PARENT INFORMATION AND INFORMED CONSENT FORM

for

Protect-NOW

Non-Interventional Study GENA-25

PRactical utilization of **O**ctapharma FVIII Concentrates in Previously Untreated and Minimally **T**reated Haemophilia A Patients **E**ntering Routine **C**linical **T**reatment (with **N**uwiq, **O**ctanate or **W**ilate)
A Real-World Efficacy and Safety Observational Study

Sponsor:	**Octapharma AG** Lachen, Switzerland
Principal Investigator:	**<name>** <institution> <address>

Dear Parent(s),

Your child's doctor has prescribed treatment with one of Octapharma's factor VIII (FVIII) products (i.e., *Octanate*®, *Wilate*®, or *Nuwiq*®) to your child. The purpose of treatment with a FVIII product is to control and prevent bleedings that may occur as a result of your child's haemophilia.

We now invite your child to take part in a non-interventional study. A study is a way of gathering information on a treatment and answering questions about something that is not well enough understood. In a non-interventional study, a medicine is used in accordance with the terms of the marketing authorization of that product. Thus, the selection of a particular therapy or medicine is clearly separated from the decision to include a patient in the study. Therefore, participation in this non-interventional study will have no influence on the treatment your child will be receiving. Your child's doctor will, however, record your child's treatment data in standardised forms so that the data can later be analysed by an independent statistics institute.

Please take the time to read this **Information Sheet** on this carefully and feel free to ask questions about anything you don't understand before deciding whether or not you wish your child to participate.

Taking part in this study is voluntary. Even if you now choose to have your child in the study, you have the right to stop at any time. If you decide not to have your child participate or to leave the study early, your child's usual health care will not be affected.

1 Why is my child asked to participate in this study?

Your child is being asked to consider participating in this study because it has haemophilia A. Haemophilia A results from an abnormality in the blood that affects its ability to clot. Blood clotting is the process that controls bleeding. It changes blood from a liquid to a solid form. This is a complex process involving many different blood chemicals or proteins, known as clotting factors. When certain clotting factors are missing or don't work properly, clotting of blood doesn't occur as it should.

In people with severe haemophilia A, an important clotting factor called 'factor 8' or 'factor VIII' (FVIII) is missing or doesn't work the way it should. This causes people with haemophilia A to bleed for a longer time than people whose blood FVIII levels are normal. The preferred treatment for haemophilia A is a FVIII replacement therapy.

2 Why is this study being done?

You and your study doctor have decided that your child will undergo treatment with one of Octapharma's FVIII products. This decision has been made independently of this study. The only difference between routine FVIII treatment and this study is that, in this study, all treatment details will be carefully documented not only in your child's medical records, but also in standardised forms for later statistical analysis.

The data will be analysed to answer the following questions (see **Section 7.1**):

- How well does the FVIII product treat or prevent bleedings in patients with haemophilia A?
- How well is the product tolerated?
- How effective is the product at controlling blood loss during surgeries?
- What FVIII treatment schedules and dosages are used in clinical practice?

In addition to the data routinely recorded during FVIII treatment, you can also choose to have some additional parameters assessed. These will be analysed to answer the following questions (see **Section 7.2**):

- What is the role of non-inhibiting anti-FVIII antibodies in the treatment of haemophilia A?
- How do anti-FVIII antibodies bind to their binding sites ('epitopes') on the FVIII molecule?
- Do certain genetic mutations have an effect on the risk of bleeding or inhibitor development?

3 Does my child have to undergo FVIII therapy?

Your doctor has recommended FVIII replacement therapy for your child because this is the preferred treatment for haemophilia A. Injecting FVIII makes the clotting factor immediately available in the bloodstream, and the body can activate it to continue the clotting cascade and control the bleeding risk.

People with haemophilia A are treated either with FVIII products that are made from **donated human blood** (such as *Octanate*® or *Wilate*®) or with **recombinant FVIII products** that are produced from cell lines (such as *Nuwiq*®).

Also, there are two basic options for FVIII treatment, i.e., treatment may be given at the time a bleed occurs (known as **'on-demand therapy'**), or it may be given regularly to prevent bleeds from occurring (known as **'prophylactic therapy'**).

Your child's doctor will select the treatment regimen s/he considers the best option for your child.

4 How many patients will participate in this study?

Overall, 140 patients with haemophilia A from approximately 50 treatment centres worldwide will be enrolled into this study.

5 What are the main criteria for participating in this study?

This study is open to participation to patients with severe haemophilia A who have:

- never before received a FVIII product
- received a FVIII product on fewer than 5 days, with the first administration having taken place after 1 January 2015.

There are also a number of reasons that prevent your child from participating in this study, namely the presence of a blood clotting disorder other than haemophilia A, the presence of a FVIII inhibitor, the treatment with drugs that act on the immune system, or participation in an interventional clinical study.

6 How long will the study last?

To obtain solid results, each patient should be in the study for 100 'exposure days' (i.e., days on which the FVIII product is administered) or a maximum time of 3 years.

7 What will be done in this clinical study?

Before any study-specific documentation will take place, your doctor will discuss the study with you, and you will be asked to read this **Information Sheet** and sign the **Informed Consent Form** at the end of this document.

7.1 Routine FVIII treatment

First visit

During the first visit, your doctor will explain all treatment and study details to you and answer any of your questions. The **demographic and baseline data**, such as your child's body weight, height, age, medical and bleeding history, laboratory parameters, and any additional diseases, will be documented.

You will be handed out a **Treatment Diary** in which to record any observations in connection with your child's health. Your doctor will explain to you how to fill in the diary and emphasize the importance of carefully documenting all treatment details, bleeding episodes, side effects of treatment, illnesses, or hospitalizations as well as any additional medications your child may be taking throughout the study.

If bleedings occur, you will also be asked to assess the effectiveness of FVIII treatment in the Treatment Diary once the bleeding has stopped. Please bring your child's Treatment Diary along to each study visit so that your doctor can monitor the effectiveness of treatment, adapt recommendations and record and transcribe the data.

Follow-up visits

During routine standard visits, the frequency of which will be discussed between you and your doctor, your doctor will document results of examinations and laboratory tests. Especially during the start of a regular treatment with a FVIII concentrate, the FVIII level and the presence of inhibitors are routinely checked more frequently.

During these visits, your doctor will also review the Treatment Diary to find out whether the prescribed treatment regimen works well for your child. You will also be asked about any side effects that may have occurred since your last visit.

In addition to the regular visits described above, you and your child may need to visit the treatment centre in case of severe bleedings, emergencies, surgeries, or if you suspect that your child may have developed a FVIII inhibitor.

7.2 Additional assessments

In addition to the assessments routinely performed almost worldwide during FVIII treatment start and further follow up, you may decide to have some additional not yet golden standard parameters recorded. These parameters could, in the future, help to further individualise haemophilia A treatment, predict a patient's risk of developing inhibitors, or even prevent the formation of inhibitors:

Measurement of non-inhibiting anti-FVIII antibodies

In this study, it is intended to check for the presence of non-inhibiting anti-FVIII antibodies. In contrast to inhibiting antibodies, the role of non-inhibiting antibodies is currently not clear. If you agree to this type of testing, *no* additional blood samples will have to be taken, because these antibodies can be tested by using the samples taken for routine inhibitor testing as described above.

Epitope mapping

'Epitopes' are small regions on the FVIII molecule that are recognised by anti-FVIII antibodies and that these antibodies bind to. Through this binding mechanism, the antibodies attack the FVIII molecule so that it cannot fulfil its desired function of setting off a chain of reactions that ultimately form a blood clot. Characterization of these regions may improve the understanding of the mechanisms of inhibitor activity and may aid in the development of new therapies. If you agree to this type of testing, a small aliquot of a routinely taken blood sample will be provided to a central laboratory in Germany at predefined times during the study.

F8 genotyping

'Genotyping' has become golden standard in analysing haemophilia A patients for many years, already. It is the process of identifying specific genetic changes responsible for a person's disorder. Within this study, a blood sample can be provided to a central laboratory in Germany, if agreed upon. Gene mutation analysis will be used to test for any mutations in your child's FVIII gene. For example, certain F8 genotypes have been linked with an increased risk of severe bleeding or inhibitor development.

8 What are the possible benefits of the study?

Your child's participation in this study will help to obtain additional information on the effectiveness and safety of the prescribed FVIII product, and the dosage regimens used.

The study may also allow to assess the effect of non-inhibiting anti-FVIII antibodies, FVIII epitopes, and certain genetic characteristics affecting the bleeding risk and treatment outcome. In this way, your child may contribute towards the development of effective treatment strategies for future haemophilia A patients.

9 What are the possible risks and discomforts when taking part in this study?

Because this is a non-interventional study assessing a routine treatment, no additional risks are expected from your child of being in the study. The FVIII product your child will receive for treatment has been licensed in your country. Please ask your doctor if you would like to know more about this product.

10 What are the costs of your participation in this study?

All costs related to this study are covered under your medical care plan. The haemophilia treatment centre will provide you with the FVIII product and additional items needed to infuse the product, such as syringes or needles. You will not be paid for your child being in this study.

11 Confidentiality

All data will be kept confidential and only your child's doctor will have access to personal data. All blood samples and study documents will be number-coded to prevent disclosure of personal information.

Although everything will be done to keep your records a secret, this cannot be fully guaranteed. Both the records that identify your child and the consent form you signed may be looked at by others, e.g.:

- People at the Research Ethics Board (REB)
- Your study doctor and his/her team of researchers

Also, this study and its results may be subject to meetings, or may be published in relevant journals. However, the names of all study participants will always be kept private. You and your child have the right to request access to any personal health information from the study doctor.

This authorization of data use does not expire. However, you may withdraw this authorization of disclosure of your child's personal health information. If you withdraw this authorization, the doctor, research staff, and sponsor of this study will no longer be able to use or disclose your child's personal health information from this study from that date, except so far as that they have already relied on this information to conduct the study.

12 Who do I call if I have questions?

If you have additional questions regarding this study, please contact the study doctor:

Study doctor

Name:	
Address:	
Phone:	
Fax:	

Thank you for reading this Information Sheet.

If you decide to have your child take part in this study,
please enter your name on the attached
Informed Consent Form and sign and date it.

Informed Consent Form

I am aware that personal data, in particular medical reports, will be collected, stored, and evaluated in the course of this project. Any information about my child's health will be used in compliance with the statutory regulations, and its use is subject to my voluntary informed consent prior to participation in the project, i.e., my child cannot participate in the project if I do not sign the following consent.

1. I herewith agree that the data collected within the scope of this project, in particular information about my child's health, may be recorded on paper and on electronic data carriers. The collected data may only be disclosed to the project manager or his agents for the purpose of scientific evaluation in pseudonymised form (encrypted).
2. I further agree that authorised agents, who are sworn to secrecy may inspect the available personal data, in particular the health data, to the extent that this is necessary to verify the correct implementation of this project. For this purpose, I herewith release the attending physician from his/her obligation to maintain confidentiality.
3. My consent to the collection and processing of personal data, in particular data about my child's health, is irrevocable. I have been informed that I may terminate my child's participation in the project at any time. In the event of such a termination, I herewith agree that any data stored up to this point in time may continue to be used without my child's name being used, provided that my child's protected interests are not violated thereby.
4. I herewith agree that my child's data shall be stored for at least ten years after termination or discontinuation of the project. Thereafter, the personal data will be deleted, unless required otherwise by law, statutes, or contractual provisions.
5. I have been informed about the following statutory regulation: If I withdraw my consent to my child's participation in this project, all agencies that have stored any personal data, in particular health data, must immediately review to what extent the stored data is still required. Any data no longer required must be deleted forthwith.

Please mark appropriate check box(es) below.

Based on the information available to me,

☐ **Yes**, I agree to have my child take part in the project.

☐ **Yes**, I agree to have my child take part in "Additional Assessments" of this project.

Signatures

Patient's parent(s) or legal guardian:

I agree to have my child take part in this study as stated above.

Print name	Signature	Date

Patient's parent(s) or legal guardian:

I agree to have my child take part in this study as stated above.

Print name	Signature	Date

Treating Physician:

Print name	Signature	Date