Revised Protocol of Non-Interventional Study (NIS)

Drug Substance	SEROQUEL® /XR
Study Code	D1443C00057
Edition Number	3
Date	[redacted]

A Multinational, Multicenter, Retrospective, Observational Drug Utilisation Study of Seroquel® Extended Release (XR) Prescribed by Psychiatrists as Treatment for Major Depressive Disorder (MDD) in Selected Countries in the European Union (EU)

Sponsor: AstraZeneca LP. [redacted]

The following Amendment(s) and Administrative Changes are included in this revised protocol:

Amendment No.	Date of Amendment	Local Amendment No.	Date of local Amendment
1	[redacted]		
2	[redacted]		

Administrative change No.	Date of Administrative Change	Local Administrative change No.	Date of local Administrative Change

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LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

The following abbreviations and special terms are used in this study Non-interventional Study Protocol.

Abbreviation or special term	**Explanation**
AE	Adverse event
CHMP	Committee for Medicinal Products for Human Use
CRF	Case Report Form (electronic/paper)
EC	Ethics Committee, synonymous to Institutional Review Board (IRB) and Independent Ethics Committee (IEC)
EU	European Union
GCP	Good Clinical Practice
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
MHC	Mental Health Centers
MDD	Major Depressive Disorder
PASS	Post Authorization Safety Surveillance
PHARMO	Institute for Drug Outcomes Research
PI	Principal Investigator
SAE	Serious adverse event
WBDC	Web Based Data Capture
WHO	World Health Organization
XR	Extended Release

1. INTRODUCTION

The study design presented in this non-interventional study protocol will provide an evaluation of the characteristics of patients under specialist (psychiatrist) care receiving Seroquel XR as treatment for MDD. The study will also summarize data on prescribing and drug utilisation of therapeutic regimens used to treat MDD that include Seroquel XR, and document any differences in prescribing patterns between the countries included in the study. This study will be conducted in 5 European Union countries representing different geographic regions.

1.1 Study objectives

The study objectives include:

- documenting characteristics of patients under specialist (psychiatric) care who are prescribed Seroquel XR as treatment for MDD in each of the selected countries over a 9 month period, starting 3 months following the launch of the product for its approved indication.

- describing the differences between countries concerning treatment practices involving use of Seroquel XR through the use of a drug utilisation questionnaire of psychiatrist in 5 European countries.

2. STUDY DESIGN

This non-interventional study protocol has been subject to a peer review according to AstraZeneca standard procedures.

2.1 Overall study design

This is a multinational, multicenter, retrospective, observational study of antidepressant drug utilisation among an inception cohort of patients under specialists (psychiatrists) care who are prescribed Seroquel XR for treatment of major depressive episodes associated with MDD following launch of the indication in each country. The study will be conducted in 5 European countries: Germany, Italy, Romania, Spain, and Sweden to ensure geographic representation across European member states. The sponsor may include alternate EU country(ies) based upon limited use of Seroquel XR for MDD in the countries listed and whose selection will maintain geographic representation among EU countries.

The inception cohort is defined as patients initiating Seroquel XR (as add-on therapy or as monotherapy) during a 9 month period corresponding to 3 to 12 months following the launch of the product in each country for the MDD indication. In the period immediately after launch, physicians may not be aware of the approval of Seroquel XR for add-on treatment for MDD. Therefore, patients treated with Seroquel XR within the 3 months after launch will not be included in the inception cohort because they are not likely to be representative of patients

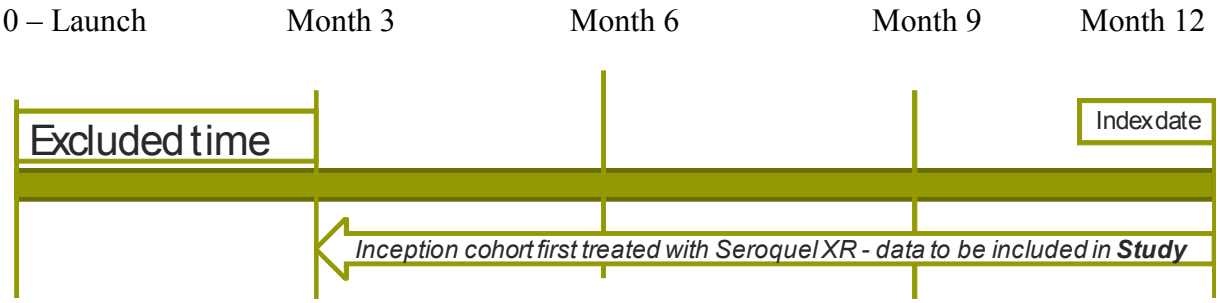
treated in subsequent periods. A drug utilisation questionnaire will be used to collect study data. Data collection will be initiated following a study-defined index date, approximately 12 months after product launch. All study sites within a country will be assigned the same index date and will not be contacted prior to the index date.* Initiation of site-specific activities for selection of patient records meeting study selection criteria will commence on or following the index date. Data on drug utilisation will be censored on the index date. This approach will ensure that study procedures do not influence prescribing practices.

2.1.1 Sampling Design

Sampling to identify patients will follow a two-step process. Study sites and investigators will be selected in the first step and individual patients in the second.

A sample of psychiatry practices within a country will be selected to reflect the overall distribution of practice settings in that country. This approach permits the inclusion of patients prescribed Seroquel XR by physicians practicing across different care settings where the medical management of MDD might differ.

Figure 1 – Overall Study Design



Note - In the period immediately after launch, physicians may not be aware of the approval of Seroquel XR for add-on treatment for MDD. Therefore patients treated with Seroquel XR within the 3 months after launch will not be included in the inception cohort because they are not likely to be representative of patients treated in subsequent cohorts.

* Local ethics approval for this protocol will be obtained prior to study start and prior to the study-defined index date.

3. SITE AND PATIENT SELECTION CRITERIA

3.1 Site and Investigator Selection

MDD patients may seek psychiatric care in a variety of settings, including mental health centers (MHC), university-affiliated hospitals, community hospitals, and in private practice settings. The distribution of psychiatry practice settings by country is expected to approximate the data provided in Table 1. Additional information on the settings of specialist care for MDD patients in each country will be obtained through consultation with Science Advisory Board Members. Any advice and updated information on the distribution of practice settings will be considered in investigational site recruitment in each country.

Approximately 25 sites/investigators will be selected in each country to permit the selection of MDD patients that are broadly representative of the overall MDD population.

Table 1 Distribution of Psychiatry Practice Settings by Country

Country	Number of Psychiatrists	MHC	Private Practice	University Hospital	Community Hospital
Germany	6040	N/A	40%	30%	30%
Spain	5782	41%	7%	36%	16%
Sweden	2196	45%	10%	45%	N/A
Italy	9117	40%	10%	20%	20%
Romania	1013	60%	10%	30%	N/A

Source for estimated number of psychiatrists (except Sweden and Romania): IMS. Sources for Sweden and Romania: WHO Report Policies and practices for mental health in Europe: meeting the challenges, 2008, xiii and The World Bank population statistics. The distribution of psychiatry practice settings was derived through disease-specific surveys, panels of independent scientific advisors for other neuroscience studies conducted by AstraZeneca, and based upon the literature. Based upon feedback from Science Advisory Board Members the proportion of patients treated for MDD could differ from the distribution of psychiatry practice settings provided in Table 1.

Investigators who have participated in the Seroquel XR clinical development program for MDD will be excluded from participation in this study.

3.2 Patient Selection

Each investigator will identify patients who meet criteria as having received SEROQUEL XR for MDD at any time in the 3-12 month period following launch in each country, and contact the patients to obtain informed consent. A listing of subjects will be generated according to patients' last name (or other convenient identifier).

Up to 30 subjects will be selected per site. The selection of eligible patients will proceed as follows:

1. For sites with 30 or fewer eligible patients, all will be included, provided that informed consent is given where required.

2. For sites with more than 30 eligible patients, random selection to assure lack of bias in the selection of 30 patients will be accomplished using an algorithm provided by AstraZeneca. Informed consent will be obtained to provide up to a maximum of 30 selected patients.

The limit of 30 patients per site is proposed to support the objective of having adequate representation of patients within a given country.

Site specific activities related to the selection of patient records will start on or following the index date. This approach should ensure that selection of patients will not be influenced by prescribing practices prior to the index date and prescribing practices are not influenced by study procedures.

If the number of eligible patients refusing to take part in the study exceeds 20% of the total sample in a country, readily identifiable basic demographic information (age range and gender) from patients refusing to participate will be requested and collated. This will permit an evaluation of the distribution of non-participants across sites and countries.

3.3 Inclusion and Exclusion Criteria for Patients and Investigators

Each patient and investigator should meet all inclusion criteria and none of the exclusion criteria for this study. Under no circumstances can there be any exceptions to this rule.

3.3.1 Inclusion Criteria for Patients

1. Provision of informed consent before initiation of any collection of questionnaire data.

2. Female and male aged 18 years and over.

3. Documented clinical diagnosis of Major Depressive Disorder, Single Episode, or Recurrent.

4. Initiation of Seroquel XR for treatment of MDD during the period defining the inception cohort, i.e. from 3 months after launch until the index date.

The prescription of the medicinal product is clearly separated from the decision to include the patients in the study.

3.3.2 Exclusion criteria for Patients

If participating in any clinical trial during the time from 3 months after launch until the index date, the patient cannot take part in this study.

3.3.3 Exclusion Criteria for Investigators

Investigator must not be or must not have been an employee of AstraZeneca or participated as an investigator in the Seroquel XR clinical program for MDD.

4. STUDY CONDUCT

4.1 Questionnaire Validation Plan

In order to effectively evaluate the drug utilisation questionnaire prior to implementation, questionnaire validation will be implemented with a sample of psychiatrists and pilot testing of the questionnaire will be performed. Face validity assessment and pilot testing will be done in a single language.

4.1.1 Face Validity

Prior to administering the questionnaire, an evaluation by two practicing psychiatrists will be performed. The purpose of this evaluation will be to determine whether there are any items that are not readily understood or where the response requested may be misinterpreted. Face validity will be assumed if ≤5% of items on the questionnaire are flagged as problematic by both psychiatrists.

4.1.2 Pilot Testing

Pilot testing of the questionnaire is intended to test the instrument's utility and the methods employed for abstraction of data in different practice settings. Pilot testing of the questionnaire will be conducted in multiple sites that are representative of practice settings. The pilot testing will be performed using different sites/investigators than those participating in this study. Sites included in pilot testing are contacted on a separate time schedule than those in this study to ensure that any modifications required are completed and tested prior to the start of this study.

The pilot testing will consist of the completion of the questionnaire for up to 20 patients. In conjunction with the local Ethics Committee the requirements for collection of Informed Consent during the pilot testing of the questionnaire will be determined.

AstraZeneca may update the drug utilization questionnaires based on pilot study results and recommendation of the Scientific Advisory Board.

4.1.3 Translation of the drug utilisation questionnaire

Translation will be done after the validation of the questionnaire. All translations to the respective languages will be done using forward and backward translations.

4.2 Questionnaire Administration

4.2.1 Timeline for questionnaire administration

The exact index date for each country will be selected to optimise preparations leading to completion of drug utilisation questionnaires at all sites within a country following Good Pharmacoepidemiology Practices (PDS 2008).

Contact with investigators and site preparatory activities are initiated following the index date, which will correspond to a date approximately 12 months following the launch of Seroquel XR for MDD in each country.

Preparatory activities for completion of the drug utilisation questionnaires at each site will rely on automated and manual review of data from patient medical records in order to identify patients meeting study inclusion criteria. This selection includes consideration of the inception cohort definition (i.e., initiation of treatment with Seroquel XR in the time interval 3 months after launch up to the index date).

Once site preparatory activities are concluded, including the obtaining of informed consent from the patient, data abstraction of patient medical records using the drug utilisation questionnaire will begin.

Information on the Physician questionnaire related to physician characteristics will be completed based upon the best available recollection by the investigator. Patient questionnaire data will be abstracted from the medical records of the patients maintained at the official location for storage of records for the site/investigator and will be performed by a representative of AstraZeneca.

4.2.2 Key Variables - Psychiatrists, Subjects, and Drug Utilisation

The drug utilisation questionnaire is constructed to collect key variables on characteristics of physicians, patients and the drugs utilised in the medical management of depressive episodes in MDD where the treatment regimen includes Seroquel XR.

Information on participating psychiatrists will include:

- location of practice (i.e., country, region, and city or town)
- age
- gender
- years in practice
- practice setting (i.e., mental health clinic, university-affiliated hospital, community hospital, private practice office, other)
- proportion of patient volume in hospital versus non-hospital

- approximate proportion of patients with a diagnosis of MDD in their practice

Information on patients will include:

- demographics (date of birth, gender, race)
- source and reason for referral of the patient
- general medical and psychiatric history (i.e., date of first depressive episode, start date of most recent depressive episode, month and year of diagnosis of MDD, total number of depressive episodes over lifetime, number of depressive episodes during the 12 months up to the latest consultation, presence of psychotic symptoms in the past, psychiatric co-morbidities (anxiety disorders, substance use, other Axis I, or other Axis II disorder), other medical co-morbidities (i.e., hypertension, obesity, diabetes, other cardiovascular), ever been hospitalised for a psychiatric condition, ever hospitalised for MDD, and whether hospitalised during most recent depressive episode)

Information on drug utilisation will include, where recorded:

- treatment history including details on current and past drug treatments for MDD (including Seroquel XR) within the past 12 months (historical information based on patient reported drug use may be required if physician has been treating the patient for < 12 months), dose/duration of drugs used to treat MDD (including any drug treatments for MDD noted in the patient's medical record that were prescribed by other physicians), including changes in medication, date of initiation/end for each drug; and whether drug treatments for MDD prescribed with Seroquel XR were still prescribed on the index date; for Seroquel XR treatment details include frequency of prescriptions by dose, prescribed days supply by dose, initial dose, usual (modal) dose, maximum dose
- diagnosis for which Seroquel XR is being prescribed
- number of visits to the psychiatrist during the timeframe that Seroquel XR has been prescribed
- Presence of psychotic symptoms at time of prescription of Seroquel XR
- Clinical Global Impression of the patient prior to initiation of Seroquel XR

Data will be collected either via a paper questionnaire for completion by the treating psychiatrist, or be extracted from medical records or related records by AstraZeneca representative using an electronic Case Report Form (eCRF).

The Questionnaire designed for collecting Physician and Patient-level data are provided in Appendix B. The Patient-level questionnaire may be revised based upon the findings of the pilot study and the recommendations of the Scientific Advisory Board.

4.3 Role of scientific advisory board

A board comprised of independent, external psychiatrists from each of the participating EU countries will provide scientific support to AstraZeneca.

The scope of the services will include:

- Provide scientific advice regarding the protocol and conduct of the study
- Ensure that the selected population included in the study are representative of the distribution in each country

5. SAMPLE SIZE AND PRECISION

Data will be collected from a total of 100-400 patients per country. As a questionnaire will be used to collect the data, the precision around responses is further discussed.

The proportion of patients prescribed a specified daily dose of Seroquel XR is of particular interest. The PHARMO Report (Institute for Drug Outcomes Research) Part 1 described the distribution of doses of Seroquel XR prescribed to individuals in the Netherlands. The proportion of patients taking Seroquel XR at various dose levels varied from 1% to 67%. The 95% confidence interval for the estimate of a proportion can be calculated for a general situation (i.e., and as applied in this study, the proportion of patients receiving a given dose of Seroquel XR in the sample from each country); for sample sizes of 100, 200, 300 and 400 is provided in Table 2.

Sample sizes of 100-400 patients will provide reasonable precision for a wide range of the estimated proportions of patients receiving a given dose of Seroquel XR in a given country.

Table 2 Precision of Estimated Proportions for a Sample Size of 100 to 400 (2-sided 95% Confidence Intervals)

Estimated Proportion	Sample size = 100	Sample size = 200	Sample size = 300	Sample size = 400
6%	(1.3%,10.7%)	(2.7%,9.3%)	(3.3%,8.7%)	(3.7%,8.3%)
11%	(4.9%,17.1%)	(6.7%,15.3%)	(7.5%,14.5%)	(7.9%,14.1%)
16%	(8.8%,23.2%)	(10.9%,21.1%)	(11.9%,20.1%)	(12.4%,19.6%)
21%	(13%,29%)	(15.4%,26.6%)	(16.4%,25.6%)	(17%,25%)
26%	(17.4%,34.6%)	(19.9%,32.1%)	(21%,31%)	(21.7%,30.3%)

31%	(21.9%,40.1%)	(24.6%,37.4%)	(25.8%,36.2%)	(26.5%,35.5%)
36%	(26.6%,45.4%)	(29.3%,42.7%)	(30.6%,41.4%)	(31.3%,40.7%)
41%	(31.4%,50.6%)	(34.2%,47.8%)	(35.4%,46.6%)	(36.2%,45.8%)
46%	(36.2%,55.8%)	(39.1%,52.9%)	(40.4%,51.6%)	(41.1%,50.9%)
51%	(41.2%,60.8%)	(44.1%,57.9%)	(45.3%,56.7%)	(46.1%,55.9%)
56%	(46.3%,65.7%)	(49.1%,62.9%)	(50.4%,61.6%)	(51.1%,60.9%)
61%	(51.4%,70.6%)	(54.2%,67.8%)	(55.5%,66.5%)	(56.2%,65.8%)
66%	(56.7%,75.3%)	(59.4%,72.6%)	(60.6%,71.4%)	(61.4%,70.6%)
71%	(62.1%,79.9%)	(64.7%,77.3%)	(65.9%,76.1%)	(66.6%,75.4%)
76%	(67.6%,84.4%)	(70.1%,81.9%)	(71.2%,80.8%)	(71.8%,80.2%)
81%	(73.3%,88.7%)	(75.6%,86.4%)	(76.6%,85.4%)	(77.2%,84.8%)

5.1 Measures to Minimize Bias

A number of measures will be implemented to ensure the completion of the drug utilisation questionnaire is conducted in a systematic, professional, and unbiased manner:

- The drug utilisation questionnaire will be evaluated through pilot testing of the questionnaire with medical records of psychiatrists treating MDD patients to ensure that questions are understood, and not ambiguous or misleading
- Programming of the Electronic Data Capture version of the questionnaire (eCRF) will be reviewed by a quality control process and simulation prior to implementing the questionnaire
- Standard scripts will provide consistent instruction on completion of the questionnaire
- All individuals performing abstraction of data from medical records will be trained on appropriate data abstraction techniques
- Physicians who participated as an investigator for the Seroquel XR clinical development program for MDD will not be eligible to participate

6. ETHICAL AND REGULATORY REQUIREMENTS

6.1 Ethical conduct of the study

The Study will be performed in accordance with ethical principles that are consistent with the Declaration of Helsinki, ICH GCPs and the applicable legislation on Non-Interventional Studies.

The Investigator will perform the study in accordance with the regulations and guidelines governing medical practice and ethics in the country and in accordance with currently acceptable techniques and know-how.

6.1.1 Ethics review

The final protocol of the Study, including the final version of the Subject Informed Consent Form, must be approved or given a favourable opinion in writing by the Ethics Committee.

The Ethics Committee must also approve any amendment to the protocol, according to local regulations.

6.2 Subject data protection

The Subject Informed Consent Form will incorporate wording that complies with relevant data protection and privacy legislation. Pursuant to this wording, subjects will authorise the collection, use and disclosure of their personal data by the Investigator and by those persons who need that information for the purposes of the study.

The Subject Informed Consent Form will explain that study data will be stored in a computer database, maintaining confidentiality in accordance with the local law for Data Protection.

The Subject Informed Consent Form will also explain that a monitor of AZ or a monitor of company representing AZ, will require direct access to the signed subject informed consent forms. The Subject Informed Consent Form will explain that for data verification purposes, monitor will require direct access to source documents that are part of the hospital or practice records relevant to the Study.

6.3 Informed consent

Principal Investigator(s) at each site will:

- Ensure each patient is given full and adequate oral and written information about the nature, purpose, possible risk and benefit of the study
- Ensure each patient is notified that they are free to discontinue from the study at any time
- Ensure each patient is given the opportunity to ask questions and allowed time to consider the information provided
- Ensure each patient provides signed and dated informed consent before collecting any data from the patient's record
- Ensure the original, signed Informed Consent Form(s) is/are stored in the Investigator's Study File
- Ensure a copy of the signed Informed Consent Form is given to the subject

- Ensure that the provision of anything of value to the patients who participate in the study as well as any provisions for subjects harmed as a consequence of study participation are described in the informed consent form that is approved by an Ethics Committee

6.4 Changes to the protocol and informed consent form

If there are any substantial changes to the study protocol, then these changes will be documented in a study protocol amendment and where required in a new version of the study protocol.

The amendment should be approved by each Ethics Committee and if applicable, also the national regulatory authority, before implementation. Local requirements should be followed for revised protocols.

AstraZeneca will distribute any subsequent amendments and new versions of the protocol to each Principal Investigator.

If a protocol amendment requires a change to a site's Informed Consent Form, AstraZeneca and the site's Ethics Committee should approve the revise Informed Consent Form before the revised form is used.

If local regulations require, any administrative change will be communicated to or approved by each Ethics Committee.

6.5 Audits and inspections

Authorized representatives of AstraZeneca, a regulatory authority, or an Ethics Committee may perform audits or inspections at the site, including source data verification. The purpose of an audit or inspection is to systematically and independently examine all study-related activities and documents, to determine whether these activities were conducted, and data were recorded, analysed, and accurately reported according to the protocol, GCP, guidelines of the ICH, and any applicable regulatory requirements. The investigator will contact AstraZeneca immediately if contacted by a regulatory agency about an inspection at the site.

7. STUDY MANAGEMENT BY ASTRAZENECA

7.1 Pre-study activities

Before the first patient is selected for the study and retrospective data are abstracted, it is necessary for a representative of AstraZeneca to visit the investigational study site to:

- Determine the nature of the medical records storage retrieval
- Determine availability of appropriate patients for the study

- Discuss with the investigator(s) (and other personnel involved with the study) their responsibilities with regard to protocol adherence, and the responsibilities of AstraZeneca or its representatives.

7.2 Training of study site personnel

Before the first patient is entered into the cohort, an AstraZeneca representative will review and discuss the requirements of the protocol and related documents with the investigational staff and also train them in any specific procedures.

The Principal Investigator will ensure that appropriate training relevant to the study is given to all of these staff, and that any new information relevant to the performance of this study is forwarded to the staff involved.

The Principal Investigator will maintain a record of all individuals involved in the study.

7.3 Monitoring of the study

During the study, an AstraZeneca representative will have regular contacts with the study site including visits to:

- Provide information and support to the investigator(s)
- Confirm that the investigational team is adhering to the protocol, that data are being accurately collected and recorded in the physician part of the questionnaire
- Ensure that the subject informed consent forms are signed and stored at the investigator site
- Extract patient data from subject's medical records or other records relevant to the study, using questionnaire in the eCRF. This will require direct access to all original records for each subject (i.e., clinic charts)
- Perform source data verification (a comparison of the data in the questionnaire with the subject's medical records at the hospital or practice, and other records relevant to the study). This will require direct access to all original records for each subject (i.e., clinic charts).

The AstraZeneca representative will be available between visits if the investigator or other staff at the site need information and advice about the study conduct.

8. DATA MANAGEMENT

8.1 Collection, monitoring, processing of data and archiving

The investigator will complete the physician part of the drug utilisation paper questionnaire. The monitor will visit the site to extract data from the completed physician questionnaires.

The monitor will have direct access to medical records and other related information for consented study patients. Patient drug utilization data will be entered in the study eCRF by the monitor at the Investigator's site.

Data entered in the eCRF system will be immediately saved to a central database and changes tracked to provide an audit trail. When data have been entered reviewed and edited, data will be locked to prevent further editing. A copy of the e-CRF will be archived at the Investigator's site.

The data will be manually reviewed and queries raised as appropriate to correct inconsistencies or errors. Medical history and medications will be coded using relevant dictionaries.

8.2 Reporting and publication of data

AstraZeneca is obliged to analyse and report all study data as described in the protocol.

In accordance with the Declaration of Helsinki, both authors and publishers have ethical obligations. In publication of the results of the study, the authors are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. AstraZeneca endeavours to publish the results of study and is committed to ensure that the data are reported in a responsible and coherent manner.

9. ANALYSIS

Data obtained from the drug utilisation questionnaire will be reported descriptively. No statistical comparison will be conducted. Summary statistics will be provided. There will be no imputation for any missing values. For continuous variables, the number of responses, mean, median, minimum, maximum, and standard deviation will be provided. For discrete variables, the number of responses and proportion represented by each category will be summarized. Prescribing practices and drug utilisation data will be reported by country permitting comparisons across countries.

9.1 Participating psychiatrists data

Number of participating psychiatrists, and their age, gender, years in practice, practice setting, psychiatric patient volume, approximate proportion of patients with a diagnosis of MDD in their practice will be summarized descriptively by country and overall.

9.2 Patient's demographic data and psychiatric history

Summary statistics will be provided by country and overall for patient's demographics data including age, gender, and race, and for patient's medical history including years since first depressive episode, year of MDD diagnosis, number of depressed episodes over lifetime, number of depressive episodes during the 12 months up to the latest consultation, presence of psychotic symptoms in the past, presence of psychotic symptoms at start of Seroquel XR

treatment, psychiatric co-morbidities (anxiety disorders, substance use, other Axis I, or other Axis II disorder), other medical co-morbidity (hypertension, obesity, diabetes, other cardiovascular disorder), ever been hospitalised for a psychiatric condition), as well as for the number of visits to the psychiatrist during the timeframe that Seroquel XR has been prescribed.

9.3 Seroquel XR utilisation

At the time of initiation of Seroquel XR, the diagnosis for which Seroquel XR was prescribed, whether the patient was experiencing psychotic symptoms, Clinical Global Impression, the initial daily dose of Seroquel XR prescribed and any concomitant antidepressant drug(s) and dose(s) prescribed will be summarized descriptively by country and overall.

The last prescribed daily dose prior to the index date, the maximum daily dose prescribed, modal daily dose, and the duration for each dose of Seroquel XR as prescribed will be summarized descriptively by country and overall.

Doses described above will be summarized in two ways.

- As continuous variable: the following will be calculated: number mean, mode, median, minimum, maximum, and standard deviation

- As a categorical variable: number and % of patients will be provided for each of the following dose levels: 50 mg, 100 mg, 150 mg, 300 mg and other.

9.4 Other drug utilisation for MDD

The following will be summarized for treatments other than Seroquel XR for MDD the daily dose at the first initiation, whether a dose change accompanied initiation of Seroquel XR, latest dose following Seroquel XR initiation, interval from initiation of Seroquel XR to latest dose change and whether the prescription was continuing on the index date.

10. SAFETY EVENT REPORTING

10.1 Safety Reporting for Investigators

Due to the non-interventional and retrospective design of this drug utilisation study, adverse event (AE), serious adverse event (SAE) and other safety data are not proactively collected. Instead investigators should report any adverse events noted during routine medical practice according to the standard spontaneous reporting procedures for marketed products in their country. The questionnaire associated with this study should not be used to record or report adverse event data.

If there are any questions regarding AE and SAE reporting obligations, the local AstraZeneca representative should be contacted.

11. LIST OF REFERENCES

PDS 2008
ISPE. Good Pharmacoepidemiology Practices. Pharmacoepidemiology and Drug Safety 2008: 17: 200-208.

PHARMO Report
PHARMO Institute. Seroquel compared to other antipsychotics. Part A: Drug utilisation study as pre-study for design of safety study. Version 2.0, May 2010.

WHO Report
WHO Report – Policies and practices for mental health in Europe: meeting the challenges 2008, xiii.

Revised Protocol of Non-Interventional Study (NIS)
Appendix A

Drug Substance	SEROQUEL® XR
Study Code	D1443C00057
Edition Number	2
Date	[redacted]
Protocol Dated	[redacted]

Appendix A
Signatures

ASTRAZENECA SIGNATURE(S)

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This Non-Interventional Study Protocol and all Amendments to the Non-Interventional Study Protocol have been subjected to an internal AstraZeneca peer review.

I agree to the terms of this revised protocol.

AstraZeneca Research and Development site representative

[redacted]

[redacted]

Date
(Day Month Year)

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Revised Protocol of Non-Interventional Study (NIS)
Appendix B

Drug Substance	SEROQUEL® XR
Study Code	D1443C00057
Edition Number	3
Date	[redacted]

Appendix B
Drug Utilisation Questionnaire

Doctor Information – MDD Survey

Instruction for completion: The following are general questions about you and your practice. Please answer to the best of your knowledge.

General Demographics

What country do you practice in?

_____

What region do you practice in?

_____

What city or town do you practice in?

_____

What is your gender?
☐ Male
☐ Female

What is your year of birth?

_ _ _ _

How long have you been in practice as a medical doctor?
_ _ years

How long have you been working in your current speciality?
_ _ years

Practice Details

If you now think about the practice from which you are selecting patient records for this study:

How would you describe the location from which you are selecting patient records for this study?
Select one answer only.
☐ Urban centre
☐ Suburban
☐ Rural

Please select out of the following options the one that best describes this setting:
Select one only.
☐ General Hospital (public & private)
☐ University Hospital
☐ Mental health centre
☐ Other open care facilities (ambulatory, out-patient clinic, community clinic)
☐ Private office
☐ Mixed (hospital & office/community/clinic):
☐ Other – Please specify

In this setting, what proportion of patients are diagnosed with MDD _ _ _%

What proportion in this setting are in-patients?
_ _ _%

The following two questions are to be answered for physician practices that are based in a hospital setting:

Could you specify the total number of hospital beds in the hospital where you spend the majority of your time?
_ _ _ _ beds

Could you specify the number of beds that are dedicated to psychiatry?
_ _ _ beds

Location of Medical Record

Please select the location that the patient's medical record for this study is from:
☐ outpatient clinic or private practice
☐ hospital or in-patient setting
☐ other specify:

Patient Form – MDD Survey - To be completed by data extraction monitor unless indicated as 'Investigator Assessment'

Instructions for completion: Please respond to the following questions about patients prescribed Seroquel XR treatment for MDD at any time between *date 1 and date 2 [INDEX DATE].* Additional detailed instructions provided in other sections of this questionnaire.

General Patient Demographics

What is the patient's month and year of birth?
_ _ / _ _ _ _
mo / year

What is the patient's gender?
☐ Male
☐ Female

What is the patient's height?
_ _ _ cm
☐ Unknown

If you have specified a height for this patient, has it been:
☐ Measured?
☐ Estimated?
☐ Not specified?

What was the patient's weight at the visit closest to *date 1 (date 1 = 9 months prior to [INDEX DATE])*
_ _ _ kg
☐ Not specified?

Date that weight was:
☐ measured?
☐ reported by patient ?
☐ not specified?
_ _ / _ _ / _ _ _ _
day / mo / year

What is the race of this patient?
☐ White
☐ Black
☐ Asian
☐ Other (including native people or mixed races) – please specify _____
☐ Not specified

Referral Pathways

When did the investigator see this patient for the first time?
_ _ / _ _ _ _ (month / year)
mo / year

Who referred this patient to the investigator?
Please select one answer only
☐ Primary care physician
☐ Another psychiatrist (in-patient)
☐ Another psychiatrist (out-patient)
☐ Law enforcement
☐ Family member
☐ Accident & emergency
☐ Social services
☐ Self-referral
☐ Other – please specify _____

Why was this patient referred to the investigator?
Please select all that apply
☐ Specific need for psychiatric care
☐ Access to specific treatments
☐ Severity of MDD
☐ Concomitant disorders / complexity of psychiatric state
☐ Other – please specify _____

Medical/Psychiatric History

In the table below, please record if, according to the medical record, the patient has ever reported/experienced any of the following concomitant disorders? *Please select all that apply*
Has the patient received **drug treatment** (in the past or current) for any of these conditions?
Please select all that apply

	Ever Experienced	If experienced, is the condition past /current Circle all that apply?	Received Drug treatment (in the past)	Receiving Drug treatment (currently)
Anxiety disorder(s)	Yes / No / Unknown	Past / Current	Yes / No / Unknown	Yes / No / Unknown
Alcohol abuse	Yes / No / Unknown	Past / Current	Yes / No / Unknown	Yes / No / Unknown
Nicotine use	Yes / No / Unknown	Past / Current	Yes / No / Unknown	Yes / No / Unknown
Illicit substance abuse	Yes / No / Unknown	Past / Current	Yes / No / Unknown	Yes / No / Unknown
Other Axis 1	Yes / No / Unknown Please specify 1) _____ 2) _____ 3) _____	 Past / Current Past / Current Past / Current	 Yes / No / Unknown Yes / No / Unknown Yes / No / Unknown	 Yes / No / Unknown Yes / No / Unknown Yes / No / Unknown
Other Axis 2	Yes / No / Unknown Please specify 1) _____ 2) _____ 3) _____	 Past / Current Past / Current Past / Current	 Yes / No / Unknown Yes / No / Unknown Yes / No / Unknown	 Yes / No / Unknown Yes / No / Unknown Yes / No / Unknown
Hypertension	Yes / No / Unknown	Past / Current	Yes / No / Unknown	Yes / No / Unknown
Obesity	Yes / No / Unknown	Past / Current	Yes / No / Unknown	Yes / No / Unknown
Dyslipidemia	Yes / No / Unknown	Past / Current	Yes / No / Unknown	Yes / No / Unknown
Other cardiovascular	Yes / No / Unknown Please specify 1) _____ 2) _____ 3) _____	 Past / Current Past / Current Past / Current	 Yes / No / Unknown Yes / No / Unknown Yes / No / Unknown	 Yes / No / Unknown Yes / No / Unknown Yes / No / Unknown
Diabetes	Yes / No / Unknown	Past / Current	Yes / No / Unknown	Yes / No / Unknown

Diagnosis of MDD

What was the date of the **1st depressive episode** experienced by this patient (if known)?
_ _ / _ _ _ _
mo / year
☐ Unknown

What was the date of **diagnosis of MDD**?
_ _ / _ _ _ _
mo / year
☐ Unknown

Who initially diagnosed this patient with MDD?
Please select one answer only
☐ The investigator
☐ Another psychiatrist
☐ Primary care physician
☐ Other specialist – please specify _____
☐ Unknown

How many **depressive episodes** has this patient experienced in his / her lifetime?
☐ 0
☐ 1
☐ 2
☐ 3 or more
☐ Unknown

How many depressive episodes has this patient suffered in the **12 months up to the latest consultation**?
☐ 0
☐ 1
☐ 2
☐ 3 or more
☐ Unknown

When did the last depressive episode (prior to the *INDEX DATE*) start?
_ _ / _ _ _ _
mo / year
☐ Unknown

Has this patient ever been hospitalised for **any** psychiatric condition(s)?
☐ Yes, please specify _____
☐ No
☐ Unknown

In the table below, please specify if this patient has ever been hospitalised for MDD?

Ever Hospitalised for MDD	Number of hospitalisations for MDD
☐ Yes ☐ No ☐ Unknown	____ (no. of times)

What is the date of the most recent hospitalisation for MDD?
_ _ / _ _ _ _
mo / year
☐ Unknown

How long was the patient hospitalised for?
_ _ _ days
☐ Unknown

In the table below, please specify if, according to the medical record, whether this patient has experienced psychotic episodes? Has this patient experienced psychotic manifestation in the last depressive episode?

Ever experienced psychotic symptoms during a depressive episode?	Experienced during the last depressive episode?
☐ Yes ☐ No ☐ Unknown	☐ Yes ☐ No ☐ Unknown

MDD Treatment

This section is dedicated to recording **drug treatments** received by this patient for his / her MDD in the **12 months up to *[INDEX DATE]***.

In the table below, please list **ALL drug treatments for MDD that started and ended before the initiation of Seroquel XR** received by the patient in the 12 months up to *[INDEX DATE]*. ***Please include any drug treatments for MDD noted in the patient's medical record that were prescribed either by the investigator or by other physicians.*** Also, for each drug treatment, please specify information on start and end date and dosing. Please record **all changes in dose** as separate line entries.

(1) Specific drug name *(generic or brand names)*	**(2)** Start date *(day/mth/year)* *Check for "on demand" or prn use*	**(3)** End Date *(day/mth/year)*	**(4)** Dose *(specify Unit)*
	_ _/_ _/_ _ _ _ ☐ prn	_ _/_ _/_ _ _ _	_____
	_ _/_ _/_ _ _ _ ☐ prn	_ _/_ _/_ _ _ _	_____
	_ _/_ _/_ _ _ _ ☐ prn	_ _/_ _/_ _ _ _	_____
	_ _/_ _/_ _ _ _ ☐ prn	_ _/_ _/_ _ _ _	_____
	_ _/_ _/_ _ _ _ ☐ prn	_ _/_ _/_ _ _ _	_____
	_ _/_ _/_ _ _ _ ☐ prn	_ _/_ _/_ _ _ _	_____

In the table below, please list **ALL drug treatments for MDD** that were **prescribed concurrently with Seroquel XR** (including Seroquel XR) received by the patient in the 12 months up to *[INDEX DATE]*. ***Please include any drug treatments for MDD noted in the patient's medical record that were prescribed either by the investigator or by other physicians.*** Also, for each drug treatment, please specify information on start and end date (if applicable), dosing and dates of dose changes.

For Seroquel XR prescriptions, please record **all changes in dose** as separate line entries using columns **(1) – (4)**.

Instructions: Please answer these questions for **ALL drug treatments for MDD that were prescribed *by the investigator or other physicians* concurrently with Seroquel XR** For **Seroquel XR**, please record all changes in dose as separate line entries				**Instructions:** Please answer these questions only for **drug treatments for MDD that were prescribed *by the investigator or other physicians* concurrently with Seroquel XR**		
(1) Specific drug name *(generic or brand names)*	**(2)** Start date *(day/mth/year Check for "on demand" or prn use)*	**(3)** End Date *(day/mth/year)*	**(4)** Dose *(specify Unit)*	**(5)** Did the dose change at **<u>initiation of Seroquel XR?</u>**	**(6)** Most recent dose prior to *[INDEX DATE]* *(if different than at initiation)*	**(7)** Date of most recent dose change *(day/mth/year)*
	_ _/_ _/_ _ _ _ ☐ prn	_ _/_ _/_ _ _ _ ☐ Still prescribed at *[INDEX DATE]*	__________	☐ Increase ☐ Decrease ☐ Remained the same ☐ Not applicable	__________ ☐ Not applicable	_ _/_ _/_ _ _ _ ☐ Not applicable
	_ _/_ _/_ _ _ _ ☐ prn	_ _/_ _/_ _ _ _ ☐ Still prescribed at *[INDEX DATE]*	__________	☐ Increase ☐ Decrease ☐ Remained the same ☐ Not applicable	__________ ☐ Not applicable	_ _/_ _/_ _ _ _ ☐ Not applicable
	_ _/_ _/_ _ _ _ ☐ prn	_ _/_ _/_ _ _ _ ☐ Still prescribed at *[INDEX DATE]*	__________	☐ Increase ☐ Decrease ☐ Remained the same ☐ Not applicable	__________ ☐ Not applicable	_ _/_ _/_ _ _ _ ☐ Not applicable
	_ _/_ _/_ _ _ _ ☐ prn	_ _/_ _/_ _ _ _ ☐ Still prescribed at *[INDEX DATE]*	__________	☐ Increase ☐ Decrease ☐ Remained the same ☐ Not applicable	__________ ☐ Not applicable	_ _/_ _/_ _ _ _ ☐ Not applicable

Seroquel XR Treatment

Was the patient experiencing psychotic symptoms at initiation of Seroquel XR?
☐ Yes
☐ No
☐ Unknown

Which disorder was Seroquel XR prescribed for?
Please select all that apply
☐ MDD
☐ Schizophrenia
☐ Bipolar disorder
☐ Other – please specify _____

How many times has the investigator seen this patient since initiation of Seroquel XR?
_ _ visits

What is your estimate of patient adherence to the prescribed treatment regimen that included Seroquel XR for depression?

__ __ __ % of time adherent to prescribed dose(s) (range: 0 – 100%)
(Investigator assessment)

In the table below record the number of different **dosages of Seroquel XR** prescribed for this patient. Please indicate by ticking in the appropriate boxes the **different dosages** that this patient has experienced, then please enter the **number of prescriptions** for each selected dosage and the **duration (or days supply) of each prescription**.

Dosage of Seroquel XR prescribed	Number of prescription for each dosage	Duration of each prescription (in days)
☐ 50 mg / day	_ _ scripts	Script 1: _ _ days, Script 2: _ _ days, Script 3: _ _ days, Script 4: _ _ days Script 5: _ _ days, Script 6: _ _ days, Script 7: _ _ days, Script 8: _ _ days
☐ 100 mg / day	_ _ scripts	Script 1: _ _ days, Script 2: _ _ days, Script 3: _ _ days, Script 4: _ _ days Script 5: _ _ days, Script 6: _ _ days, Script 7: _ _ days, Script 8: _ _ days
☐ 150 mg / day	_ _ scripts	Script 1: _ _ days, Script 2: _ _ days, Script 3: _ _ days, Script 4: _ _ days Script 5: _ _ days, Script 6: _ _ days, Script 7: _ _ days, Script 8: _ _ days
☐ 200 mg / day	_ _ scripts	Script 1: _ _ days, Script 2: _ _ days, Script 3: _ _ days, Script 4: _ _ days Script 5: _ _ days, Script 6: _ _ days, Script 7: _ _ days, Script 8: _ _ days
☐ 250 mg / day	_ _ scripts	Script 1: _ _ days, Script 2: _ _ days, Script 3: _ _ days, Script 4: _ _ days Script 5: _ _ days, Script 6: _ _ days, Script 7: _ _ days, Script 8: _ _ days
☐ 300 mg / day	_ _ scripts	Script 1: _ _ days, Script 2: _ _ days, Script 3: _ _ days, Script 4: _ _ days Script 5: _ _ days, Script 6: _ _ days, Script 7: _ _ days, Script 8: _ _ days
Other 1: _ _ _ _ mg / day	_ _ scripts	Script 1: _ _ days, Script 2: _ _ days, Script 3: _ _ days, Script 4: _ _ days Script 5: _ _ days, Script 6: _ _ days, Script 7: _ _ days, Script 8: _ _ days
Other 2: _ _ _ _ mg / day	_ _ scripts	Script 1: _ _ days, Script 2: _ _ days, Script 3: _ _ days, Script 4: _ _ days Script 5: _ _ days, Script 6: _ _ days, Script 7: _ _ days, Script 8: _ _ days
Other 3: _ _ _ _ mg / day	_ _ scripts	Script 1: _ _ days, Script 2: _ _ days, Script 3: _ _ days, Script 4: _ _ days Script 5: _ _ days, Script 6: _ _ days, Script 7: _ _ days, Script 8: _ _ days

Prior to initiating SEROQUEL XR, what was the patient response to their most recent prior antidepressant treatment?

		Side effects			
		None	Did not significantly interfere with Subject's functioning	Significantly interfered with Subject's functioning	Outweighed therapeutic effect (Not tolerable, Needed to stop medication)
Therapeutic effect	Marked vast improvement. Complete or nearly complete remission of all symptoms				
	Moderate improvement. Partial remission of symptoms				
	Minimal slight improvement				
	Unchanged or worse				

Unknown or Not assessed ☐
(Investigator assessment)

When was the last consultation date for this patient?
_ _/ _ _/ _ _ _ _
day / mo / year

Revised Protocol of Non-Interventional Study (NIS)
Appendix C

Drug Substance	SEROQUEL® XR
Study Code	D1443C00057
Edition Number	3
Date	[redacted]

Appendix C
Sample Patient Information and Consent Form

PATIENT INFORMATION AND CONSENT FORM

Sponsor : AstraZeneca

Study Code: D1443C00057

Centre No: << >> Enrolment Code: << >>

Title of the study: A Multinational, Multicenter Retrospective, Observational Drug Utilisation Study of Seroquel® Extended Release (XR) Prescribed by Psychiatrists as Treatment for Major Depressive Disorder (MDD) in selected countries in the European Union (EU)

Dear patient,

We kindly want to ask if you would be willing to take part in an observational study. This observational study is mandated by AstraZeneca LP [redacted] Observational studies (from now on called 'study') are those where doctors collect information from your medical records only. In this case to understand how medications are being used to treat your Major Depressive Disorder (MDD, from English meaning 'Major Depressive Disorder'). Your medical care will not in any way be affected or altered by your decision to participate (or not participate) in this trial.

Before you decide if you want to take part it is important for you to understand why this study is being done, how your information will be used and what the study will involve. Please take time to read the following information carefully and discuss it with your family doctor. If you were already in a clinical trial at the time of interest you cannot take part in this study. In this document the term "Study Doctor" refers to your psychiatrist.

WHAT IS THE BACKGROUND TO AND PURPOSE OF THE STUDY?

You are diagnosed with major depressive disorder that can be treated in various ways, including sometimes with medicines. This study is being carried out to find out how individuals suffering from this disease are medically treated by their psychiatrists.

This study is being carried out across different countries in Europe. Approximately 500 to 2000 other subjects like you will take part.

DO I HAVE TO TAKE PART?

If you do decide to take part in this registry, you will be asked to sign this Informed Consent Form. The participation at this registry is totally voluntary. If you decide to take part, not to take part at the registry or decide to withdraw from this study at a later point in time, this will not have any negative affects on your further medical care.

The sponsor of the registry or a regulatory authority can stop the registry earlier than planned. In this case, the investigator will inform you immediately about it and explain to you the reasons for the discontinuation. No further personal data will be abstracted and saved. You will be medically treated as usual.

WHAT DO I HAVE TO DO?

If you decide to participate in the study, your psychiatrist will discuss this consent form with you and ask you to sign it.

If you want to participate in this study, your psychiatrist will access your medical records to gather some data on your medical history and information needed to determine whether you meet the inclusion criteria for the study. If you meet the inclusion criteria for the study, then your Study Doctor, the responsible Clinical Research Associate of the Contract Research Organization Outcome (the AstraZeneca representative for this study) and AstraZeneca Auditors if applicable will have access to your medical records. It is possible, that regulatory authorities have to do so as well. The responsible Clinical Research Associate from the Contract Research Organization Outcome (AstraZeneca representative) will use the information from your medical records to complete the study questionnaire.

If you are a woman and you discover you are pregnant during your participation in this study, you will need to notify your doctor at the earliest opportunity. Your doctor may request some additional information related to your pregnancy and the Seroquel XR treatment that you have been receiving. Your health during pregnancy will still be followed up according to the usual standard of care by your treating doctor.

WHAT ARE THE POSSIBLE SIDE EFFECTS, RISKS AND BENEFITS OF TAKING PART?

Your participation in this study does not require or include any specific medical procedure or tests; nor will any medicines be changed. It requires the accessing of medical records only. There is no specific risk related to your participation in the study.

There is no immediate clinical benefit for you. Nevertheless the information we get from this study may help us to better understand how individuals with major depressive disorder are currently managed in real-life practice and how management could be improved in the future.

HOW WILL MY PERSONAL DATA BE USED?

By signing this form you consent to the Study Doctor and his or her staff and the CRO Outcome and its agents (the AstraZeneca representative for this study) collecting and using your personal data for the study ("Study Data"). Data collected from your medical records will include your age, your sex, your ethnic origin, information regarding your diagnosis, treatment used, dose and prescription of medication, and additional personal data on your physical or mental health or condition. Your consent to the use of the Study Data does not have a specific expiration date, but you may withdraw your consent at any time without

providing a reasons, and this withdrawal will not have any negative affects on your further medical care. Please notify the Study Doctor, if you withdraw your consent.

The Study Data shared with AstraZeneca is protected by the use of a code (the "Code"), which is a number specific to you and which helps to keep your personal data pseudonymous. The Study Doctor is in control of the Code key, which is needed to connect the Study Data to you. A person appointed by AstraZeneca, regulatory authorities or other supervisory bodies might review any of the Study Data held by the Study Doctor.

The Study Doctor and Outcome (the AstraZeneca representative) and its agents, will use the Study Data to conduct the Study. AstraZeneca may use the Study Data to support research related to the development of pharmaceutical products, diagnostics or medical aids. The Study Doctor's institution and AstraZeneca are each responsible for their handling and ensuring the privacy of your Study Data in accordance with applicable Data Protection law(s).

AstraZeneca may share the Study Data with other companies within its group such as a partner company. AstraZeneca may also share Study Data with its service providers and contractors such as for example Outcome that is representing AstraZeneca for this study, or with other research institutions. Such shared Study Data will be used only for the purpose to support research related to the development of pharmaceutical products, diagnostics or medical aids. The Study Data will remain pseudonymous at all times.

AstraZeneca may transfer your Study Data to countries outside of Germany and the European Union (EU), for the purposes described in this document. Please be aware that the laws in such countries may not provide the same level of data protection as in Germany and may not stop the Study Data from being shared with others. All data that is transferred will be coded. Please note, the results of the study may be published in medical literature, but you will not be identified.

You have the right to request information about your Study Data held by the Study Doctor and AstraZeneca. You also have the right to request that any inaccuracies in such data be corrected. If you wish to make a request, then please contact the Study Doctor, who can help you contact AstraZeneca if necessary.

If you withdraw your consent, the Study Doctor will no longer use your Study Data or share it with others. AstraZeneca may still use Study Data that was shared with it before you withdrew your consent.

By signing this form I consent to the use of Study Data as described in this form.

WHOM SHOULD I CONTACT IF I NEED MORE INFORMATION OR HELP?

Should you need additional information, please contact:

Dr <<Name>>Phone No. << >>

Address << >>

PATIENT INFORMED CONSENT

- I have been cleared up by the physician on the above study and have read the attached written information.
- I have been given the sufficient time to discuss the study and ask questions.
- I understand that I may refuse consent without my current or future medical care being affected.
- I consent to taking part in the study and I am aware that my participation is entirely voluntary.
- I understand that I may withdraw at any time without this affecting my current or future medical care.
- By signing this information and consent form I agree that my personal data (data collected from my medical records, including my age, my gender, my ethnic origin, information regarding my diagnosis, treatment used, dose and prescription of medication and data regarding my physical or mental health) may be transferred to countries outside of Germany and the European Union (EU) in exclusively pseudonymised form, which means without mentioning my name, my initials, my birthday date and my address.
- All personal data will be recorded and sent out in a pseudonymised form. A conclusion on my person is not possible.
- I understand I will receive a copy of this information and consent form.

_____ _____

Signature of patient Date of Signature

To be signed and dated by the patient

_____

Printed name of patient (BLOCK CAPITALS)

_____ _____

Signature of person conducting the informed consent discussion

Date of Signature

_____

Printed name of person conducting the informed consent discussion (BLOCK CAPITALS)