INFORMED CONSENT FORM

The Clinical Study for Evaluating The Safety AndEfficacy Of Epodion® During Maintenance Period Until Evaluation Period On CKD (Chronic Kidney Disease) Patients: An Open Label, Randomized, Active Drug-Comparative, Parallel-Designed, Multi-Center Clinical Study

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DAEWOONG PHARMACEUTICAL CO., LTD.

2019

EXPLANATION SHEET

1. Study Title:

The clinical study for evaluating the safety and efficacy of Epodion on CKD (Chronic Kidney Disease) patients: an open label, randomized, active drug-comparative, parallel-designed, multi-center clinical study.

2. Informed Consent Form:

This explanatory sheet provides general information and explanations of the clinical trial and trial drug, providing relevant information to help you decide whether you will participate in this clinical trial or not. If you have questions that are not clearly understood in this statement, or if you have additional questions about this trial, you can ask your doctor and the representative listed at the end of the statement.

3. Activities :

Team at the Internal Medicine Department of RSPAD Gatot Soebroto, Internal Medicine Department of RSAU dr. Esnawan Antariksa, and Internal Medicine Department of RSIJ Cempaka Putih is conducting a study to determine the safety and efficacy of EPODION® (Recombinant Human Erythropoietin Alfa), the production of PT. Daewoong Infion in patients with Chronic Kidney Disease (CKD) with anemia. A hundred subjects who met the criteria will be included in this study.

You meet the criteria to participate in this study, therefore you are requested to participate in this study.

4. Purpose:

The purpose of this study is to determine the safety and efficacy of EPODION in patients with Chronic Kidney Disease (CKD) with a treatment period of 44 weeks.

5. Study Procedure:

Drug Information

This study compares the efficacy and safety of Eprex® and Epodion®. Both Eprex® and Epodion® both contain Recombinant Human Erythropoetin Alfa. Erythropoetin functions to help the formation of red blood cells. In patients with chronic kidney disease (CKD), the formation of the hormone erythropoetin will decrease, the reduction resulting in inhibition of red blood cell production. Giving Eprex® and Epodion® will help meet the needs of the hormone erythropoetin in patients with chronic kidney disease (CKD), so that patients do not lack blood (anemia).

5.1. Study Flow:

Before the study begins you will be asked for approval. The study will be divided into5 stages consisting of:

1. The screening period for 4 weeks
2. The dosage adjustment period for 4 to 8 weeks
3. Baseline evaluation period for 4 weeks
4. The maintenance period for 24 weeks
5. Final evaluation period for 4 weeks

The first phase of the study is the screening period. In the screening period your condition will be evaluated for 4 weeks, you will get a blood examination, examination for hepatitis, HIV, and pregnancy test as free. If you meet the criteria you will be able to join the study and get hemodialysis treatment 3 times a week during the study

period.

The second period of the study a dose adjustment period, at this stage you will get Eprex®. If at the 4th week of your hemoglobin study the treatment target (10-12 g / dL) you will enter the baseline evaluation period, but if your hemoglobin has not reached the target dose adjustment period it will be extended for 4 weeks. If for 8 weeks your hemoglobin has not met the treatment target, the study procedure will be stopped and you will no longer participate in this study.

Before entering the next period, the doctor will conduct an assessment, if according to the doctor you meet the criteria of the baseline evaluation period you will be asked to participate further into the maintenance period. If the doctor consider that your condition is not appropriate you cannot participate in the maintenance phase and all study procedures will be terminated.

The fourth stage of the study is the maintenance period, you will be randomized into one of the 2 groups:

a) The first group received Eprex®
b) The second group received Epodion®

The final stages of the study is the final evaluation period. After treatment evaluation period of 4 weeks finished, the study will be completed.

The dose of Epodion® and Eprex® given will be adjusted based on your body weight and hemoglobin level which will be examined once every 2 weeks.

6. Potential risks and discomfort

Some side effects that can occur but not for everyone, include skin reactions (itching, redness), nausea, dizziness, vomiting, diarrhea, and irritation at the injection site. Some of the serious side effects that can occur are allergic reactions. If a reaction occurs, the doctor will immediately take care. Another effect that often arises is an increase in blood pressure and the doctor will handle the increase in blood pressure.

Study in animal subjects shows that administration of erythropoietin does not pose a teratogenic risk (disrupting the fetus), but there is no adequate experience regarding the use of erythropoietin in pregnant women. Therefore women who are willing to participate in this study are required to use contraception to prevent pregnancy (IUD or Hormonal).

7. Benefits for the subject

You will get hemodialysis treatment 3 times a week, blood examination every 2 weeks, and get free Epoetin (Epodion® or Eprex®) medication.

8. Drop Out Procedure

At the screening period you will get a blood check, hepatitis, HIV, and a pregnancy test. The doctor will evaluate the results and if your condition is not appropriate you cannot take part in the study.

At the baseline evaluation stage the doctor will evaluate your condition, if your condition is appropriate then you are asked to go to the maintenance period until the treatment evaluation period. If the doctor considers your condition to be incompatible then you cannot go to the maintenance or evaluation period of treatment, *but the quality of service you receive from the hospital will not change.*

If during the study you did not obey the instructions given by the doctors and / or a condition happen which according to the doctor does not allow you to continue the study, you can be excluded at any time in this study.

Termination of the study procedure will not affect the quality of the service you will receive from the hospital.

9. Confidentiality

All of this study data will be treated confidentially so it does not allow other people to connect with you.

10. Compensation

While you are participating in this study, you will get compensation in the amount of **IDR 94.000** per visit or total of **IDR 13.160.00** for the 44 weeks of the study period. Compensation will be given proportionally according to the stages of the study. The compensation is paid through the Contract Research Organization (CRO) in 4 terms:

1. At the initial week you are listed to participate in the study, in the amount of **IDR 658,000**
2. After you randomized into one of the 2 groups, in the amount of **IDR 1.974.000**
3. After 30 weeks since you participate in the study, in the amount of **IDR 3.948.000**
4. At the final week of treatment evaluation, in the amount of **IDR 6.580.000**

Subject compensation has been deducted by 6% income tax.

11. Guarantee

Treatment costs related to study activities will be borne by the sponsor based on the agreement.

If an unwanted reaction occurs that is proven to be a related or resulted by the study for up to 3 months after the study ends, the cost of the required treatment will be paid by the sponsor.

12. Voluntary Participation

You are free to refuse to participate in this study. If you have decided to join, you are also free to resign at any time without causing a change in the quality of services of your doctor. You are given the opportunity to ask all things that are not clear regarding this study.

The name and address of the study team

If at any time there are side effects or need an explanation, you can contact:

1. **Internal Medicine Department at the RSPAD Gatot Soebroto**
   dr. Jonny, Sp. PD-KGH, M.Kes, MM in Jl. Abdul Rahman Saleh Raya No.24, Jakarta Pusat
2. **Internal Medicine Department RSAU dr. Esnawan Antariksa**
   dr. Widodo Sutandar, Sp. PD-KGH in Jl. Merpati No.2, Jakarta Timur
3. **Internal Medicine Department RSIJ Cempaka Putih**
   dr. Kuspuji Dwitanto, Sp. PD-KGH in Jl. Cemp. Putih Tengah I No.1, Jakarta Pusat

APPROVAL SHEET

1. I_____, the undersigned voluntarily agree to take part in the studyof safety and efficacy of Epodion (Recombinant Human Erythropoietin, produced by PT. Daewoong-Infion) in patients with Chronic Kidney Disease (CKD). I understand that this study will involve using EPODION® and EPREX®.
2. I have been given a full explanation by the members of the study team, about the natural goals and the possible duration of the study and what will be done. I have been told of any inconveniences and possible adverse effects on health or well-being that might occur.
3. I have been given the opportunity to ask the study team about aspects of the study and have understood the suggestions and information provided as answers.
4. I agree to follow the instructions given during the study and to work with the study team, and to immediately notify, if there is a change in health that I feel, or an unexpected or unusual symptom, and if planning a trip far outside the reach of the hospital where the study takes place.
5. I agree and accept not to limit the use of drugs studied during this study, and I accept to publish the results of this study to an approved institution.
6. I understand that I am free to withdraw from this study at any time without needing to explain my decision.
7. I agree to participate in this study in accordance with my free will.

Subject		**Investigator**	
Name	: _____	Name	: _____
		Institution	: _____
Date	: _____	Date	: _____
Signature	: _____	Signature	: _____