the community, decreased need for crisis management, increased ability to participate in psychosocial treatment activities, or independent living.

5. **CONTRAINDICATIONS.** The patient has none of the following contraindications:

A. a myeloproliferative disorder,

B. history of Clozaril-induced severe leukopenia or agranulocytosis,

C. a current WBC count of less than 3500/cu mm or a granulocyte count of less than 1500/cu mm,

D. severe CNS depression or comatose state,

E. a debilitated physical state,

F. currently taking a medication that may suppress bone marrow function, or another neuroleptic (after initial titration),

G. is currently or plans to become pregnant,

H. has a history of seizures that cannot be controlled on anticonvulsants other then carbamazapine (Tegretol).

APPENDIX E

Budget Addendum Request Justification:

a. This addendum request is to cover costs of a pilot program which will support the use of Clozaril (Sandoz Pharmaceuticals) in DMHMRSAS patients. Given the high cost of the drug and the large number of potentially eligible patients, it is very important to have a structured pilot program to allow the assessment of the potential benefits as well as possible problems related to the use of this new pharmacological agent. The funding requested will cover the cost of purchasing Clozaril for approximately 100 patients with schizophrenia who are in treatment in our system during the next two fiscal years. Additionally, the funding will be used to set up a central monitoring system so that appropriate data can be collected and reports generated to follow the progress of the Clozaril program. The Food and Drug Administration approved package insert continues to require a weekly blood test for each patient so that the white blood cell count can be monitored. This laboratory monitoring is used to prevent serious decreases in the white blood cell count, a known side effect of Clozaril. Laboratory costs will largely be included in current facility budgets and will not be included in this addendum request.

   All services to be provided through this funding are new services, and all are necessary if we are to begin utilizing Clozaril in our system facilities and clinics. Clozaril is not currently available to patients in our system (except for certain patients who were volunteers in initial investigative studies done at Western State Hospital and who have been continued on the drug). Given the cost of the drug, approximately $5,000 per patient per year, Clozaril cannot be added to our hospital and Aftercare Pharmacy formularies without the requested funding.

b. Significant benefits have been predicted for the patient population receiving Clozaril. Research studies as well as early clinical experiences have shown that, in some 30 per cent of patients with severe symptoms of schizophrenia which have not been responsive to conventional antipsychotics, there have been major signs of improvement on Clozaril. Many patients have improved sufficiently to be able to live in the community and participate in less intensive and less expensive programming. Some studies have demonstrated significant cost savings in later years due to this less intensive treatment.

c. $556,000 has been requested for each of the next two fiscal years, FY93 and FY94. No new positions will be funded under this request. This pilot program will support the initiation and continuation of Clozaril for approximately 100 patients during both years. The average per patient cost of Clozaril is $5500 annually.

d. The funding requested in the addendum is from general funds. As increasing numbers of patients are followed on Clozaril in system clinics, it would be expected that we would collect some revenue from those patients covered under Medicaid or other insurance carriers.

e. Clozaril is a new program and has not been included in previous budgets.

f. There are many patients in our system with severe schizophrenia or serious side effects from neuroleptics that will receive benefit from Clozaril. For some, all other treatment options have been tried unsuccessfully, and the patients, their families, and others are experiencing significant suffering as a result. For them, Clozaril holds some hope, and should be provided as soon as is reasonable and safe.

g. As noted above, studies have predicted significant cost savings per patient in those who have a good response to Clozaril and are able to move to less intensive levels of care.

h. No other sources of funding for Clozaril have been identified. No other pharmacological options have been identified for those patients who have been found to be unresponsive to conventional drugs.

i. No changes in the Code of Virginia are proposed or anticipated related to the use of Clozaril for DMHMRSAS patients.

j. This addendum has no requirements for new or revised language for the Appropriations Act.