TITLE PAGE

INFORMED CONSENT FORM

Multicenter, Randomized, Open-Label, Comparative Study of Therapeutic Efficacy, Safety and Tolerability of Imupret application in the therapeutic concept of delayed prescription of antibiotics in children, aged 6-12 with severe acute tonsillitis.

Working Title:
ATi-2

Imupret in tonsillitis
Clinical phase: IV
Date: 07.02.2019

Name of the investigational product: Imupret®

Coordinating Investigator: Prof. Dr. Vasyl Ivanovych Popovych

Sponsor:
Ivano-Frankivsk National Medical University
Prof. Dr. Vasyl Popovych
2, Galytska str.,
Ivano-Frankivsk,
Ukraine, 76000

PATIENT INFORMATION SHEET
(FOR PARENTS OR THE LEGAL REPRESENTATIVE OF THE CHILD)

Title of the study: "Study of the clinical efficacy, safety and tolerability of the drug Imupret in the technology of delayed administration of antibiotics in patients with acute tonsillitis"

Name and surname of the investigator: _____

Phone number and contact information _____

_____

Read this document carefully before signing it.

Dear patient / parents !

You are invited to take part in a local study of the herbal medicine Imupret, which contains chamomile flowers, marshmallow, yarrow herb, walnut leaves, dandelion root, horsetail herb (trade name Imupret). The organizer of the study is Professor Vasyl Ivanovych Popovych.

This document contains information about the purpose of the study, its duration, the treatment proposed, the research procedures (actions you will be asked to take), the risks and benefits of participating in this study.

You have already been invited to participate in this clinical trial. Read the following information carefully before deciding to participate in the study. After reading this document, your research doctor will explain the content of this study and you will be able to ask questions to the doctor or staff involved in the study to find out any aspects of the study at any time. You will have plenty of time to decide whether to participate in this study.

Participation in this study is entirely voluntary. If you refuse to participate, this decision will not have a negative impact on the medical care provided to you now or will be provided in the future.

This study was praised by the Ethics Commissions.

1. The purpose of the study

This study examines the effectiveness of a combined herbal medicine in reducing the time and complete elimination of symptoms of acute tonsillitis, the frequency of the need for antibiotics in children aged 6-18 years.

The over-the-counter Imupret is used to treat acute and chronic inflammatory diseases of the throat, as well as to treat ARTI and prevent their complications, and is available in 19 countries, including Germany and Ukraine.

You / your child are candidates for this study because you have an uncomplicated upper respiratory infection. This study will be conducted in several centers in Ukraine. Approximately 100 patients with acute tonsillitis will be involved in this study.

2. Characteristics of the drug

Imupret is a herbal preparation that contains such active ingredients as chamomile flowers, marshmallow, yarrow herb, walnut leaves, dandelion root, horsetail herb in the form of tablets or drops for oral use. Previous clinical studies with Imupret have shown that the use of these ingredients is safe and well tolerated. Interaction with other drugs was not detected. Imupret® due to polysaccharides of chamomile and marshmallow stimulates a non- specific response of the immune system by increasing the phagocytosis of macrophages and granulocytes. These active ingredients also increase the intracellular destruction of bacteria during phagocytosis due to increased secretion of active oxygen metabolites that have bactericidal properties.

Polysaccharides, essential oils and flavonoids (chamomile, marshmallow and yarrow) reduce mucosal edema in respiratory infections. In vitro studies have shown that oak bark, which contains a lot of tannins, has an antiviral effect on influenza virus.

Horsetail, which is part of the drug, enhances these effects due to its well-known healing and prophylactic properties.

3. Research procedures

If you / your child is eligible to participate in the study, you will be asked to sign this form to give your consent. You / your child will be randomly prescribed (similar to tossing a coin) one of two treatment regimens (conventional therapy, or conventional therapy with Imupret). The probability of receiving the drug Imupret is 50%.

Your participation in this study will last up to 10 (± 1) days and will include four visits to the investigating physician to assess your health: Visit 1 (at the beginning of the study), Visit 2 (36-48 hours after the start of therapy for the previous control of the effectiveness of the prescribed treatment), Visit 3 (control, after 5 days), Visit 4 (after 10 days: end of treatment and control of its effectiveness), Visit 5 (28 days: remote control of the effectiveness of treatment).

4. Research-related benefits

During treatment, the patient will receive standard treatment and, in addition, the test drug.

The data obtained in this study will help to clarify the information on the use of Imupret for the treatment of acute tonsillitis as a manifestation of upper respiratory tract infections; this knowledge will be useful for physicians and will improve the treatment of future patients.

5. Standard treatment

Uncomplicated acute tonsillitis of non-bacterial etiology is usually treated without antibiotics because it has been proven that they are ineffective and have a negative effect on the body when there is no bacterial infection.

1. Thrifty diet (eating 5-6 times a day in small portions with the exception of spicy, spicy, difficult to digest products);
2. Elimination of factors that irritate the pharyngeal mucosa (thermal, chemical, mechanical genesis) - if necessary;
3. Anti-inflammatory therapy (Acetaminophen (paracetamol) in a single dose up to 500 mg 3-4 times a day;
4. Local NAIDs - benzydamine.

6. Risks and potential side effects

The appearance of side effects can be caused by the use of any drug. Unknown side effects associated with starting treatment may also occur during the study.

The following side effects may occur while taking Imupret:
Rare: gastrointestinal disorders (eg abdominal pain, nausea, vomiting). Allergic reactions (such as rash, itching, shortness of breath) may also occur.
When used in combination with drugs containing chamomile flowers, allergic reactions may occur, as well as in patients with hypersensitivity to other plants of the family Compositae (eg yarrow (Achillea Millefolium)).
If you experience any side effects, you should stop using the drug and be sure to consult your doctor.

At the first sign of an allergic reaction (urticaria, itching and redness of the skin), you should stop taking the drug immediately.

Tell your investigator doctor or research team immediately about any side effects while taking the study drug during the study or any adverse medical events and / or changes in your health.

7. Treatment after the end of the study or premature withdrawal from the study

If you have decided to discontinue this clinical trial before or if you discontinue at the suggestion of the investigating physician, try your best to come for Visit 4. The investigating physician will discuss possible treatment options with you. Premature termination of participation will not have a negative impact on health care in the future.

The research doctor will discuss other treatment options with you if you still have symptoms after the test.

During the study you will be asked to minimize the intake of other drugs.

8. The right to withdraw from the study

Participation in this study is voluntary. You can withdraw your consent at any time without explanation and without paying any fines or adversely affecting your further medical care. The investigating physician may terminate your participation in the study, with or without your consent, if it is considered that further participation in it will harm your health.

Once you have given your consent, you will be informed if new information or results relevant to this study become available.

9. Data protection

During this study, medical results and personal information about you or your child will be collected and recorded in your personal records or stored electronically at the study center. Important clinical trial data will also be stored, analyzed, and used for statistical processing and analysis.

You will have the right to review the medical records kept by the investigating physician and to correct incorrect information.

Some research documents (medical history) will be kept for at least 25 years after the study is stopped or completed. If consent is withdrawn during the study, new data will not be collected after that date, but data collected so far may be used if necessary.

According to the Law of Ukraine № 2297-VI of June 1, 2010 "On Personal Data Protection", your personal data - information or a set of information about an individual who is identified or can be specifically identified using this data; Your personal information may not be used or transferred without your written consent, except as provided by the laws of Ukraine. The results of this clinical trial, which will be used to write a scientific publication, will not contain names, addresses, personal identification numbers that may allow the identification of your person or child.
By signing the Clinical Tribunal Consent Form provided at the end of this patient information, you agree that:
Your personal data / child's data will be used to process the results of the clinical trial and provide evidence of the clinical trial in accordance with current legislation of Ukraine, taking into account the requirements of Directives and regulations of the European Parliament and the Council; International Standards for Good Medical Practice (ICH GCP); international ethical principles of biomedical research, including medical ethics and other applicable rules.

The owner of personal data that includes your personal information is the health care facility that conducts the current clinical trial in which you participate. This healthcare institution is responsible for the processing of your personal data, including their collection, systematization, accumulation, storage, adaptation, improvement, updating, use, distribution (distribution, transfer) and destruction.
The following persons will have access to your personal data: the research doctor and other persons directly involved in the conduct, supervision and control of the clinical trial, from the staff of the health care institutions in which you participate in this clinical trial. You have the right to review and copy health data related to your participation in this clinical trial, but in order to ensure the scientific integrity of the clinical trial, you will not have access to some medical records related to this clinical trial. its completion.

You will not be able to participate in this study unless you consent to the collection, recording and transfer of your data to the extent necessary.

10. Evaluation of data collected in this study

The researcher will evaluate the results of the surveys and, if necessary, publish them in scientific journals.

11. Your personal connection

Your research doctor or research team will be happy to answer any questions you may have about this study, as well as your rights as a participant or possible risks and precautions. In the event of an injury related to the study, the need for emergency medical care, or an urgent question about a health problem, contact your research physician immediately. Contact information and telephone numbers are given on page 1.

Round-the-clock hotline number (printed or handwritten):

_____

CONSENT TO PARTICIPATE IN A CLINICAL TRIAL

Title of the study: "Study of the clinical efficacy, safety and tolerability of the drug Imupret in the technology of delayed administration of antibiotics in patients with acute tonsillitis"

First and last name of investigator: ……
Phone and Contact Information: ……

.....
Name and surname of the research participant in capital letters

Date of birth ..... Screening number: .....

I confirm that I have read and understood the fact sheet on the above study and the data protection statement printed below. I had the opportunity to review this information and discuss it with the research doctor, ask questions and get satisfactory answers to all questions. I know I can ask questions at any time during the study. I was given enough time to make a decision.

In particular:

(1) I understand the nature, importance and scope of this study and the related rights and responsibilities.
(2) I know that participation in this study is voluntary and that I have the right to withdraw from the study at any time without explanation and without paying any fines or loss of benefits. I know that a researcher can also stop research at any time and that inappropriate collaboration on my part can lead to my withdrawal from research.
(3) I agree with the study plan and will follow the research physician's instructions to the extent necessary to conduct the study.

Data protection

I know that during this clinical trial, my personal data, including medical data, will be collected, stored and analyzed. These data will be used in accordance with legal requirements that require voluntary informed consent to participate in a clinical trial prior to participation. This means that I cannot participate in clinical trials without the consent below.

1) I agree that in the context of this clinical trial, my personal data, in particular information on ethnic origin, should be collected and stored in paper form and on electronic media for storage in the research center..... ....[] *(specify facility / center for data collection)*. If necessary, the collected data can be transmitted using a pseudonym (in encrypted form) to the following persons:
a) Specialists in medical statistics
b) to the Organizer
c) Other research doctors appointed by the organizer
In addition, I agree that the authorized representatives of the organizer are bound by the confidentiality agreement, and the competent health authorities and foreign authorities can review my personal data stored by the research doctor (especially information about my health).), if necessary to verify the proper conduct of the study. For this reason, I release the research physician from the obligation to maintain the principle of confidentiality between physician and patient.

2) I have been informed that I can complete the clinical trial at any time. However, I cannot revoke my consent to the collection and processing of my personal data, including information about my health. I understand that if I withdraw consent to participate in a clinical trial, the data held at the time of withdrawal of consent may continue to be used if necessary for the following purposes:
a) determining the effect of the study drug;

b) protection of my legitimate interests;
c) compliance with the requirements for providing complete documentation to obtain a registration certificate.
I agree that my personal data will be kept for at least 25 years after the end or termination of the study, in accordance with the rules applicable to medicines. After that, my personal data will be deleted, unless otherwise provided by legal, regulatory or contractual retention periods.

2) I have been informed of the following legal provisions: if I withdraw my consent to participate in the study, all centers in which my personal data, including medical data, are stored, must immediately check the extent to which the data stored are necessary for the purposes listed in section 3, items a) –c). Data that is no longer needed should be deleted immediately.

3) I agree that health data may be collected and accessed by treatment physicians, the investigating physician, and others directly involved in the conduct, supervision, and control of the clinical trial, and by health care professionals. In which I participate in this clinical trial, representatives of the sponsor, including audit firms, independent auditors and independent experts, representatives of the State Expert Center of the Ministry of Health of Ukraine, the Ethics Commission in the health care institution in which I Representatives of national and international, national and / or governmental authorities, if necessary for the proper conduct of the study and its control, participate in this clinical trial.
4) Please select one option:
☐ I agree to have my family doctor informed of my involvement in the clinical trial.
.....
Name and contact phone:

Or
☐ I do not agree to have my family doctor informed about my participation in the clinical trial.

I declare that I will voluntarily participate in the above study.

I was informed about the study and I read the information above. I had time to consider my decision before deciding to participate in the study. I received a copy of the patient information sheet and a signed copy of this form of consent to participate in the clinical trial. I am also aware that I may withdraw my consent at any time, without the need to provide any explanation and without any consequences for the medical care I receive. I received a copy of the insurance certificate, including the insurance conditions.

To be filled in by the research participant personally:

.....
Name and surname of the research participant (in capital letters)

..... …….. ……
Date Time Signature **of the research participant**

To be filled in by the doctor - investigator:

I informed the patient about the study and got consent.

.....
Name and surname of the physician -investigator in capital letters

....

Date Signature of doctor- investigator

One original copy of the informed consent form will be kept at the research center and another will be issued to the patient / patient's representative.