Informed Consent Form

Dear Sir/Madam,

Hello!

Because you are a patient with uremia combined with Restless Legs Syndrome (RLS), you are invited to participate in a study led by Dr. Xia Yunfeng from the Department of Nephrology, The First Affiliated Hospital of Chongqing Medical University: "A Self-Controlled Study of Dipyridamole in the Treatment of Uremic Restless Legs Syndrome." This study primarily aims to observe the efficacy and safety of dipyridamole in patients with uremia and RLS, and to understand the extent to which this drug can improve RLS symptoms and sleep conditions in patients. The expected course of treatment is 3 months.

This informed consent form provides you with information to help you decide whether to participate in this clinical research. Your participation in this study is voluntary. This study has been reviewed and approved by the Ethics Review Committee of our institution. If you agree to join this study, please read the following instructions carefully.

If you have any questions, please ask the principal investigator responsible for this study.

I. Research Background

Restless Legs Syndrome (RLS) is a common complication in uremic patients, significantly impacting their quality of life and prognosis. Many studies have found that RLS is closely related to nocturnal hypertension and the occurrence of cardiovascular events in uremic patients, affects patients' sleep, leads to anxiety, depression, and decreased quality of life. The mortality rate of hemodialysis (HD) patients with RLS is significantly higher than those without RLS. Over the past few decades, dopaminergic drugs have been the mainstay of first-line treatment for RLS. Although these drugs show significant short-term efficacy, long-term use is characterized by short half-life, tendency to cause early morning rebound, and poor long-term efficacy. Recent studies suggest that nucleoside equilibrium transporter inhibitors, such as dipyridamole and ticagrelor, may control RLS symptoms by increasing endogenous adenosine-mediated tonic A1 receptor activation, potentially representing a new treatment strategy for RLS. Preliminary clinical studies have shown that dipyridamole significantly improves sleep quality and quality of life in patients.

We will only screen patients who meet both the inclusion and exclusion criteria to participate in this study. Eligible patients will receive dipyridamole free of charge, 50mg each time, three times a day, for a total of 12 weeks. During the treatment period, we will regularly follow up on your condition. You will need to undergo assessments using the International Restless Legs Syndrome Study Group Rating Scale (IRLSSG), Clinical Global Impression (CGI) scale, and Medical Outcomes Study Sleep Scale (MOS-SS) before and after treatment to evaluate the degree of symptom changes. Through this treatment, we aim to understand the specific efficacy of dipyridamole in uremic patients with RLS, the extent to which it improves RLS sensory and motor symptoms and

sleep conditions, while also observing its effects on concomitant depression, anxiety, quality of life, etc., in maintenance dialysis patients, as well as the clinical efficacy and common adverse reactions of dipyridamole in this population.

II. Research Purpose

To understand the efficacy and adverse reactions of dipyridamole in uremic patients with RLS, and its effects on concomitant depression, anxiety, sleep disorders, and quality of life in these patients.

III. Research Process and Methods

* **Study Design Type:** Single-center, self-controlled study. This study plans to enroll 80 subjects, with an observation period of 12 weeks. The study period is planned from June 1, 2025, to December 31, 2026.
* **Sample Collection:** At the beginning of the study and after 12 weeks of medication, we will collect general clinical data and laboratory parameters before and after the study, including age, gender, body mass index, Charlson Comorbidity Index score, dialysis duration, serum iron, ferritin, serum parathyroid hormone, hemoglobin, albumin, and dialysis adequacy. We will also use the International Restless Legs Syndrome Study Group Rating Scale (IRLSSG), Pittsburgh Sleep Quality Index (PSQI), Hamilton Depression Rating Scale (HAMD), Hamilton Anxiety Rating Scale (HAMA), Clinical Global Impression (CGI) scale, Medical Outcomes Study Sleep Scale (MOS-SS), Epworth Sleepiness Scale (ESS), and KDQOL-SF™-36 scale to assess changes in the patient's condition before and after treatment. We will collect information on the occurrence of drug-related adverse reactions during the study period, such as nausea, headache, dizziness, diarrhea, insomnia, fatigue, bleeding, etc.

Inclusion and Exclusion Criteria

Inclusion Criteria:
(1) Maintenance hemodialysis ⩾ 3 months;
(2) Age between 18-75 years;
(3) Diagnosed with Restless Legs Syndrome (RLS) according to the IRLSSG criteria and with an IRLSSG score > 15 points;
(4) Willing to cooperate with this study.

Exclusion Criteria:
(1) Comorbid with other cerebrovascular, muscular, or motor system diseases that affect the assessment of RLS severity;
(2) Comorbid with active bleeding, such as gastrointestinal bleeding, cerebral hemorrhage, etc.;
(3) Patients already taking dipyridamole long-term;
(4) Patients who have taken other medications that may affect RLS severity within the last 3 weeks, such as dopamine receptor agonists/antagonists, tricyclic antidepressants, lithium, etc.;
(5) Patients with a history of psychiatric illness;

(6) Pregnant or lactating women;
(7) Patients allergic to or intolerant of dipyridamole;
(8) Patients unable or unwilling to cooperate with this study.

Mid-study Withdrawal: Subjects may withdraw from the study at any time if they experience severe adverse reactions or voluntarily request to withdraw for any reason.

Research Duration and Follow-up:
* **Duration:** Your participation in this study will last for 12 weeks.
* **Condition Follow-up:** During your participation, the investigator will conduct follow-up visits at least once a month, scheduled at your convenience during dialysis. During each visit, research staff will use relevant clinical observation forms to collect all required data.

IV. Potential Benefits of the Research:

* **Personal Benefit:** You may directly benefit from the treatment or interventions in this study, such as symptom relief or more effective disease control.
* **Indirect Benefit:** Your participation will provide valuable data for medical research, helping to advance treatment methods for related diseases and potentially benefiting more patients in the future.

V. Research Risks and Discomforts:

* **Adverse Drug Reactions:** Dipyridamole is a commonly used clinical drug. However, due to individual differences in drug response, a very small number of patients may experience adverse reactions such as nausea, headache, dizziness, diarrhea, insomnia, fatigue, bleeding, etc. Most adverse reactions resolve after stopping the medication. The investigator will take appropriate treatment measures based on your specific situation.

VI. Alternative Treatment Options (Applicable only to interventional studies):

Apart from participating in this research, there are other treatment options currently available for your condition, such as dopaminergic drugs. You can discuss the advantages and disadvantages of these options further with your doctor.

VII. Privacy Issues:

If you decide to participate in this study, your participation and personal data will be kept confidential. All information pertaining to you will be confidential. All research members and the study sponsor are required to keep your identity confidential. Your records will be stored in a locked cabinet accessible only to the research staff. To ensure the study is conducted according to regulations, representatives of government regulatory authorities or the Ethics Review Committee may inspect your personal data at the research site as required by law.
If the results of this research are published, the researchers are also required to commit to

maintaining confidentiality.

VIII. Costs and Compensation:

Funding for this project is provided by the 2025 Graduate Student Research Innovation Project of The First Affiliated Hospital of Chongqing Medical University. The required medication, dipyridamole tablets, will be provided free of charge by the research team. The project will also purchase corresponding liability insurance for you. Provided you follow the research doctor's instructions, if you experience a drug-related adverse event confirmed to be caused by the study drug or diagnostic tests and treatments required by the study protocol, resulting in harm to you, the doctor will provide active treatment. The research team will bear the related medical costs and other expenses stipulated by law, including portions not covered by insurance. Treatments and examinations required for other concurrent diseases you have are not covered. Additionally, we will provide long-term follow-up of your condition and long-term free treatment guidance free of charge, striving to improve RLS sensory and motor symptoms as well as sleep disorders. Since enrolled patients receive regular hemodialysis treatment at the Hemodialysis Center of The First Affiliated Hospital of Chongqing Medical University, and are already under regular treatment and laboratory follow-up there, our study only collects routine serological test results from patients and will not impose additional financial burden. Furthermore, as our efficacy evaluation indicators are primarily based on scales, there is no corresponding compensation.

IX. Voluntary Withdrawal:

As a participant, you have the right to be informed about information related to this study and its progress. You can voluntarily decide to continue or discontinue participation. After joining, regardless of whether any harm occurs or its severity, you can choose to withdraw from the study at any time without giving any reason by notifying the investigator. Your data will not be included in the research results, and your medical treatment and rights will not be affected as a result. If continuing participation would cause you significant harm, the investigator will also terminate your involvement in the study.
However, during your participation, please provide truthful information about your medical history and current physical condition; inform the research doctor of any discomfort you experience during the study; refrain from taking restricted drugs or foods; and inform the research doctor if you have recently participated in or are currently participating in other studies. The research doctor may discontinue your participation in this study if you fail to comply with the research plan, if you experience a study-related injury, or for any other reason.

X. Contact Information:

If you have questions related to this study, or if you experience any discomfort or injury during the study, or have questions regarding the rights of participants in this study, you can contact Dr. Xia Yunfeng, Tel: 023-89011356, or the Medical Research Ethics Review Committee Office of The First Affiliated Hospital of Chongqing Medical University, Tel: 023-89011876.

XI. Sharing of Results:

After the study concludes, all relevant results will be published in scientific journals and may be presented at academic conferences; findings will be shared with the global scientific community to promote academic exchange and knowledge updates in this field.

XII. Consent Signature:

I have read this informed consent form, and my doctor, Dr. Xia Yunfeng, has explained the purpose, procedures, risks, and benefits of this clinical trial to me in detail. All questions I have asked have been answered. I understand this clinical research and voluntarily agree to participate.

Subject Signature: _____ **Date:** _____ **Contact Phone:** _____

Guardian Signature: _____ **Date:** _____ **Contact Phone:** _____

Relationship to Subject: _____

Investigator Signature: _____ **Date:** _____ **Contact Phone:** _____