

Xinnaoning Capsule for Chronic Stable Angina Pectoris (Qi Stagnation and Blood Stasis Syndrome) Informed consent for post-marketing clinical trials.

Informed Information Page

Respected patient: Hello!

Your doctor has diagnosed you with chronic stable angina. Welcome to participate in the post-marketing clinical trial of Xinnaoning Capsule voluntarily, and express our heartfelt thanks for your participation. Before deciding whether to participate, it is necessary for you to understand the purpose of the test, the test drugs, the risks that may be brought to you, what you are expected to do during the test and your rights as a subject. Please read the instructions carefully.

1、 Research Background

Xinnaoning Capsule (Z20025697), a traditional Chinese medicine produced by Guizhou Jingcheng Pharmaceutical Co., Ltd., has been on the market for many years. This product is a hard capsule with brown to brown powder or granules. The prescription is composed of Ginkgo biloba leaves, Salvia miltiorrhiza, Populus lobularis, ginger root and Allium alba. It has the functions of activating blood circulation, promoting qi, dredging collaterals and relieving pain. It is used for chest tightness, tingling, palpitation, dizziness, and angina pectoris of coronary heart disease. To carry out the clinical trial of Xinnaoning Capsule in treating chronic stable angina pectoris (Qi stagnation and blood stasis syndrome) is to make an objective evaluation of the efficacy and safety of Xinnaoning Capsule in clinical application.

From February 2011 to October 2011, Xinnaoning Capsule was used to treat angina pectoris of coronary heart disease of Qi stagnation and blood stasis type in 309 Hospital of PLA. Methods: 182 patients with angina pectoris of Qi stagnation and blood stasis type were randomly divided into treatment group (102 cases) and control group (80 cases). The control group was treated with routine treatment group (isosorbide mononitrate tablets, aspirin enteric-coated tablets). Group B was treated with Xinnaoning Capsule on the basis of routine treatment. The results showed that the total effective rate of angina pectoris in the treatment group, the time of angina attack and the improvement of TCM symptoms were better than those in the control group, especially in the improvement of chest pain, chest tightness, dizziness, headache and other symptoms. There were no obvious adverse reactions during the treatment, suggesting that the drug is safe.

From June 2012 to June 2014, the Cardiovascular Disease Center of Xiyuan Hospital, Chinese Academy of Traditional Chinese Medicine (CATCM) conducted a study on Xinnaoning Capsule in the treatment of recurrent angina pectoris after coronary stent implantation. Methods: 160 patients diagnosed as recurrent angina pectoris after coronary artery disease stent implantation were randomly divided into treatment group (80 cases) and control group (80 cases). Control group: aspirin enteric-coated tablets 100 mg, once a day, isosorbide mononitrate tablets 20 mg, twice a day, atorvastatin calcium tablets 20 mg, once a day. Treatment group: On the basis of the control group, Xinnaoning capsule was added. The observation results were as follows: Xinnaoning capsule played a good clinical effect on angina pectoris patients after coronary artery stent implantation by improving myocardial microcirculation, promoting the opening of collateral circulation,

inhibiting platelet aggregation, reducing blood lipid and stabilizing platelet.

2、 Research Introduction

This study was conducted by Xiyuan Hospital, Chinese Academy of Traditional Chinese Medicine, with a multi-center clinical study. It is expected to be carried out in Beijing, Shanghai, Shaanxi, Tianjin and other related departments, such as the comprehensive internal medicine department of Xiyuan Hospital. It is expected that 240 subjects will participate in the study with you. This study has been approved by the Ethics Committee of Xiyuan Hospital, Chinese Academy of Traditional Chinese Medicine. This study is in line with the principles of the Helsinki Declaration and medical ethics.

In this study, the efficacy and safety of Xinnaoning capsule in the treatment of chronic stable angina pectoris (Qi stagnation and blood stasis syndrome) were evaluated with placebo as control. A randomized, double-blind, parallel controlled, multi-center clinical study was conducted.

3、 Who is suitable to participate in the study

1) According to the Guidelines for the Diagnosis and Treatment of Chronic Stable Angina issued by the Chinese Medical Association in 2007, western medicine has been diagnosed as a patient with coronary heart disease (which can meet any of the following criteria):

- There is a clear history of old myocardial infarction, PCI or bypass.
- Coronary angiography (results indicate that at least one coronary artery is stenosed and the lumen is stenosed more than 50%) or coronary CTA suggests that the lumen is stenosed more than 50%.

2) According to the diagnostic criteria of chronic stable angina pectoris: the history of angina pectoris attack is more than one month, and the degree, frequency, nature and inducing factors of angina pectoris attack have no obvious changes.

3) The severity of angina pectoris of the Canadian Cardiovascular Society (CCS) was classified as Grade I-III, and the number of attacks of angina pectoris was more than twice a week.

- 4) To meet the TCM syndrome differentiation criteria of Qi stagnation and blood stasis syndrome;
- 5) Age between 30 and 79 years old;
- 6) Sign the informed consent.

4、 Who should not participate in the study

- 1) Severe cardiopulmonary insufficiency (grade III, IV, severe abnormal pulmonary function);
- 2) Poor control of hypertension (systolic blood pressure (> 160 mmHg) or diastolic blood pressure (> 100 mmHg) after treatment;
- 3) Complicated with liver and kidney dysfunction, ALT, AST (> 1.5 times the upper limit of normal value), or Cr ($>$ the upper limit of normal value), combined with hematopoietic system and other serious primary diseases;
- 4) Acute myocardial infarction within 3 months after interventional therapy;
- 5) pacemaker;
- 6) Pregnancy, lactation or pregnancy planning;
- 7) allergic constitution or allergic to known components of research drugs;

- 8) Chest pain caused by other causes (moderate anemia, hyperthyroidism, etc.)
- 9) Those who participated in other clinical drug trials within one month;
- 10) Researchers consider it inappropriate to participate in clinical research.
- 11) Other factors affecting ST-T changes in ECG, such as myocardial hypertrophy, left bundle branch block, etc. 重度心肺功能不全者(心功能III、IV级、肺功能重度异常);

5. Overall process

If you are willing to participate in clinical trials and sign the informed consent. Before you enter the study, you will undergo the following checks to determine whether you can participate. The research doctor will inquire about and record your medical history and treatment history, conduct vital signs, physical examination, score symptoms of angina pectoris, and electrocardiogram examination. After passing the examination, you need to take Xinnaoning capsule simulator for 2 weeks, and then have a physical examination for you again, including blood routine, urine routine, stool routine + Occult blood, liver and kidney function, blood coagulation, fasting blood glucose, blood HCY, electrocardiogram and blood lipid.

If you pass the above inspection, the following steps will be taken to study:

At the beginning of the study, according to the random number provided by the computer, you will be treated with Xinnaoning capsule or Xinnaoning capsule simulator. 50% of you will be treated with Xinnaoning capsule simulator. 50% of you will be treated with Xinnaoning capsule simulator. Neither you nor your doctor can know and choose any treatment method beforehand. Therapeutic observation will last for 12 weeks. You need to go back to the hospital for 4 follow-up visits.

After 4 weeks of medication: You should go to the hospital to see a doctor, and truthfully reflect to the doctor the change of the condition, the doctor will collect your condition information.

After 8 weeks of medication: you should go to the hospital to see a doctor, and truthfully reflect to the doctor the change of the condition, the doctor will collect your condition information.

After 12 weeks of medication: you need to go to the hospital again and report the change of your condition to the doctor truthfully. The doctor collects your condition information again and gives you blood routine, urine routine, stool routine + Occult blood, liver and kidney function, blood coagulation, HCY, fasting blood sugar and electrocardiogram examination.

After this follow-up, your research will be over. If you have any questions about this research, you can still contact your research doctor.

Other matters requiring your cooperation:

During the trial period, please come to the hospital according to the follow-up time agreed by the doctor and you. Your follow-up is very important and your doctor will determine whether the treatment you receive really works. Every time you go back to the hospital, you need to bring back the unused medicines and packages, return them to the researchers, and inform the doctor of the other medicines you are taking, including those you need to continue taking for other complications. If you need any other treatment, please contact your doctor beforehand.

Long-acting nitrates can continue to be used as antiplatelet agents, angiotensin-converting enzyme inhibitors (ACEI) or angiotensin II receptor antagonists (ARB), statins, calcium antagonists, beta-blockers and can not be adjusted by themselves. During the study period, it is forbidden to add any other Chinese and

Western medicines which have therapeutic effects on angina pectoris of coronary heart disease. If you need to adjust the medication, please contact your doctor in charge in time and do not adjust it by yourself.

When deciding whether to participate in this study, please carefully consider the impact of the above items on your daily work and family life, as well as the traffic problems of each return visit. If you have any questions about the examination and procedure in the study, consult your research doctor.

6、 Your rights and interests

1) The researcher will introduce you to the testing drugs and the testing arrangements, whether or not the participants fully follow the principle of voluntary participation. In the course of the trial, we may get new information about the treatment. We will inform you in time to decide whether to continue the research or withdraw. If you have any questions, you can call or consult the researcher directly. You will receive good medical services during the study period. You may refuse to participate in the study or withdraw from the study at any time in the course of the study, which will not affect your relationship with the doctor, your medical treatment or other interests. You may withdraw from the study at any time without discrimination or unfair treatment, and your medical treatment and rights will not be affected. You do not have to choose to participate in this study in order to treat your disease. If you withdraw from the study due to drug reasons, it will be very beneficial to your health and the whole study if you tell your doctor about the changes of your condition and complete the corresponding physical and chemical examinations.

2) You and society may benefit from this experiment. You will get a free treatment for angina pectoris. You will get free experimental drugs and laboratory tests related to this test. Your condition may be improved, but we can't guarantee that your condition will be improved. We hope that the information from the research you participated in will benefit patients with the same condition as you in the future.

3) If you combine the treatment and examination needed for other diseases at the same time, it will not be free of charge.

4) Compensation: This study will pay you a certain amount of transportation fee.

7、 Your obligation

1) Adhere to the principle of voluntary participation and sign the informed consent before the start of the experiment. Provide accurate information about past medical history and current condition.

2) Tell the research doctor about any health conditions you took during the study. Tell your doctor about any medications you take during the study

3) Not participating in other medical research.

4) Please return unused research medicines and all empty packages to the doctor at each required visit. Follow the unified arrangement of researchers, follow the guidance of researchers and research doctors, and cooperate with researchers to complete the experimental task.

5) Store research drugs at room temperature, keep them out of reach of children, and don't give them to

anyone.

6) Take appropriate contraceptive measures during the study period.

8、 Possible adverse reactions and safety measures

All therapeutic drugs may have adverse reactions, and this research drug is no exception, but the adverse reactions of Xinnaoning capsule are not clear at present. No adverse reactions related to Xinnaoning capsule have been found in literature, magazines, websites, etc. Your research doctor will pay close attention to the adverse reactions of the research drug. During the trial, you will have any discomfort or new changes in your condition, or any unexpected situation, whether or not it is related to drugs, please report to your competent doctor immediately, and the doctor will make judgments and medical treatment.

Sample collection will be performed strictly in accordance with aseptic requirements in the course of the study. Sample collection may have some very small risks, including temporary pain, local cyanosis, mild dizziness in a few people, or extremely rare needle infection, which does not exclude abnormal damage or unexpected adverse events. You need to visit the hospital on time during the study period, which may cause trouble or inconvenience to you.

If you take a placebo, your condition may not improve. In addition, any treatment may be ineffective, as well as because of ineffective treatment or because of the merger of other diseases and other reasons leading to the continued progress of the disease. This is the treatment risk that every patient will face, even if they do not participate in this clinical study, treatment risk will exist.

If there is a slight adverse reaction during the study, which does not affect the continuation of the study, please cooperate with the researchers to complete the study.

If serious adverse reactions occur, the researchers will terminate your study as appropriate.

Doctors and Guizhou Jingcheng Pharmaceutical Co., Ltd. will do their best to prevent and treat the possible harm caused by this study.

9、 Reasons for Terminating Your Participation in the Trial

If something happens, you will be asked to terminate your research.

- 1) Certain tests show that you are not suitable to participate in this study or take this drug.
- 2) During the study period, you had some new health problems.
- 3) You can't cooperate or return your visit in time.
- 4) For 7 consecutive days, you did not take the research drugs or did not take the research drugs correctly.
- 5) Be pregnant or decide to be pregnant.
- 6) Severe adverse reactions occurred during the study.
- 7) For your best interests, the research doctor thinks it should stop.
- 8) Clinical trials were cancelled by the State Food and Drug Administration/the relevant state departments.

If this happens, the researcher has the right to terminate your participation without your consent.

10、 Confidentiality

All information about you, including your identity, medical history, condition, physical examination and laboratory results, will be kept strictly confidential within the limits permitted by law. Only authorized researchers, ethics committees and research institutes can access your records. Food and Drug Administration

is allowed to access your medical records related to this study to verify the authenticity and accuracy of the data collected in this study, but not your personal details. Your name will not appear in any public information or reports related to this study. We will make every effort to protect the privacy of your personal medical data within the scope permitted by law.

11、 Publishment

Whatever the results, we will try our best to publish them.

Thank you for reading the above information. If you decide to participate in clinical research, please inform your doctor that he or she will arrange for you all matters related to clinical research. Please keep this information.

Informed consent signature page

Title: A randomized, double-blind, parallel-controlled, multicenter clinical study to evaluate the efficacy and safety of Xinnaoning capsule in the treatment of chronic stable angina pectoris (Qi stagnation and blood stasis syndrome).

Bidder: Guizhou Jingcheng Pharmaceutical Co., Ltd.

Consent statement

I have read the above introduction to this study and have the opportunity to discuss and ask questions with my doctor about this study. All my questions have been answered satisfactorily.

I know the risks and benefits of participating in this study. I know it's voluntary to participate in research, and I'm sure I've had enough time to think about it and understand that:

I can consult my doctor for more information at any time.

I can withdraw from this study at any time without discrimination or unfair treatment, and medical treatment and rights will not be affected.

I also know that if I quit the study halfway, especially when I quit the study due to medication, it will be very beneficial for me and the whole study if I tell the doctor about the changes of the condition and complete the corresponding physical and chemical examinations.

If I need to take any other medication because of the change of my condition, I will consult the doctor in advance or tell the doctor truthfully afterwards.

I will get a signed and dated copy of the informed consent. At the same time, I allow the State Food and Drug Administration/relevant state departments, ethics committees and relevant researchers to review the records.

Finally, I decided to agree to participate in the study.

Signature of patient: _____ ID□□□□□□□□□□□□□□□□

Patient Contact Telephone: _____ Date: _____

Legal Agent Signature: _____ ID□□□□□□□□□□□□□□□□

Telephone: _____ Date: _____

I confirm that I have explained to the patient the details of the trial, including its rights, possible benefits and risks, and have given him a signed copy of the informed consent.

Doctor's signature: _____ Date: __ __ __ __

Doctor's Work Telephone: _____

Contact telephone number of Xiyuan Hospital Medical Ethics Committee Office: 010-62835646

Informed consent process record

When the subject is unable to read or sign the informed consent, the designated agent/guardian records this page.

How does the subject agree with the information?	<input type="checkbox"/> Doctors/nurses read the contents of the informed consent to the subjects and answered their questions. <input type="checkbox"/> The agent reads the content of the informed consent to the subject and the doctor answers the subject's questions. <input type="checkbox"/> The legal representative of the subject reads the instructions of the subject and all questions have been answered by the doctor. <input type="checkbox"/> Other: _____ _____
Does the subject already know all the information about the subject?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> not applicable
Does the participant agree to participate in the experiment?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> not applicable
Do the subjects agree to all the declarations on the Informed Consent Page?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> not applicable
Reasons why subjects were unable to sign this informed consent	<input type="checkbox"/> A disability <input type="checkbox"/> illiteracy <input type="checkbox"/> Under age <input type="checkbox"/> other: _____
Relationship between Agent and Subject	<input type="checkbox"/> spouse <input type="checkbox"/> parent <input type="checkbox"/> children <input type="checkbox"/> Brother <input type="checkbox"/> other: _____
Remark:	_____ _____ _____

Subject Agent/Guardian Signature:

Date: / /
