# Effectiveness of Xiapex® educational material for healthcare professionals in the treatment of Peyronie's disease - a non-interventional post-authorization safety study

# PASS information

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| **Title** | Effectiveness of Xiapex® educational material for healthcare professionals in the treatment of Peyronie's disease - a non-interventional post-authorization safety study |
| **Protocol version identifier** | Sobi.Xiapex-PASS01 |
| **Date of last version of protocol** | 20 April 2015 |
| **EU PAS register number** | ENCEPP/SDPP/9339 |
| **Active substance** | M09AB02<br>Collagenase *Clostridium histolyticum* |
| **Medicinal product** | Xiapex |
| **Product reference** | Xiapex-2048 |
| **Procedure number** | EMEA/H/C/002048/II/0044 |
| **Marketing authorization holder(s)** | Swedish Orphan Biovitrum AB (publ) |
| **Joint PASS** | No |
| **Research question and objectives** | The study objective is to evaluate the effectiveness of the Xiapex® educational material as an additional risk minimization measure for healthcare professionals in the treatment of Peyronie's disease.<br>The effectiveness will be assessed by the following endpoints:<br>1. Survey response of "disagree" or "strongly disagree" to survey question on **treatment procedure**; Question 2 (comprising 4 items) of the Implementation survey and the Follow-up survey.<br>2. Survey response of "not effective" to survey question on:<br>a. **Safe and precise administration and adverse event reporting**; Question 4 (comprising 5 items) of the Implementation survey.<br>b. **Identified safety risks**; Question 5 of the Implementation survey and Question 3 of the Follow-up survey. |

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| **Research question and objectives, continued** | 3. Type of adverse events not sufficiently described in the education material, as assessed by the responders.<br>4. Education material in need of revision to prevent adverse events, as assessed by the responders. |
| **Country(-ies) of study** | Minimum 5 countries where local Regulatory Approval of Xiapex Peyronie's education material has been obtained.<br>Approval has been obtained in Austria, Denmark, Finland, Iceland, Ireland, Norway, Poland, Sweden, and UK. |
| **Author** | Sari von Reedtz, Clinical Program Leader<br>Swedish Orphan Biovitrum AB<br>SE-112 76 Stockholm, Sweden |

# Marketing authorization holder(s)

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|---|---|
| **Marketing authorization holder(s)** | Swedish Orphan Biovitrum AB (publ)<br>SE-112 76 Stockholm, Sweden |
| **MAH contact person** | Marianne Keisu, QPPV |

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# 1 List of abbreviations

| | |
|---|---|
| MAH | Marketing authorization holder |
| QC | Quality control |
| Sobi | Swedish Orphan Biovitrum AB |

# 2 Responsible parties

The marketing authorization holder (MAH), Swedish Orphan Biovitrum AB (Sobi) is responsible for the design, conduct and data evaluation of this post-authorization study. This is a non-interventional safety study, eliciting information from health care professionals that complete the Xiapex Peyronie's education material. There are hence no principal investigator or study sites.

# 3 Abstract

**Title**

Effectiveness of Xiapex® educational material for healthcare professionals in the treatment of Peyronie's disease - a non-interventional post-authorization safety study

Study protocol no. Sobi.Xiapex-PASS01, Version 1, 20-Apr-2015

Sari von Reedtz, Swedish Orphan Biovitrum AB, SE-112 76 Stockholm, Sweden

**Rationale and background**

Comprehensive education material has been developed to minimize identified and potential risks associated with Xiapex treatment and to ensure that all physicians who are expected to prescribe/use Xiapex in Peyronie's disease are appropriately trained in the correct administration of the product. Trained physicians will be registered in a Peyronie´s database held by the MAH in Europe (i.e., Sobi) confirming that he/she has fulfilled the physician training program requirements by reading the treatment training brochure. Thus, the education material constitutes an additional risk minimisation measure.

This study will evaluate the effectiveness of the additional risk minimization measure, i.e., the educational material for healthcare professionals. The effectiveness will be assessed through surveys administered to physicians completing the treatment education material. The surveys are designed to capture the physicians' perception of how useful the education material has been to:

- ensure safe and correct administration of Xiapex
- make the physician aware of the identified risks associated with the use of Xiapex

Based on the results of this study, the education material may hence be revised, as deemed appropriate.

**Research question and objectives**

The study objective is to evaluate the effectiveness of the Xiapex® educational material as an additional risk minimization measure for healthcare professionals in the treatment of Peyronie's disease. The effectiveness will be assessed by the following endpoints:

1. Survey response of "disagree" or "strongly disagree" to survey question on **treatment procedure**; Question 2 (comprising 4 items) of the Implementation survey and the Follow-up survey.
2. Survey response of "not effective" to survey question on:
    a. **Safe and precise administration and adverse event reporting**; Question 4 (comprising 5 items) of the Implementation survey.
    b. **Identified safety risks**; Question 5 of the Implementation survey and Question 3 of the Follow-up survey.
3. Type of adverse events not sufficiently described in the education material, as assessed by the responders.
4. Education material in need of revision to prevent adverse events, as assessed by the responders.

**Study design**

This is a non-interventional post-authorization safety study evaluating the effectiveness of the implemented additional risk minimization measure, i.e., the Xiapex educational material for healthcare professionals for treatment of Peyronie's disease. The effectiveness will be assessed through a survey program which includes an Implementation survey and a Follow-up survey.

The Implementation survey will be sent to the physician in a feasible time frame after the physician's registration in the Xiapex Peyronie's Trained Physicians database, maintained by Sobi, or provided upon completion of a training event that includes review of the education material. The Follow-up survey will be sent approximately 6 months after the physician's registration in the Xiapex Peyronie's Trained Physicians database.

**Population** Healthcare professionals completing the Xiapex education program for usage of Xiapex in the treatment of Peyronie's disease that receive, complete and submit the Implementation and/or Follow-up Surveys.

**Variables** Responses to survey questions.

**Data sources** Completed surveys.

**Study size** Minimum 30 Implementation Surveys and 30 Follow-up Surveys

**Data analysis** Categorical data from the Implementation survey (all items in Questions 1, 2, 4, 5) and the Follow-up survey (all items in Questions 1, 2, 3) will be summarized using frequency counts and percentages using the categories defined in the survey. For all items in Question 2 of

the Implementation and Follow-up surveys, the number and proportion of physicians responding "disagree" or "strongly disagree" merged as one category will also be presented.

Adverse events identified in question 4 of the Follow-up survey will be coded using MedDRA. The number and proportion of physicians reporting each individual event (on a preferred term level) will be presented.

**Milestones** Start of data collection: 15-Feb-2015; End of data collection: 30-Nov-2016; Registration in the EU PAS register: 15-Apr-2015; Final report of study results; 30-Nov-2017

# 4 Amendments and updates

None.

# 5 Milestones

| Milestone | Planned date |
|---|---|
| **Start of data collection** | 15-Feb-2015 |
| **End of data collection** | 30-Nov-2016 |
| **Registration in the EU PAS register** | 15-Apr-2015 |
| **Final report of study results** | 30-Nov-2017 |

# 6 Rationale and background

As agreed with the European Medicines Agency, only those physicians who are experienced in the treatment of male urological diseases and who have been appropriately trained in the usage of Xiapex® in the treatment of Peyronie's disease shall use Xiapex. Comprehensive education material has been developed to minimize the identified and potential risks associated with Xiapex treatment. Trained physicians will be registered in a Peyronie's database held by the MAH in Europe (i.e., Sobi) confirming that he/she has fulfilled the physician training program requirements by reading the treatment training brochure. Thus, the education material constitutes an additional risk minimisation measure.

In addition to the training brochure, other training activities may be included in local training programs, e.g., peer-to-peer Xiapex administration training events, web-based tutorials, etc.

The effectiveness of the risk minimization measure will be evaluated through surveys. Upon registering in the Peyronie's Trained Physicians database, or upon completing a training event including review of the education material, the physician will be asked to complete and submit an Implementation survey. Six months after registering in the Peyronie's Trained Physicians database, the physician will be asked to complete a Follow-up survey.

The surveys are designed to capture the physicians' perception of how useful the education material has been to:

- ensure safe and correct administration of Xiapex
- make the physician aware of the identified risks associated with the use of Xiapex

In addition, the Follow-up survey will capture adverse events that were not described in the education material and suggestions on mitigations to prevent such adverse events.

Based on the results of this study (i.e., the survey responses), the education material may hence be revised, as deemed appropriate.

A similar training and survey approach was used for Xiapex treatment of Dupuytren's contracture.

# 7 Research question and objectives

The study objective is to evaluate the effectiveness of the Xiapex educational material as an additional risk minimization measure for healthcare professionals in the treatment of Peyronie's disease. The effectiveness will be assessed by the following endpoints:

1. Survey response of "disagree" or "strongly disagree" to survey question on **treatment procedure**; Question 2 (comprising 4 items) of the Implementation survey and the Follow-up survey.
2. Survey response of "not effective" to survey question on:
    a. **Safe and precise administration and adverse event reporting**; Question 4 (comprising 5 items) of the Implementation survey.
    b. **Identified safety risks**; Question 5 of the Implementation survey and Question 3 of the Follow-up survey.
3. Type of adverse events not sufficiently described in the education material, as assessed by the responders.
4. Education material in need of revision to prevent adverse events, as assessed by the responders.

# 8 Research methods

## 8.1 Study design

This is a non-interventional post-authorization safety study evaluating the effectiveness of the implemented additional risk minimization measure, i.e., the Xiapex educational material for healthcare professionals for treatment of Peyronie's disease. The effectiveness will be assessed through a survey program which includes an Implementation survey and a Follow-up survey.

The Implementation survey will be sent to the physician in a feasible time frame after the physician's registration in the Xiapex Peyronie's Trained Physicians database, maintained by Sobi, or provided upon completion of a training event that includes review of the education material. The Follow-up survey will be sent approximately 6 months after the physician's registration in the Xiapex Peyronie's Trained Physicians database. The Implementation survey is provided in Appendix 1. The Follow-up Survey is provided in Appendix 2.

## 8.2 Setting

The Xiapex Peyronie's Trained Physicians database will capture information on name, speciality, institution and country. Upon registration, the physician will consent to Sobi maintaining his/her information. A separate log will be set up to track the provision and return of completed surveys in order to assess the response-rate and to allow distribution of systematic reminders to non-responding physicians.

The physician's will fax, mail or e-mail the completed surveys to Sobi, or hand it over to a Sobi representative. To facilitate the tracking of survey completion, the physicians will be asked to provide their name on the completed surveys. Reminders will be sent to those physicians that have not responded to the survey (one reminder per survey). The names of the responding physicians will not be entered in the study database. Any completed anonymous surveys will be entered in the study database.

Prior to distribution, the education material translated into local language, will be reviewed and approved by each country's Regulatory Authority. The timing of approved education materials will therefore vary by country. The first education material approvals were obtained in February 2015. By 10 April 2015 approval has been obtained in Austria, Denmark, Finland, Iceland, Ireland, Norway, Poland, Sweden, and UK.

## 8.3 Variables

The study database will contain information on the specialty of responding physicians (provided that the name of the responding physician is obtained and that the responding physician is registered in the Xiapex Peyronie's Trained Physicians database) and the data captured in the surveys (refer to Appendices 1 and 2). Comments provided in local language will be translated into English prior to data entry. The tracking log of provided and returned surveys will be used to assess the response rate.

## 8.4 Data sources

The data source will be the completed surveys, provided to Sobi through fax, mail or e-mail, or in person to a Sobi representative. Text in local language will be translated to English prior to entry into the study database.

## 8.5 Study size

Implementation surveys will be provided to all physicians registering in the Xiapex Peyronie's Trained Physicians database and/or upon completion of a training event including review of the education material over the time period of 15-Feb-2015 to 30-May-2016. Overall, up to 100 physicians are expected to have completed the training program within this time period.

The collection of Follow-up surveys is planned to be completed by 30-Nov-2016.

The survey collection period will be extended if a minimum of 30 Implementation surveys and 30 Follow-up surveys have not been obtained by 30-Nov-2016. Furthermore, the collection period may be extended if surveys from less than 5 countries have been obtained by 1-May-2016.

## 8.6 Data management

### 8.6.1 Data collection

Survey forms in PDF format will be distributed to physicians via email or as printed handouts.

Survey forms distributed via email will be fillable so that the physician can enter data directly, save the form and return it to Sobi via email. The form can also be printed, completed, scanned and returned to Sobi via email, mail, fax or in person to a Sobi representative.

The completed forms will be received by Sobi and free text will be translated into English. Original and translated survey forms will be stored on a restricted access Sharepoint site.

### 8.6.2 Data entry

After translation, the data and free text will be entered into an Excel database. Free text will be entered exactly as translated into English. Free text in the original language will not be entered into the database. The names of the responding physicians will not be entered in the study database.

Data entry will be performed by Sobi data management.

## 8.7 Data analysis

Categorical data from the Implementation survey (all items in Questions 1, 2, 4, 5) and the Follow-up survey (all items in Questions 1, 2, 3) will be summarized using frequency counts and percentages using the categories defined in the survey. For all items in Question 2 of the Implementation and Follow-up surveys, the number and proportion of physicians responding "disagree" or "strongly disagree" merged as one category will also be presented.

Adverse events identified in Question 4 of the Follow-up survey will be coded using MedDRA. The number and proportion of physicians reporting each individual event (on a preferred term level) will be presented.

All data will be listed.

## 8.8 Quality control

### 8.8.1 Source data verification

Data will be verified by proof reading of 100 % of the collected source data versus the study database. Proof reading will not be performed by the person entering the data in the database. All discrepancies will be checked against the source PDF forms and where required the database will be updated.

### 8.8.2 Data quality control

Quality Control (QC) of data will be performed to ensure that data entry and verification have been performed adequately.

- 5% of the entered records will be randomly selected and all variables will be checked against source for accuracy with the allowed error rate of 1%. Errors found will be updated.

If the allowed error rate is exceeded the process will be repeated until the error rate is below or equal to the set limit.

The result of the QC will be documented and archived as a separate document.

### 8.8.3 Database lock

When all data is entered, source data verified and quality controlled with an accepted error rate the excel database is locked.

### 8.8.4 Analysis database

After database lock the excel database is converted to SAS format to allow statistical analysis of the data.

The Excel database, the SAS database and associated programs and outputs will be stored in the Sobi clinical data repository.

## 8.9 Limitations of the research methods

It is expected that there may be a difference in the physicians' response rate depending on how useful they find the education material. Thus, physicians perceiving the education material to be inadequate and/or identifying adverse events or medication errors that could be avoided by revised education material can be more motivated to complete and submit the survey compared to physicians finding the material adequate. This will however not affect the primary objective of the study, as the objective is to identify any potential areas of the education material that would benefit from revision in order to avoid adverse events and medication errors.

## 8.10 Other aspects

Not applicable.

# 9 Protection of human subjects

The personal data protection rights of study participants, i.e., the responding physicians, will be ensured by providing a limited number of Sobi personnel with access to the Trained Physicians database. Each registering physician will need to consent to Sobi maintaining his/her information.

Should any completed survey contain any personally identifiable information, then that information will be deducted from the completed form and will not be entered into the study database.

# 10 Management and reporting of adverse events/adverse reactions

This study is not designed to capture all observed adverse events in a study database for the purpose of safety evaluation of Xiapex treatment. The objective of this study is to evaluate the effectiveness of risk minimization measures and accordingly this study only captures information on any adverse events that, in the opinion of the investigator, could possibly be avoided by an improved education material.

The physicians are instructed in the survey to separately report adverse reactions associated with Xiapex to Sobi Drug Safety, either through email or by fax and to the local Regulatory Authority according to national requirements. Any received case reports will be entered into the global safety database and included in the routine pharmacovigilance activities for Xiapex including signal detection, regulatory reporting and inclusion in PSURs as applicable.

# 11 Plans for disseminating and communicating study results

The final study report will be submitted to the EMA.

# 12 References – Not applicable

# Appendix 1 Implementation Survey

## XIAPEX EDUCATION PROGRAM IN PEYRONIE´S DISEASE IMPLEMENTATION SURVEY.

**Please complete ALL questions below, and return**

**By mail:**
Medical Information,
Swedish Orphan Biovitrum AB (publ)
SE-11276 Stockholm, Sweden

**By fax:**
+46 8 697 32 30
**By email:**
medical.info@sobi.com

Name:

### 1. PLEASE IDENTIFY YOUR COUNTRY

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Austria | ☐ | France | ☐ | Lithuania | ☐ | Slovenia | ☐ |
| Belgium | ☐ | Germany | ☐ | Luxembourg | ☐ | Spain | ☐ |
| Croatia | ☐ | Greece | ☐ | Malta | ☐ | Sweden | ☐ |
| Cyprus | ☐ | Hungary | ☐ | Netherlands | ☐ | Switzerland | ☐ |
| Czech Republic | ☐ | Iceland | ☐ | Norway | ☐ | United Kingdom | ☐ |
| Denmark | ☐ | Ireland | ☐ | Poland | ☐ | Other | ☐ |
| Estonia | ☐ | Italy | ☐ | Portugal | ☐ | | |
| Finland | ☐ | Latvia | ☐ | Slovakia | ☐ | | |

### 2. WOULD YOU PLEASE INDICATE YOUR LEVEL OF AGREEMENT WITH THE STATEMENTS BELOW?

| | STRONGLY AGREE | AGREE | DISAGREE | STRONGLY DISAGREE |
|---|---|---|---|---|
| The training package was clear and comprehensive | | | | |
| The training package was effective in helping me to understand the reconstitution protocol | | | | |
| The training package was effective in helping me to understand the administration procedure | | | | |
| The training package was effective in helping me to understand the modelling procedure and out-patient treatment | | | | |

If you answered any of the questions, Disagree, Strongly Disagree please comment below.

EDUCATIONAL ITEMS

Depending on local regulations, each training package received may contain some or all of the following components.

3. PLEASE INDICATE WHICH OF THESE COMPONENTS OF THE PACKAGE WERE

A) RECEIVED
B) USED (OR ATTENDED IN THE CASE OF LIVE PEER TO PEER MEETINGS).

| EDUCATIONAL ITEMS | RECEIVED | USED OR ATTENDED |
|---|---|---|
| Xiapex Publications (with reprint carriers) | | |
| Xiapex administration training brochure | | |
| Provided website for Xiapex administration training | | |
| Invitation to attend a local live peer to peer Xiapex administration training event | | |
| Other items (if additional materials were provided, please also describe in question 5) | | |

These materials were designed to ensure safe and precise administration of Xiapex and facilitate reporting of adverse events experienced by the patient.

4. HOW EFFECTIVE WERE THE MATERIALS IN ACHIEVING THIS OBJECTIVE? Please rank the top 3 materials that were most helpful in achieving the objective by entering 1, 2, and 3 in the appropriate boxes below.

| EDUCATIONAL ITEMS | VERY EFFECTIVE | EFFECTIVE | PARTLY EFFECTIVE | NOT EFFECTIVE | MOST EFFECTIVE MATERIALS (choose 3 and rank 1- |
|---|---|---|---|---|---|
| Xiapex Publications (with reprint carriers) | | | | | ☐ |
| Xiapex administration training brochure | | | | | ☐ |
| Website for Xiapex administration training | | | | | ☐ |
| Local live peer to peer Xiapex administration training event | | | | | ☐ |
| Other items (if additio-nal materials were provided, please also describe in question 6) | | | | | ☐ |

**5. HOW EFFECTIVE WERE THE MATERIALS IN PRESENTING THE SAFETY RISKS ASSOCIATED WITH THE USE OF XIAPEX?**

| IDENTIFIED SAFETY RISK | EFFECTIVE | NOT EFFECTIVE |
|---|---|---|
| Risk of corporal rupture (penile fracture) | | |
| Risk of local reactions | | |
| Risk of medication errors | | |
| Potential risk of injury to the urethra, including in patients with hourglass deformities and ventral plaques | | |
| Potential risk for hypersensitivity/anaphylaxis | | |
| Potential risk with injection site bleeding in patients with coagulation disorders including those on concurrent anti-coagulation therapy | | |
| Potential risk for reactions related to cross-reactivity with endogenous human matrix metalloproteinases (including musculoskeletal syndrome and development/exacerbation of autoimmune disorders) | | |

If you answered "not effective" on any of the statements, please comment below.

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**6. IF ANY ADDITIONAL MATERIALS WERE PROVIDED THAT ARE NOT LISTED IN QUESTION 3, PLEASE LIST THEM BELOW, AND DESCRIBE THEIR OVERALL USEFULNESS IN MEETING THE OBJECTIVE OF THIS PROGRAM.** Also, are there any further materials that you think would help to achieve the objective of the program?

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**THANK YOU FOR PROVIDING YOUR VALUABLE INPUT.**

# Appendix 2 Follow-up Survey

## XIAPEX EDUCATION PROGRAM IN PEYRONIE'S DISEASE. FOLLOW-UP SURVEY 6 MONTHS AFTER IMPLEMENTATION

Please complete ALL questions below, and return

By mail:
Medical Information,
Swedish Orphan Biovitrum AB (publ)
SE-11276 Stockholm, Sweden

By fax:
+46 8 697 32 30

By email:
medical.info@sobi.com

Name:

### 1. PLEASE IDENTIFY YOUR COUNTRY

| | | | |
|---|---|---|---|
| Austria ☐ | France ☐ | Lithuania ☐ | Slovenia ☐ |
| Belgium ☐ | Germany ☐ | Luxembourg ☐ | Spain ☐ |
| Croatia ☐ | Greece ☐ | Malta ☐ | Sweden ☐ |
| Cyprus ☐ | Hungary ☐ | Netherlands ☐ | Switzerland ☐ |
| Czech Republic ☐ | Iceland ☐ | Norway ☐ | United Kingdom ☐ |
| Denmark ☐ | Ireland ☐ | Poland ☐ | Other ☐ |
| Estonia ☐ | Italy ☐ | Portugal ☐ | |
| Finland ☐ | Latvia ☐ | Slovakia ☐ | |

### 2. WOULD YOU PLEASE INDICATE YOUR LEVEL OF AGREEMENT WITH THE STATEMENTS BELOW?

| | STRONGLY AGREE | AGREE | DISAGREE | STRONGLY DISAGREE |
|---|---|---|---|---|
| The training package was sufficiently clear and comprehensive to enable me to administer Xiapex with confidence in my practice since the training | | | | |
| The training package was effective in helping me to understand the reconstitution protocol to enable me to administer Xiapex with confidence in my practice since the training | | | | |
| The training package was effective in helping me to understand the administration procedure to enable me to safely administer Xiapex with confidence in my practice since the training | | | | |
| The training package was sufficiently effective in helping me to understand the modelling procedure to enable me to perform and instruct my patients about it with confidence since the training | | | | |

If you answered any of the questions, Disagree, Strongly Disagree please comment below.

Please continue on next page if needed.

(continued from page 1)

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EDUCATIONAL ITEMS

3. HOW EFFECTIVE WERE THE MATERIALS IN PRESENTING THE SAFETY RISKS ASSOCIATED WITH THE USE OF XIAPEX AND THE MEASURES INTENDED TO PREVENT THESE RISKS?

| IDENTIFIED SAFETY RISK | EFFECTIVE | NOT EFFECTIVE |
|---|---|---|
| Risk of corporal rupture (penile fracture) | | |
| Risk of local reactions | | |
| Risk of medication errors | | |
| Potential risk of injury to the urethra, including in patients with hourglass deformities and ventral plaques | | |
| Potential risk for hypersensitivity/anaphylaxis | | |
| Potential risk with injection site bleeding in patients with coagulation disorders including those on concurrent anti-coagulation therapy | | |
| Potential risk for reactions related to cross-reactivity with endogenous human matrix metalloproteinases (including musculoskeletal syndrome and development/exacerbation of autoimmune disorders) | | |
| Making me realize the importance of reporting Adverse reactions in connection with treatment | | |

If you answered "not effective" on any of the statements, please comment below.

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4. IN RETROSPECT, HAVE YOU HAD PATIENTS EXPERIENCING ADVERSE EVENTS THAT WERE NOT DESCRIBED IN THE TRAINING MATERIAL, OR EVENTS THAT COULD HAVE BEEN AVOIDED IF THEY HAD BEEN MORE ACCURATELY DESCRIBED OR WARNED FOR IN THE TRAINING MATERIAL? If so, we ask you to summarize the type of event (s) here (without patient data). We also ask you to report them, as well as all other not yet reported adverse reactions you may have experienced, according to question 6 below.

| DESCRIPTION OF EVENT(S) THAT IS NOT SUFFICIENTLY DESCRIBED IN THE TRAINING MATERIAL AND THEREFORE COULD HAVE BEEN AVOIDED | NUMBER OF PATIENTS | Reported: YES/NO (If NO, please refer to question 6.) |
|---|---|---|
| | | |

5. IN CASE OF OCCURRENCE OF ADVERSE EVENTS OR MEDICATION ERRORS, DO YOU HAVE AN IDEA WHICH PART OF THE EDUCATIONAL MATERIAL SHOULD BE AMENDED TO BE ABLE TO PREVENT THESE EVENTS?

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6. IN CASE YOU HAVE OBSERVED ANY ADVERSE REACTIONS IN RESPONSE TO THE TREATMENT THAT YOU SO FAR HAVE NOT REPORTED, SOBI ASKS YOU TO DO SO ACCORDINGLY:

BY MAIL: drugsafety@sobi.com
OR BY FAX: +46 8 697 32 30

AND TO YOUR LOCAL AUTHORITY IN ACCORDANCE WITH NATIONAL REGULATIONS.

7. IN RETROSPECT, ARE THERE ANY FURTHER MATERIALS OR INSTRUCTIONS THAT YOU THINK WOULD HAVE BEEN HELPFUL TO ENSURE A CONSISTENT COMPREHENSION OF THE SAFE ADMINISTRATION OF XIAPEX IN YOUR CLINIC?

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THANK YOU FOR PROVIDING YOUR VALUABLE INPUT.

# Appendix 3 Consent form - Xiapex Physicians Training Database

Dear Healthcare Provider,

Thank you for requesting training in the administration of Xiapex for patients with Peyronie´s disease.

As agreed with the European Medicines Authority, a database of physicians who have completed the training programme is being maintained to ensure that only those physicians who are appropriately trained in the correct administration of the product and experienced in the diagnosis and treatment of male urological diseases can have access to Xiapex.

As also agreed with the European Medicines Authority, Sobi will assess the effectiveness of the training programme through surveys. You will be asked to complete a questionnaire upon completion of the training programme and a follow-up questionnaire 6 months later.

In order to fulfil this agreement with the EMA, Sobi is requesting your confirmation of the following . Please read this letter, including the terms and conditions, sign and return as below.

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1) By signing below I attest that I have fulfilled the physician training programme requirements by reading the treatment training brochure.

2) As you have completed your training Sobi requires your permission to:
   a. keep your details in a database
   b. track the provision and return of two training questionnaires

**Terms and Conditions:** You agree that your information will be held on a database administered by Sobi and that Sobi may contact you (including by email) in relation to the administration or updating of the database or in relation to any other licence requirement. You also agree that we may use your details to record that you have completed the Xiapex training programme and for the evaluation of the programme. Sobi respect the confidentiality of personal information. Only Sobi, or organisations working with the company in the administration of the above information will have access to your information. It will not be disclosed to any other third parties unless specifically agreed above. Your responses to the questionnairs will be handled anonymously. As Sobi is a global organisation, your information may be transferred within or outside of the European Economic Area (including to the US) where privacy laws may be different to those in the EU. You will at any time have the right to access your information, you can request that your information on the database is amended, or you can withdraw any of the consents that you have given at any time by writing to us at Swedish Orphan Biovitrum AB (publ), att. Medical Information, 112 76 Stockholm, Sweden.

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| | |
|---|---|
| **Name of Physician** | Click here to enter text. |
| **Title** | Click here to enter text. |
| **Specialty** | Click here to enter text. |
| **Institution** | Click here to enter text. |
| **Address** | Click here to enter text. |
| **City** | Click here to enter text. |
| **Post code** | Click here to enter text. |
| **Country** | Click here to enter text. |
| **Telephone number** | Click here to enter text. |
| **Mobile phone number** | Click here to enter text. |
| **e-mail** | Click here to enter text. |

I agree to items 1 and 2 and the associated terms and conditions set out above:

Signed: .....

Date: .....

Print name: .....

Name of practice: .....

Name of institution: .....

**Return to Sobi at the following address**:

Swedish Orphan Biovitrum AB (publ)
Att. Medical Information
112 76 Stockholm, Sweden

**OR scan/email OR fax this form to:**

medical.info@sobi.com
fax: +46 8 697 2330

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Yours sincerely,

SOBI AB