

SUBJECT INFORMATION SHEET

A Double-Blind, Multicenter, Multinational, Randomized, Active-Controlled, Two-Arm Parallel-Group Comparative Study of the Efficacy and Safety of oral HMR 3647 (800 mg once daily) versus oral Amoxicillin (1000 mg thrice daily) in the Treatment of Community-Acquired Pneumonia in Adults

HMR 3647A/3001

Our medical center participates in an investigation of a new drug, which aims to evaluate safety and efficacy of a new antibiotic (ketolide) HMR 3647 in the treatment of community-acquired pneumonia (CAP) in comparison with amoxicillin. .

Disease

You have been diagnosed as having contracted a community-acquired pneumonia of mild to moderate severity. This disease causes the symptoms you may have such as productive or unproductive cough, fever, pain when breathing, shortness of breath, fatigue, and laboratory abnormalities. CAP is an infection of the lung caused by microorganisms in our common surrounding which can be treated with antibiotics available on the market. Amoxicillin is an antibiotic which has since long been shown efficacious in the treatment of CAP. Experimental data show that it can be expected that HMR3647 will be at least as efficacious. However, in order to be able to compare both drugs in an unbiased way, neither you nor your doctor will know which drug you will be treated with, i.e. drugs will be masked and taken with the same dosage schedule as explained below.

HMR3647 and amoxicillin

The HMR3647 antibiotic is still not approved by the authorities. Thus, this antibiotic is not yet on the market, and your doctor will not be able to prescribe it after the completion of the treatment.

HMR3647 has been shown to be safe in healthy volunteers studies, in which the drug was administered at a dose of 50 to 1200 mg. In experimental animal models, it has been shown to be as effective as or superior to other antibiotics against pathogens responsible for CAP including pneumococcus resistant to other antibiotics for which the frequency has recently increased.

Adverse reactions to be potentially anticipated with amoxicillin are cutaneous eruptions, gastrointestinal effects (nausea, vomiting, abdominal pain, diarrhea), increase in hepatic enzymes and, rarely, allergic reactions.

Adverse reactions to be potentially anticipated with HMR 3647 are gastrointestinal effects (nausea, vomiting, abdominal pain, diarrhea), increase in hepatic enzymes and, rarely, allergic reactions.

If you are a woman, it is requested that you avoid becoming pregnant during your participation in the study. Abstinence or an additional method of contraception must be used (spermicide and barrier methods or another accepted method of contraception), even if you are taking oral contraceptive. In the case you suspect that you are pregnant or if you are not using a contraceptive method, you must inform your doctor immediately and you will be, for your own safety, withdrawn from study

medication. If you become pregnant you will have to be followed until the end of the pregnancy to assess the effects of the drug.

Study

A total of 400 subjects will take part in this study and receive two (2) capsules three times per day during 10 days. Subjects receiving amoxicillin will take 1000mg of active substance (amoxicillin) three (3) times per day. Subjects treated with HMR3647 will take 800 mg of active substance 1 time per day and inactive substance 2 times per day in order to keep the treatment confidential. You will also be asked to record your intake of capsules on a specially designed card and to note the time of drug intake the day before and at the day of visit 2 and 3.

Overall, your participation in the study will be approximately 40 days and if you decide to take part, your doctor will see you at 4 or 5 visits during this period of time. Your doctor will examine you at every visit with the exception of the last one which may be done by phone. In addition, the visits will include the following procedures:

Visit1 / Inclusion

Your doctor will ask you about your medical history and currently taken drugs. An ECG (electrocardiogram) will be performed. Before the start of the treatment, a chest x-ray will be performed and sputum, urine, and blood samples will be collected.

Visit2 / On therapy

At Day 3-5 visit, sputum, urine, ECG and blood samples will be repeated. Your doctor will ask you about the time of drug intake.

Visit3 / End on therapy

After the completion of treatment, at day Day 11 to 13, sputum, urine, ECG and blood samples will be repeated. Your doctor will ask you about the time of drug intake.

Visit4 / Post therapy

Seventeen (17) to 24 days after your first visit, chest x-ray and these examinations will be repeated. ECG will be done only if not performed at Visit3 or if significant modifications were seen at Visit3.

Visit5 / Late post therapy

Thirty-one (31) to 38 days after your first visit, a telephone call will be done. Following this phone call, the investigator may ask you to come back, otherwise this is your last contact with your doctor for this study.

The total amount of blood collected throughout the study will be approximately 200 ml.

Participation in this study is entirely voluntary; you are not obliged to take part. **Your treatment and the attitude of your doctor towards you will not be affected should you decide not to take part in this study.** Refusal to participate will not affect any benefits to which you are otherwise entitled. If you decide to take part, you will need to sign a document to say that you have given your consent to participate. If you agree to participate, you may nevertheless withdraw from the study at any time, although for your own safety, it is advisable to tell the investigator if you intend to do this.

The personal information obtained about you during the course of this study will remain confidential: in recording the results of the study, you will be referred to only by a code number and initials. Sponsor representatives or mandated by the sponsor, regulatory authorities, ethics committee / institutional review board will be granted access to your original medical records for verification of clinical trial procedures and / or data, without violating the confidentiality. Your identity will remain confidential even if the results of the trial are reported publicly.

You , or you legally authorised representative, will be informed in a timely manner if information becomes available that may be relevant to your willingness to continue to participate in the trial.

For the duration of the study, you must notify the investigator of any other medical treatments that may be necessary for you to undergo. In the event that you experience any adverse reaction to the investigational drug during the course of this study, you should immediately contact the investigator (for name and telephone number see below).

The sponsor has taken out insurance coverage in accordance with the requirements in your country.

Additional text for centers in Austria:

Subjects participating in this clinical trial are insured in accordance with the Austrian Medicines Act paragraph 32(1), points 11 and 12, under policy No. 64/12322/01 issued by Gerling-Konzern Allgemeine Versicherungs-AG, Hietzinger Hauptstr. 41, 1131 Vienna.

Additional text for centers in France:

A contract with Gerling-Konzern Allgemeine Versicherungs AG, Von-Werth-Str. 4-14, 50597 Cologne, No. 01 8087047 (adhesion No. 97/00028) has been subscribed to. This insurance covers the liability of the sponsor as a sponsor of biomedical research, as well as the liability of any intervening party, in accordance with article L.209.7 of the Code of Public Health.

Additional text for centers in Germany:

A subject insurance policy pursuant to paragraph 40, Section 1, Clause 8, and Section 3 of the Medicines Act has been taken out with the Gerling-Konzern Allgemeine Versicherungs AG, Von-Werth-Str. 4-14, 50597 Cologne. The policy No. is 1/016/02/13/8160186/1 (Phases I-III).

Additional text for centers in Spain:

Subjects participating in this clinical trial are insured in accordance with the conditions expressed in the Royal Decree 561/1993, article 13, under the policy issued by Gerling-Konzern, c/María de Molina, 40 6°-28006 Madrid.

You will be given a copy of this informed consent document and may ask for additional information, at any time during the study, from

_____ (insert name and telephone number of investigator).

You may also contact _____ (insert name and telephone number) if you have questions about your rights as a research subject.

INFORMED CONSENT

Multicenter, open-label study of the efficacy and safety of HMR 3647 800 mg once daily for 10 days in adult subjects with Community-Acquired Pneumonia

HMR 3647A/3001

Subject number: _____

1. I have read the informed consent document for this trial. I have received an explanation of the nature, purpose, duration, and foreseeable effects and risks of the trial and what I will be expected to do. My questions have been answered satisfactorily.
2. I agree to take part in this trial. I agree to cooperate fully with the investigator and will contact *him/her* immediately if I suffer any unexpected or unusual symptoms during the trial. For the duration of the study, I will notify the investigator of any other medical treatments that may be necessary for me to undergo. I agree that, before final inclusion in the study, laboratory tests will be performed. If any of them is not in line as required for the study, I will not be included in the study.
3. I have informed the investigator of all my previous or present illnesses and medication and of any consultation that I have had with my doctor in the last months.
4. I have further informed the investigator of any participation by me in other clinical studies in the past year.
5. I am aware that if I do not cooperate fully with the investigator's requests and directions, I may harm myself by participating in the study.
6. I understand that my participation in the trial is voluntary and that I may refuse to participate or may withdraw from the trial at any time, without penalty or loss of benefits to which I am otherwise entitled. I further understand that any information that becomes available during the course of the study that may affect my willingness to take part will be disclosed to me as soon as practicable.
7. **I agree that results of the study may be passed on to the appropriate authorities, to the sponsor, and to the manufacturer of the drug under study. My name and address will be kept confidential.**
8. **Representatives of the sponsor, independent ethics committee/institutional review board, or local or foreign regulatory authorities may wish to examine my medical records to verify the information collected. By signing this document, I give permission for this review of my records.**

Last name: _____
(block letters)

First name: _____
(block letters)

Signature: _____

Date: _____
(to be completed by subject
at time of consent)

Investigator/Sub-investigator

I confirm that I have personally explained the nature, purpose, duration, and foreseeable effects and risks of the trial to the subject named above.

Last name: _____
(block letters)

First name: _____
(block letters)

Signature: _____

Date: _____

Patient information and written agreement to participate in a clinical study that will compare the medicine HMR 3647 against amoxicillin.

At the Department of Infectious Diseases we are testing a new medicine (HMR 3647) against pneumonia. The aim is to evaluate the effect and the safety of the new medicine in comparison with one already in use (amoxicillin). HMR 3647 has previously been tested on healthy test subjects. This research project has been reviewed and approved both by The Medical Products Agency and the Ethics Committee.

Amoxicillin is a medicine which has been used extensively in the treatment against pneumonia. Experimental data indicate that HMR 3647 will be at least as effective. In order to conduct a fair comparison between the two medicines, they have been covered so that neither you, nor your doctor will know what medicine you will receive, though all participants will in this way get active antibiotics.

A total of 400 persons will participate in this study. The study will be performed in several countries.

We now ask you if you would like to participate in this study. Your doctor is of the opinion that you have pneumonia and that you can be treated with HMR 3647, alternatively amoxicillin.

Side-effects that can occur with amoxicillin are rash, nausea, vomiting, abdominal pain, diarrhoea, increased liver enzymes and, more rarely, allergic reactions. Side-effects that can occur with HMR 3647 are nausea, vomiting, abdominal pain, diarrhoea, increased liver enzymes and, more rarely, allergic reactions. These side-effects are roughly the same as those caused by standard antibiotics. If you experience any side-effects or other unexpected events, please inform us. All side-effects will be carefully registered.

If you are a woman it is mandatory to avoid pregnancy during the course of the study. An effective contraceptive method must be used (for example condom or spermicide and pessary) even when using contraceptive pills. In case you suspect that you are pregnant, or if you do not use any contraceptive methods, you must inform your doctor as soon as possible so that you can be withdrawn from the study.

You will receive two capsules of study medication three times a day. Patients who will receive amoxicillin will take 1000 mg three times a day and those who will get HMR 3647 will take 800 mg active medicine once a day and placebo twice a day to keep the treatment confidential.

Compared to standard treatment, this study involves 1 to 3 additional visits to the doctor or to the nurse.

Prior to the treatment, we will take the usual tests that we perform on all patients with pneumonia, i.e. x-ray examination of the lungs, a sputum test, urine and blood samples. Additionally an ECG will be taken. After a few days of treatment a new control will be performed, consisting of an ECG, urine and blood samples and a sputum test.

After the end of the treatment we will once again take a new ECG, sputum test and urine and blood samples. At the visit two weeks after treatment, besides taking a sputum test, as well as urine and blood samples, an x-ray of the lungs will also be performed. Possibly, even an ECG. A final visit or follow-up by phone will be performed after approximately one month. If your doctor thinks it is necessary, considering your condition, blood samples and an eventual x-ray of the lungs will then be performed. This would mean in total 4-5 visits to the clinic.

The total amount of blood that will be taken during the study is 200 ml.

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Patient nr: _____

You will get the study medication free of charge. The additional visits to the doctor are free of charge.

Your participation in the study is completely voluntary and your treatment at the Department of Infectious Diseases will in no way be affected in case you decline to participate the study. You may, at any time and without giving any specific reason, stop the study without your future treatment being affected. Your doctor may also stop your participation in the study if you experience side-effects or if the expected effect of the study medicine is not obtained. You will then be treated according to normal clinical procedures.

Information collected will be filed on computer and will be used to evaluate the effect of the medicine. Your name will not be used; you will only be registered with a code number, date of birth and initials. Otherwise the normal hospital secrecy will be followed.

You are in this study insured through "Läkmedelförsäkringen" and "Patientskadeförsäkringen".

If you have any questions regarding the study before and during its course, you are welcome to contact us:

Responsible for the study are:

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Tel:

.....

Tel:

I have been orally informed about the study and been given the above information in writing. I consent to participate in the study and know that my participation is totally voluntary and that I at any time can withdraw from the study without effect on my future treatment.

I have been informed about and consent that study specific data may be compared to my medical records by representatives from the pharmaceutical company Hoechst Marion Roussel. I am also aware and consent that Swedish and foreign authorities may want to compare data in the study to my medical records. This can be done provided that the information thus made available is not carried forward.

Signature Patient

Date

.....

Printed name

.....

I confirm that I personally have informed the patient about the study

Signature Doctor

Date

.....

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Printed name

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