Invitation to participate in the scientific study *Transfer of prednisolone into human breast milk and plasma of breastfeeding children - A study with biobanking of breast milk and plasma*

You are hereby invited to participate in a scientific study of treatment with the drug prednisolone during breastfeeding and to allow us to save the samples you provide for future research. This document is intended to provide you with information about the study and the implications of taking part. You cannot participate in the study until six weeks after giving birth and you must have taken prednisolone in the same dosage for at least one week.

What is the purpose of the project and why do you want me to participate?
You are being asked to participate in the study because you are taking prednisolone while breastfeeding. Prednisolone is an approved drug for the treatment of, among other things, various rheumatic diseases. Your doctor has prescribed this drug because the benefits of treatment outweigh the risks. However, further data are required about the extent to which the drug transfers into breast milk.

The purpose of the study is to measure the transfer of prednisolone into breast milk and the amount of the drug subsequently found in the infant's bloodstream after breastfeeding. In Sweden, 30 women will be recruited to the study. The results of the study will be reported at group level in scientific journals. The identities of study participants will not be revealed. This is a sub-study of the project ConcePTION, a public-private partnership financed by the Innovative Medicines Initiative (https://imi-conception.eu) with the aim of generating and disseminating reliable evidence-based information regarding effects of medications used during pregnancy and breastfeeding. The sponsor of the study is Uppsala University. The sponsor refers to the organisation that is responsible for the project. Collaboration partners are Region Stockholm, Karolinska University Hospital, Region Västerbotten, Center for Obstetrics and Gynecology in Umeå and Region Västra Götaland, Södra Älvsborg Hospital in Borås. The study has been reviewed and approved by the Swedish Ethical Review Authority and the Swedish Medical Products Agency (reference number: 5.1.1-2023-104170).

If you would like to participate in the study, please contact your doctor or the principal researcher via the contact details below. Before you can participate, you need to give your consent. You will also need the consent of all parents/guardians of your child for your child's participation in the study.

What does participation in the study involve?
If you decide to participate in the study, you will provide one breast milk sample and one blood sample and we will take a blood sample from your baby. You will also be asked to complete questionnaires. All samples will be taken during a single visit to one of the partners' clinics (see contact details below). You will be offered something to eat before taking your dose of Prednisolone. You will breastfeed your baby immediately before you take your

medicine and one hour after you take your medicine, in conjunction with providing the breast milk sample. It is fine if you need to breastfeed several times during your visit. The visit is expected to take approximately three hours.

Breast milk samples
You will provide one breast milk samples, one hour after taking your medication. You can take the breast milk samples yourself with the aid of an electronic breast milk pump provided by us. When you take the sample, drain all of the milk from one of your breasts until it feels empty. A total of approximately 20 ml of breast milk will be collected.

Blood samples
You will provide one blood sample, at the same time as you provide your breast milk sample. A total of 14 ml of blood will be collected.

Blood sample from your child
We will also take one blood sample from your baby. This is done to see what amount of the drug prednisolone is in the baby's bloodstream after breastfeeding. The sample is taken three hours after you take your dose of prednisolone. A total of 0.8 ml of blood will be collected from the child. The sample will be taken from the child according to the standard clinical procedure, with pain relief in the form of a sugar solution and possibly a local anesthetic (EMLA).

Questionnaire
As part of the study, we will collect and register information concerning you, your health, your child and your medication via a questionnaire that you will be asked to complete during your visit. Once you have provided your breast milk sample, you will also be asked to complete a brief questionnaire concerning the sampling procedure. Staff taking samples will also record information about the procedure for taking blood samples from you and your child. This information is required for sample analysis.

You will receive more detailed instructions about sampling if you agree to participate in the study. Samples will be stored locally before being sent to the Uppsala Biobank once all samples in the study are collected.

Potential benefits or risks associated with participating in the study
It is not anticipated that you will benefit directly from participating in the study. However, the results of the study will provide data that may help breastfeeding women to make informed decisions about taking prednisolone while breastfeeding in future. Such data will also help healthcare professionals to offer evidence-based advice to breastfeeding women on the use of prednisolone.

This study will not change your treatment in any way; participation will therefore not expose you to any additional risks. When a blood sample is taken, it is common to feel a slight prick. You may have bruising and there is always a slight risk of nerve damage, which may be

experienced as pain or numbness. A total of 14 ml of blood will be drawn. In comparison, a normal blood donation is 450 ml.

What will happen to my data?
In conjunction with the study, health data concerning you and your child will be collected and stored. Once registered, the personal health data concerning you will be used solely for the purposes of the study as described here. All personal data will be processed in accordance with the General Data Protection Regulation (GDPR 2016/679) in a manner that prevents unauthorized access. When you agree to join the study, you will be assigned a study code. The data you provide will be labelled with this code and then analyzed without your name, personal identity number or other information that can be directly linked to you. The code key will be stored separately from the health data in a secure database at Uppsala University. Your health data will be registered in Research Electronic Data Capture (REDCap), an electronic tool used by Uppsala University for secure data collection. In addition to the researchers responsible for the study, authorized staff working on the study at the Uppsala University Drug Optimization and Pharmaceutical Profiling Platform (UDOPP) at the Department of Pharmacy will also have access to your health data to the extent it is required to analyze the samples. The data they receive will however be pseudonymized so that it cannot be directly linked to you. If you do not consent to your data being saved for future research it will be stored for 10 years after the completion of the study, after which it will be erased. Your contact details will be stored at Uppsala University so that we can contact you to arrange sampling. Once all data and samples have been collected, your contact details will be erased.

The biobanks will store samples and sample information linked to your personal identity number. Samples and sample information will initially be stored in the biobank in the region where the samples are taken (Biobank West in Gothenburg, Biobank North in Umeå and Biobank and Student Support, Medical Diagnostics, Karolinska University Hospital in Stockholm) but later also in Uppsala Biobank where long-term storage of samples will take place.

The controller of your personal data is Uppsala University. You retain the right to know what data concerning you is being processed and to request the rectification of any inaccuracies. You may also request the erasure of personal data concerning you or restrictions on its processing. However, the right to erasure and the restriction of processing does not extend to the necessary processing of the data for the purposes of the research in question. If you would like access to the personal data being processed concerning you, please contact the principal investigator for the study (see contact details below). If you have comments or complaints about how your personal data is being processed, you can contact the data protection officer at Uppsala University at dataskyddsombud@uu.se or the Swedish Authority for Privacy Protection (IMY) at https://www.imy.se.

What will happen to my samples?
The samples are handled in accordance with the Biobank Act (2023:38). The samples of blood and breast milk, and information about when they were taken and processed, will be sent for

storage at the Uppsala Biobank in Uppsala, Sweden (Health and Social Care Inspectorate (IVO) registration number 827). The authority responsible for the biobank is Region Uppsala. The levels of prednisolone in the blood and breast milk will be analyzed at UDOPP at Uppsala University's Department of Pharmacy.

If you consent to your samples being saved for future research, they will be kept for 20 years and made available for medical research purposes deemed beneficial to society. At present, it is impossible to know what these specific purposes might be. The samples may only be used for the purposes to which you have consented. Should any further research other than that already planned be proposed, an ethical review board will decide whether the samples can be used and whether you need to be contacted with a request for consent. If you do not consent to your samples being saved for future research, they will be stored for 10 years and then destroyed.

You retain the right to refuse permission for the samples to be saved. If you do consent to the samples being saved, you retain the right to withdraw your consent, in which case your samples will be destroyed or anonymized. It is only permitted to anonymize samples if they cannot be destroyed without destroying other samples. If you wish to withdraw your consent, please contact the principal researcher for the study (see contact details below).

How can I find information about the results of the study?
You will not receive any individual results from the analysis of your samples. The results of the study will be presented at scientific conferences and published in scientific journals. Publications will be announced on our website (https://imi-conception.eu).

Insurance and remuneration
As a participant in the study, you are covered by the standard patient injury insurance and pharmaceutical insurance. You can keep the breast milk pump we use to take samples. You will be compensated for any travel expenses to and from the clinic where you provide samples. You will also receive remuneration in the amount of SEK 1,000 for providing blood and breast milk samples. This remuneration is tax-free.

Participation is voluntary
Your participation in the study is voluntary. You can choose to withdraw your consent and end your participation at any time. If you do so, you do not need to offer any explanation and it will not have any effect on your future care or treatment. If you decide to withdraw from the study, you may require that data concerning you be erased, as long as the data have not already been analyzed or used in scientific publications. If you wish to end your participation, please contact the principal investigator (see contact details below).

Contact information

The principal investigator for the study is Mats Hansson, senior professor of biomedical ethics.

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Commented [ES1]: Översätta?

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