Division: Worldwide Development
Retention Category: GRS019
Information Type: Worldwide Epidemiology Study Protocol

Title: European Survey of Patient and Prescriber Understanding of Risks Associated with TROBALT™

Compound Number: GW582892

Development Phase IV

Effective Date: 13-September-2012

Description: This is a cross-sectional survey of prescribers and patients on the effectiveness of the physician guide and the patient information leaflet on physician and patient understanding of the significant risks of TROBALT (retigabine). This forms part of the European Risk Management Plan (RMP) requirements.

Subject: Patient and prescriber survey of the understanding of significant risks associated with TROBALT, Physician's Guide, Patient Information Leaflet

Author(s): [redacted] (GlaxoSmithKline)

Revision Chronology:

[redacted]	2012-May-18	Original
[redacted]	2012-June-11	Amendment to add 3 countries to the survey (Norway, Spain and Slovakia) and to analyse Germany separately due to a reimbursement decision.
[redacted]	2012-Sept -13	Amendment at the request of the European regulator to provide predicted timelines for study completion, to remove patient gift, to specify physician payment for study participation, and to add a question about the titration pack (although will specify that this does not apply to Switzerland).

SPONSOR SIGNATORY:

STUDY TITLE: European Survey of Patient and Prescriber Understanding of Risks Associated with TROBALT™

Study: WEUKBRE5744

Development Phase: IV

Name of Sponsor Signatory: [redacted]

Title of Sponsor Signatory: [redacted]

Signature: _____

Date: _____

SPONSOR INFORMATION PAGE

Worldwide Epidemiology
Study Identifier:
WEUKBRE5744

[redacted]

VENDOR SIGNATORY

- I confirm agreement to conduct the study in compliance with the protocol.
- I acknowledge that I am responsible for overall study conduct. I agree to personally conduct or supervise the described study.
- I agree to ensure that all associates, colleagues and employees assisting in the conduct of the study are informed about their obligations. Mechanisms are in place to ensure that site staff receives the appropriate information throughout the study.

Vendor Name [redacted]

[redacted]

Vendor Signature

Date

TABLE OF CONTENTS

PAGE

LIST OF ABBREVIATIONS

AE	Adverse Event
AED	Anti-epileptic drug
EU	European Union
GSK	GlaxoSmithKline
HCP	Healthcare Provider
PIL	Patient Information Leaflet
REMS	Risk Evaluation and Mitigation Strategy
RMP	Risk Management Plan
SmPC	Summary of Product Characteristics
[redacted]	[redacted] Corporation
UK	United Kingdom
US	United States

Trademark Information

Trademarks of the GlaxoSmithKline group of companies	Trademarks not owned by the GlaxoSmithKline group of companies
TROBALT	

PROTOCOL SUMMARY

Rationale

As part of a European post-marketing commitment, GSK will conduct a survey of physicians' and patients' understanding of the significant risks associated with TROBALT™ (retigabine), as described in the Patient Information Leaflet (PIL) and the Physician's Guide. The goal of the surveys is to evaluate the effectiveness of the educational plan as specified in the European Risk Management Plan (RMP).

Objective(s)

The objectives of this study are to assess patients' and prescribers' understanding and knowledge of the significant risks associated with TROBALT use as evaluated by a survey instrument.

Study Design

This is a cross sectional survey of:

1) 250 patients recruited from across the following countries (United Kingdom, Sweden, Denmark, Switzerland, Spain, Slovakia and Norway) and up to 100 patients from Germany who are currently using or have filled a prescription for TROBALT at least once in the last 3 months.

2) 200 neurologists who have prescribed an anti-epileptic drug (AED) at least once in the last 3 months, and who were on the list to which a letter containing the Physician's Guide for TROBALT was distributed from across the following countries (United Kingdom, Sweden, Denmark, Switzerland, Spain, Slovakia and Norway). At least 75 of the neurologists will have prescribed TROBALT. The survey will also aim to include up to 100 neurologists from Germany of which approximately 50 will have prescribed TROBALT.

Patients eligible for the survey will be asked to take the survey online or via a telephone interview if the latter is preferred. Neurologists will be invited to take the survey online.

The selected countries were the first five countries to launch TROBALT (Germany, Denmark, United Kingdom, Switzerland and Sweden) and an additional three countries with launch in 2011, but with relatively high rates of uptake of TROBALT (Spain, Slovakia and Norway). The selection of countries includes Switzerland, which is not part of the European Union. However, the key messages regarding the risks with TROBALT are in alignment. The rationale for surveying the first five countries to launch is so that any issues identified from these countries regarding the effectiveness of the Physician's Guide and PIL in communicating the risks of TROBALT can be addressed as soon as possible, and the key messages can be revised in a timely manner. In addition, these countries are likely to provide the greatest number of neurologists with experience of prescribing TROBALT, and their patients.

Study Endpoints/Assessments

The primary outcome of the survey is the proportion of patients/neurologists providing correct responses to a series of questions concerning the significant risks associated with TROBALT. The risks evaluated will be those described in the TROBALT PIL and in the Physician's Guide.

1. INTRODUCTION

GlaxoSmithKline (GSK) will conduct a survey of patients' understanding of the significant risks associated with TROBALT™ (retigabine). The survey will concentrate on the risks described in the approved EU Patient Information Leaflet (PIL) for TROBALT, though it is recognised that the PIL is not the only source of information concerning risks associated with medication use.

GSK will also survey neurologists who are prescribing anti-epileptic drugs (AEDs) on their understanding of the significant risks associated with TROBALT. Neurologists were chosen as the target HCPs because all neurologists in each country to be surveyed were sent a letter containing the Physician's Guide and SmPC at the launch of TROBALT in that country (Appendix 1). Neurologists were targeted for this letter on the basis that they constituted the broadest group that were reasonably likely to initiate a prescription of TROBALT. Furthermore, a sub-group of neurologists commonly referred to as 'epileptologists' are known from past experience to be the specialists who first initiate prescriptions of a new AED and were therefore specifically targeted for promotional activity by GSK and are the primary target of this survey. The survey will concentrate on the risks described in the Physician's Guide for TROBALT, though it is recognised that the Physician's Guide is not the only source of information concerning risks associated with medication use.

The design for this study is based on GSK's previous experience designing risk management programs for GSK products, and on the prior experience of [redacted] Corporation ([redacted] in conducting similar surveys in the EU.

2. OBJECTIVE(S)

The objectives of this study are:

1. To assess patients' understanding of the significant risks associated with TROBALT as evaluated by a survey instrument.

2. To assess prescribers' understanding of the significant risks associated with TROBALT as evaluated by a survey instrument, for those who should have received the letter containing TROBALT Physician's Guide, and specifically for the subset of prescribers who have prescribed TROBALT.

3. INVESTIGATION PLAN

3.1. Study Design

This study is sponsored by GlaxoSmithKline (GSK), and will be conducted by [redacted] an international research consultancy.

This is a cross-sectional study of physicians' and patients' understanding of the significant risks associated with TROBALT.

Physicians will be recruited by selecting a random sample of neurologists from lists provided by GSK in each country. The list includes names of all potential TROBALT prescribers who were mailed an introductory letter including the Physician's Guide for TROBALT (Appendix 1). Following recruitment, neurologists' understanding of the potential risks associated with TROBALT will be evaluated using an online survey. Each invitation will include information on how to access the survey on-line, and will include a unique code to ensure that the invitation is used only once.

The primary method of recruiting patients is through their physicians. In countries in which a list of current TROBALT prescribers can be obtained, a random sample of prescribers in each country will be selected. Otherwise, the sample will come from the list of neurologists who were mailed the Physician's Guide, who have not participated in the neurologist survey. Sampled prescribers will be asked to provide survey invitations to their patients being treated with TROBALT. Each prescriber will be given 10 invitations and asked to provide these invitations to up to 10 consecutive patients who have been prescribed TROBALT in the last 3 months. If the patient response rate using this recruitment method is lower than expected, then other options will be identified including patient panels where available.

Following recruitment, patients' understanding of the potential risks associated with TROBALT will be evaluated using an online survey or the same survey instrument delivered during a telephone interview. The latter option aims to accommodate individuals who are not comfortable with online technology or are not computer literate. Each invitation will include information on how to access the online survey and will also provide the toll-free number for accessing the Survey Call Centre.

To ensure comprehension of each communication piece, all of the physician and patient outreach will be conducted in the local country language. Specifically, the surveys and invitation letters will all be translated by a certified translation company. In addition, when conducting the survey by telephone, the person conducting the survey will be a native language speaker.

3.2. Study Populations

3.2.1. Patients using TROBALT

This survey aims to recruit 350 patients who are currently being treated with TROBALT or who have received TROBALT within the last 3 months. These numbers reflect a trade-off between what is practical in terms of recruitment, given the relatively low predicted uptake of TROBALT, and providing sufficient precision around outcome estimates (proportion giving correct responses per question) (Section 8).

The selected countries were the first five countries to launch TROBALT (Germany, Denmark, United Kingdom, Switzerland and Sweden) and an additional three countries with launch in 2011, but with relatively high rates of uptake of TROBALT (Spain, Slovakia and Norway). The selection of countries includes Switzerland, which is not part of the European Union. However, the key messages regarding the risks with TROBALT are in alignment. The rationale for surveying the first five countries to launch is so that any issues identified from these countries regarding the effectiveness of the Physician's

Guide and PIL in communicating the risks of TROBALT can be addressed as soon as possible, and the key messages can be revised in a timely manner. In addition, these countries are likely to provide the greatest number of neurologists with experience of prescribing TROBALT, and their patients.

Two-hundred fifty patients will be recruited from across the following countries (United Kingdom, Sweden, Denmark, Switzerland, Spain, Slovakia and Norway). If required, additional EU countries may be included in the survey to reach the minimum recruitment target. Up to one hundred patients will be recruited from Germany, which was one of the earliest countries to launch and currently has the highest volume of use of TROBALT in Europe. However, it should be noted that on May 31, 2012, following the reimbursement process in Germany, GSK chose not to enter into price negotiations and TROBALT will not be available for new patients from July 2012 until further notice. Patients currently on TROBALT prior to May 31, 2012 will continue to be able to fill their TROBALT prescriptions in Germany. Therefore, by November 2012 at the start of the survey, the characteristics of the patients using TROBALT in Germany may differ from the other European countries where new patients will continue to receive TROBALT prescriptions. Additionally, the neurologists included from Germany will only be those who continue to prescribe TROBALT, and this may be a selected population. For these reasons, the survey data from Germany will be analysed with the total study population, as well as separately.

3.2.1.1. Inclusion criteria for patient survey

Patients will be required to meet all the following inclusion criteria:

1. Use of TROBALT: current use or at least one prescription filled within the previous three months.
2. 18 years of age or older.
3. Willing to take the online survey or have the survey administered via a telephone interview.

3.2.1.2. Exclusion criteria for patient survey:

Patients meeting any of the following criteria will not be eligible to take the survey:

1. Unable to understand and complete the survey by internet or phone.
2. Currently an employee of GSK [redacted]

3.2.1.3. Methods of Recruitment

Patients will be recruited by prescribers, who will be asked to provide survey invitations to their patients being treated with TROBALT. If the patient response rate using this recruitment method is lower than expected, then other options will be identified including patient panels, where available and approved by the country-specific Ethics Committee.

3.2.2. Neurologists prescribing anti-epileptic drugs

This survey aims to recruit a random sample of 300 neurologists prescribing AEDs and who have been sent the TROBALT Physician's Guide. A sample of 200 neurologists will be recruited from across the following countries (United Kingdom, Sweden, Denmark, Switzerland, Spain, Slovakia and Norway), and up to 100 neurologists will be recruited from Germany. If required, additional EU countries may be included in the survey to reach the minimum recruitment target. The recruitment will be from among those who have prescribed an anti-epileptic drug (AED) at least once in the last 3 months, and who were on the list to which a letter including the Physician's Guide TROBALT was distributed. The survey will aim to recruit at least 75 physicians (from the seven specified countries) and 50 physicians from Germany with experience of prescribing TROBALT for sub-analyses, as these individuals would be expected to be more aware of the risks of TROBALT. The sub-group of neurologists commonly referred to as 'epileptologists' are known from past experience to be the specialists who first initiate prescriptions of a new AED and were therefore specifically targeted for promotional activity by GSK and are the primary target of this survey.

As with the patient population, these numbers reflect a trade-off between what is practical in terms of recruitment, given the relatively low predicted prescribing of TROBALT, and providing sufficient precision around outcome estimates (proportion giving correct responses per question), and also to allow analysis of the sub-sample of neurologists who have prescribed TROBALT.

3.2.2.1. Inclusion criteria for physician survey

Physicians will be required to meet all the following inclusion criteria:

1. Must have prescribed an AED at least once in the last 3 months
2. Must be on the list to which the Physician's Guide for TROBALT was distributed.

3.2.2.2. Exclusion criteria for physician survey

Physicians meeting any of the following criteria will not be eligible to take the survey:

1. Currently an employee of GSK or [redacted]

3.2.2.3. Methods of Recruitment

The neurologists will be recruited through an invitation to participate in the survey. The invitation will direct the neurologist to the survey website to complete the survey. Invitations will be sent by e-mail to those neurologists for whom an e-mail address is available. For those neurologists without e-mail addresses, invitations will be sent by mail. If there is no response after the first invitation, then a second reminder invitation will be sent within 2 weeks after the first mailing.

Physicians will be paid the equivalent of €75 for their participation, which is fair market value for a survey estimated to take 20 minutes to complete.

3.3. Survey Design

The final study design is based on experience from risk management studies previously completed by GSK and [redacted] has designed and conducted assessment surveys in over 20 European countries to evaluate prescribers' understanding of risk messages. Recruitment and analytic strategies included in this proposal are similar to those programs. Further, both [redacted] and GSK have conducted similar knowledge, attitude and behavior surveys in the US to evaluate Risk Evaluation and Mitigation Strategies (REMS).

3.3.1. Questionnaire Structure

Each survey will be composed of multiple choice and close-ended questions. There will be no open-ended questions included. For statements or questions that use "true" or "yes" vs. "false" or "no" response options, the desired response for key risk messages is generally "true" or "yes" indicating knowledge of, or behavior in accordance with, the objectives of the program. However, some questions are formatted to have the respondent disagree with the statement as written by providing response options of "false" or "no" to avoid having the same affirmative answer for all desired responses.

Both physicians and patients will be provided a unique code in the survey invitation letter and will be asked to provide the unique code to gain access to the online survey or when calling the Survey Coordinating Center. The code will be deactivated after use to minimize the possibility for fraud.

3.3.2. Measures to minimise bias in the surveys

The following are measures to minimise bias in the surveys:

- Telephone interviewers are highly trained and use a standardized script to administer interviews.

- All questions will be programmed to ensure that questions are asked in the appropriate sequence. Skip patterns will be clearly indicated. Respondents cannot go back to a question once the question has been answered and cannot skip ahead. All questions must be answered in order to complete the survey.

- Response options presented in a list will be randomized to minimize positional bias.

- Programming will be reviewed by quality control and simulated users (User Acceptance Testing) prior to implementing the survey.

4. STUDY ASSESSMENTS AND PROCEDURES

4.1. Patient Screening and Assessment

The patient informed consent form is outlined in Appendix 2 and the survey instrument for the patient assessment is in Appendix 3. The questionnaire will begin with a screening module with questions to confirm eligibility. Depending on the answers to the screening questions, survey participation could either be terminated or continued. If ineligible, the respondent is immediately notified with a "thank you" message that survey participation has ended. If eligible, the respondent is allowed to continue survey participation.

After accepting the invitation to participate in the study, individual patients will be directed to take a screening questionnaire based on their preference of either online completion or via a telephone interview. The screening questionnaire will assess:

- Agreement to take the survey
- TROBALT formulation, time since last prescription.
- Demographics: age. Additional socio-demographic questions will be asked in the main survey questionnaire.
- Employment at GSK or [redacted]

4.2. Neurologist Screening and Assessment

The health care provider introduction information is outlined in Appendix 4, and the survey instrument for neurologist assessment is in Appendix 5. The neurologist questionnaire will begin with a screening module with questions to confirm eligibility. Depending on the answers to the screening questions, survey participation could either be terminated or continued. If ineligible, the respondent is immediately notified with a "thank you" message that survey participation has ended. If eligible, the respondent is allowed to continue survey participation.

The screening questions included in the prescriber survey are:

- Agreement to take the survey
- Time since the last prescription written for any AED
- Ever prescribe TROBALT*
  *Used to ensure that the sample includes at least 100 TROBALT prescribers
- Employment at GSK or [redacted]

4.3. Patient Outcomes

Patient understanding of the significant risks associated with TROBALT will be assessed using a standardised questionnaire.

The primary outcome of this study is the proportion of patients that correctly respond to individual survey questions concerning the risks associated with TROBALT. The proportion responding correctly will be tabulated separately for each item in the patient understanding survey instrument. These risks represent those described in the PIL for TROBALT.

Patient demographic information will be collected at the end of the survey in order to further characterize the respondent population. This will include gender, country of residence, education level and indication for TROBALT use.

At the conclusion of the online survey, the final screen will display a summary of the relevant information from the PIL, including a link to the PIL on the internet at http://www.gsk.com/products/prescription-medicines/trobalt.htm. Similar information will be provided by the telephone interviewer. If the patient poses any questions on the information presented, he/she will be directed to discuss the question with the treating physician.

4.4. Neurologist Outcomes

Neurologist understanding of the significant risks associated with TROBALT will be assessed using a standardised questionnaire.

The primary outcome of this study is the proportion of neurologists that correctly respond to individual survey questions concerning the risks associated with TROBALT. The proportion responding correctly will be tabulated separately for each item in the physician understanding survey instrument. These risks represent those described in the Physician's Guide for TROBALT.

Physician demographic information will be collected at the end of the survey in order to further characterise the respondent population. This will include gender and medical specialty, type of medical practice, years in medical practice. Country in which practice occurs will be collected at the beginning of the survey in order to identify respondents from Switzerland for whom not all questions apply.

At the conclusion of the online survey, the final screen will display a summary of the relevant information from the Physician's Guide.

4.5. Adverse Drug Experience/Event Measures

This study will not investigate adverse events associated with the use of TROBALT. While it is not the intention of the survey to solicit adverse events, it is possible that during a telephone survey a respondent may spontaneously provide information that meets the criteria of an adverse event. Any reported adverse events will be entered into the GSK safety database:

- Online respondents will be provided with the telephone number for the local call centre in the country of the participant at the end of the online survey and will be directed to call the centre to report any adverse events potentially associated with TROBALT.

- If, at any time during the telephone interview, the subject describes an adverse event associated with TROBALT or any GSK product, the telephone interviewer will complete an adverse event form and fax it to GSK Global Clinical Safety and Pharmacovigilance on +44 208 754 7821 within 24 hours of receiving the information. The form is included in Appendix 6.

- GSK Global Clinical Safety and Pharmacovigilance has specific guidelines detailing action to be taken if an individual reports suicidal thoughts or behavior. All telephone interviewers will be trained on these guidelines and will follow this process if a respondent reports suicidal thoughts during the interview.

At the end of the project, [redacted] will provide a summary of all adverse events that it has submitted to GSK to enable the reports to be reconciled.

5. DATA COLLECTION AND MANAGEMENT

All data collected during the survey will be held confidential. The electronic data capture (EDC) system used for data collection encrypts all identifiable information, and respondent identifiers are stored separately from the survey responses.

In all cases, patient identifiers will not be collected or transmitted to GSK according to GSK policy. All patients will be given an alphanumeric patient identifier.

6. DATA ANALYSIS

6.1. Analysis Populations

6.1.1. Patient population

The population for analysis will comprise all patients recruited into the study, meeting eligibility criteria as assessed in the survey screener, and completing all questions in the survey.

The outcomes will be summarised for all eight specified countries combined, and separately for Germany and for the seven countries combined not including Germany for the reasons outlined in Section 3.2.1.

6.1.2. Neurologist population

The population for analysis will comprise all neurologists recruited into the study, meeting eligibility criteria as assessed in the survey screener, and completing the survey.

The outcomes will be summarised for all eight specified countries combined, and separately for Germany and for the seven countries combined not including Germany for the reasons outlined in Section 3.2.1.

The sub-population for analyses will be the neurologists who have ever prescribed TROBALT.

6.2. Analyses

6.2.1. Patient survey analysis

Patient demographics and indication for TROBALT use (epilepsy/ other) will be summarised using descriptive statistics for continuous data and proportions for categorical data.

The primary outcome is the proportion of patients answering each question of patient understanding of the risks associated with TROBALT correctly. Point estimates for the proportion with correct responses, and associated confidence intervals, will be calculated for each question about the risks of TROBALT. In the case of multiple choice questions, the number and proportion of patients reporting each response will also be provided.

The proportion of correct answers to survey questions will be summarised overall, and by demographic subgroups such as country. Consideration of these subgroups may highlight differences in patients' responses. Although the sample size in some subgroups may be relatively small and have low precision, data will be grouped into 2-3 sub-categories as appropriate to identify potential trends in patient understanding including:

- Demographics (gender, age, education level)
- Country
- TROBALT use (e.g., months using TROBALT, method of obtaining TROBALT (pharmacy, neurologist, mail, internet), whether the patient read the PIL)

The survey results will be presented with Germany included in the overall study population, then separately for Germany and the remaining specified European countries.

This study is descriptive; hence there will be no formal statistical testing completed.

6.2.2. Neurologist survey analysis

The primary outcome is the proportion of neurologists answering each question of the understanding of the risks associated with TROBALT correctly. Point estimates for the proportion with correct responses, and associated confidence intervals, will be calculated for each question about the risks of TROBALT. In the case of multiple choice questions, the number and proportion of neurologists reporting each response will also be provided.

The proportion of correct answers to survey questions will be summarised overall, and separately for those neurologists who have prescribed TROBALT. Exploratory analyses may include stratification by country.

The survey results will be presented with Germany included in the overall study population, then separately for Germany and the remaining specified European countries.

7. PRECISION BY SAMPLE SIZE

Table 1 summarises the margin of error at the 95% confidence level provided by varying sample sizes and estimates of percentage of patients indicating a correct response. For example, if the estimate of the percentage of patients indicating a correct response to an individual survey question is 60%, then a sample of 250 patients will provide a margin of error of ± 6.0 percentage points of this estimate with a 95% confidence interval. Subgroups of the total sample will have smaller numbers of patients, resulting in larger margins of error and therefore provide estimates with lower precision.

Table 1 Sample size and precision estimates

Sample Size	Proportion of Correct Responses to Each Question						
	50	60	70	75	80	85	90
	Precision/ Margin of Error (±%) with 95% Confidence Interval						
50	14	14	12	11	10	9.0	8.0
100	10	10	9.0	8.0	8.0	7.0	6.0
150	8.0	8.0	7.3	7.0	6.7	5.7	4.7
200	7.0	7.0	6.5	6.0	5.5	5.0	4.0
250	6.0	6.0	5.6	5.4	4.8	4.6	3.6
300	5.7	5.7	5.3	5.0	4.7	4.0	3.3
350	5.1	5.1	4.9	4.4	4.3	3.9	3.1
400	5.0	4.8	4.5	4.3	4.0	3.5	3.0
450	4.7	4.4	4.2	3.9	3.8	3.2	2.7
500	4.4	4.2	4.0	3.8	3.6	3.2	2.6

8. STUDY LIMITATIONS

There are some limitations inherent in the study design. The patient sample may not be fully representative of patients typically prescribed TROBALT. This limitation will be addressed to the extent possible by asking the prescriber to invite up to 10 consecutive patients for whom TROBALT has been prescribed. However, the neurologists may have access to patients likely to have greater knowledge of the risks associated with TROBALT due to referral from a health care provider regularly prescribing TROBALT and aware of the ongoing study and its aims.

The patients from Germany who are included in the survey may not be representative of the total epilepsy patient population using TROBALT in Germany, since new users will only be available after May 31, 2012 by re-import, requiring justification by the prescribing physician.

The physicians who are recruited to invite their patients will be a random sample of prescribers who were mailed a letter containing the language from the Physician's Guide. Prescribers will be identified as a proportionate random sample stratified by country. The sample of prescribers asked to invite their patients will be an independent sample separate from the sample of prescribers asked to complete the survey themselves.

Another potential limitation of the study is whether or not the patient has (ever) read the PIL prior to the survey. The patient will not be provided with the PIL during the survey administration, unless by chance they happen to have it with them when taking the survey. Therefore, each patient's knowledge of the risks of TROBALT is based on his/her overall experience which may or may not include the PIL, in addition to other sources of information. Various questions have been included in the survey to try and elicit the role of the PIL in the patient's knowledge of the risks associated with TROBALT, but the responses may be subject to recall bias.

The sample of neurologists who are invited to participate will be a random sample of all neurologists who received the Physician's Guide for TROBALT. The sample of participating neurologists will be self-selected since respondents will voluntarily respond to the invitation to participate; however, the survey recruitment strategies are intended to recruit a heterogeneous sample of prescribers for participation. For Germany, as noted in section 3.2.1, TROBALT will no longer be available for new patients and so only neurologists who continue to have patients on TROBALT in November 2012 will be targeted.

9. STUDY MANAGEMENT

9.1. Ethical approval and patient consent

Survey participation is voluntary. The survey will begin with a question indicating the patient's or neurologist's agreement to participate in the survey. If the individual does not agree, the survey will be ended.

Ethics approval will be sought as required by individual countries.

9.2. Patient confidentiality

Privacy issues will be addressed and respected at each stage of the study. [redacted] will maintain strict confidentiality in handling all patient identification information. All data provided to GSK will be de-identified; no patient-level data or protected health information will be communicated to GSK.

9.3. Reporting of adverse events

See Section 4.5.

9.4. Study reporting and publications

The recruitment period is estimated to be 12 months from November 2012, though this could be earlier if the target number of participants is reached sooner than November 2013.

A final report will be written and submitted to European Medicines Agency (EMA) through the Periodic Safety Update Report (PSUR) in May 2014 (PSUR scheduled 29th September 2013 to 28th March 2014).

10. APPENDICES

Appendix 1 Template for the letter to prescribers including the TROBALT Physician's Guide

Physican address
Date

Dear Physician (or personalise with Dr and surname where possible)

Introducing new Trobalt (retigabine): a first-in-class potassium channel opener for the adjunctive treatment of epilepsy[1]

GlaxoSmithKline is pleased to announce the recent marketing authorisation of Trobalt in (country). Trobalt is licensed for partial onset seizures with or without secondary generalisation in adults aged 18 years and above with epilepsy [1]

The approval was supported by the results of the pivotal phase III studies RESTORE 1 and 2, which showed that significantly more patients with uncontrolled epilepsy saw a reduction of 50% or more in seizure frequency compared to placebo when a 600mg/day, 900mg/day or 1200mg/day dose of Trobalt was added to their current anti-epileptic drug (AED) regimen.[2,3]

Trobalt is a first-in-class AED that is thought to primarily target potassium channels in the brain[4] which play a major role in seizures and in regulating neuronal function, providing a new therapeutic option for the treatment of uncontrolled epilepsy.[5,6]

To date, 45 studies investigating Trobalt (phase I, II and III) have been completed evaluating more than 2,000 subjects, including 1,365 patients with epilepsy.[7]

Trobalt has been shown to be generally tolerated with most reported adverse events being transitory, mild to moderate in severity and occurring early during the titration period. Very common side effects were dose-related and included dizziness, somnolence and fatigue[1]

AEDs may have specific considerations to ensure appropriate prescribing. With Trobalt, the following advice should be discussed with your patients before initiating therapy.

Trobalt must be taken orally, with or without food, in three divided daily doses. Tablets should be swallowed whole and not chewed, crushed or divided. Trobalt must be titrated to reach an effective dose. The starting dose is 300 mg/day, increased by 150 mg/day weekly according to patient response and tolerability. The maximum total daily dose is 1200 mg/day.[1]

Treatment initiation packs are available for patients using the standard dose titration regimen to facilitate the first 2 weeks of therapy, and reach a potentially therapeutic dose of 600 mg/day by the third week of therapy.

Appropriate dose titration may minimise the risk of central nervous system-related adverse events, including hallucination and psychotic disorders.

GlaxoSmithKline

Prescribing Information is available on the back page

Trobalt™ retigabine tablets

Date of preparation: May 2011
NECE/RTG/0033/11

1. Urinary effects

Urinary retention, dysuria and urinary hesitation were reported in controlled clinical studies with Trobalt, generally within the first 8 weeks of treatment. Trobalt must be used with caution in patients at risk of urinary retention, and it is recommended that patients are advised about the risk of these possible effects.[1]

Does your patient have symptoms of urinary retention e.g. hesitancy, poor stream?
Does your patient take drugs that can cause urinary retention e.g. anticholinergics?
Is your patient able to communicate new symptoms of urinary retention?

2. QT interval prolongation

A study of cardiac conduction in healthy subjects has demonstrated that Trobalt titrated to 1200 mg/day produced a QT prolonging effect. A mean increase in Individual Corrected QT Interval (QTcI) of up to 6.7 ms (upper bound of 95% one-sided CI 12.6 ms) was observed within 3 hours of dosing. [1]

Caution should be taken when Trobalt is prescribed with medicinal products known to increase QT interval and in patients with known prolonged QT interval, congestive cardiac failure, ventricular hypertrophy, hypokalaemia or hypomagnesaemia and in patients initiating treatment who are 65 years of age and above. [1]

In these patients it is recommended that an electrocardiogram (ECG) is recorded before initiation of treatment with Trobalt and in those with a corrected QT interval >440 ms at baseline, an ECG should be recorded on reaching the maintenance dose. [1]

Does your patient have a history of cardiac disease?
Does your patient take drugs that are known to cause QT prolongation?

Retigabine has not been shown to cause cardiac arrhythmias in the randomised clinical trials, however patients should be advised to report new symptoms that might indicate a prolonged QT interval, for example palpitations, syncope.

3. Psychiatric effects

During controlled clinical studies, confusional state, psychotic disorders and hallucinations were reported, generally within the first 8 weeks of treatment. It is recommended that patients are

advised about the risk of these possible effects and to not exceed the recommended titration schedule. [1]

For further information please contact (country to insert specific details)

Yours faithfully,

Xxxxxxx
(Title)

References

1. Trobalt Summary of Product Characteristics. GlaxoSmithKline; 2011.
2. Brodie MJ *et al.* Efficacy and safety of adjunctive retigabine in refractory partial epilepsy. *Neurology* 2010; **75**: 1817-1824.
3. GlaxoSmithKline Data on File. (French *et al.*)
4. Main MJ *et al.* Modulation of KCNQ2/3 potassium channels by the novel anticonvulsant retigabine. *Mol Pharmacol* 2000; **58**: 253-262.
5. Cooper E, Jan L. M-Channels Neurological Diseases, Neuromodulation, and Drug Development. *Arch Neurol* 2003; **60**: 496-500.
6. Rogawski M. KCNQ2/KCNQ3 K+ channels and the molecular pathogenesis of epilepsy: implications for therapy. *Trends Neurosci* 2000; **23**: 393-398.
7. GlaxoSmithKline Data on File. (Advisory Committee Briefing document).

Insert local PI

Appendix 2 Patient informed consent form for the online survey about TROBALT

[BEGIN ONLINE/PHONE SURVEY CONTENT]

[PREAMBLE]

Before you begin, we would like to share some general information about this survey. The information collected in the survey you are about to take will help us to know if patients understand important information about taking TROBALT™. The survey will take up to 20 minutes.

There are no known risks to you in taking this survey. You may refuse to take part or withdraw at any time. Your answers to the questions or your decision to take part in the survey will not affect your ability to receive or take TROBALT.

How We Use Your Information

Your answers to the survey questions will be combined with answers given by others. All answers will be put together and reported in anonymous form to GlaxoSmithKline (GSK), the maker of TROBALT.

How We Protect Your Privacy

We respect that the privacy of your personal information is important to you.

- All information that is collected about you during the course of the survey will be kept strictly confidential. You will not be asked to provide your name or address in order to take the survey.

- Data collected during the study may be sent to researchers in countries where the laws do not protect your privacy to the same extent as the law in [enter participating country name]. However, GlaxoSmithKline will take all reasonable steps to protect your privacy.

- Your answers will be kept strictly confidential. You will not be contacted for marketing purposes based on your personal information or your answers to the survey.

- Neither GlaxoSmithKline nor its contractors will sell, transfer, or rent your information. Your privacy will be protected; however, research survey records may be inspected by the European Medicines Agency (EMA) and your country's Ethics Committee that reviews research studies to make sure they are safe for participants. The EMA and your country's Ethics Committee have reviewed and approved this research study and survey.

- Your choice to allow GlaxoSmithKline to use your information is entirely voluntary but necessary to take part in this survey.

How to Learn More About TROBALT

The information in this survey and the Patient Information Leaflet (PIL) should not take the place of talking with your health care professional.

- If you have any questions about your condition or treatment, or if you would like more information about TROBALT, talk to your health care professional.

How to Learn More About This Survey

- If you have questions about the survey or have any problems with the survey, please contact the Survey Coordinating Center at +x-xxx-xxxxxxx [NOTE: This number will be determined before the start of the survey].

Thank you for your interest in this survey.

[END]

Appendix 3 Questionnaire for Patients Prescribed TROBALT Who are Recruited by Invitation Letter through their Healthcare Professional

[Use for both Web-based and telephone survey]

Screening Questions:

1. Do you agree to take part in this survey?
   - **Yes**
   - No (Exclude)

2. Are you now taking TROBALT or did you take TROBALT within the past 3 months?
   - **Yes**
   - No (Exclude)

3. When was the last time that you filled a prescription for TROBALT?
   - Less than 1 month ago (OK)
   - Between 1-2 months ago (OK)
   - Between 2-3 months ago (OK)
   - More than 3 months ago (Exclude)
   - I do not know (Exclude)

4. What is your current age?
   - Under age 18 (Exclude)
   - 18-20 years
   - 21-30 years
   - 31-40 years
   - 41-50 years
   - 51-60 years
   - 61-70 years
   - Over age 70

5. Do you currently work for GlaxoSmithKline or [redacted] Corporation?
   - Yes (Exclude)
   - **No**

Questionnaire for Patients Prescribed TROBALT:

6. What is the reason you take TROBALT? (Select all that apply)
   - To treat my epilepsy (SKIP to Q #8)
   - To treat my headaches
   - To treat my heartburn
   - Other (please specify) [FREE TEXT]
   - I do not know

7. Do you take prescription medicine to treat epilepsy?
    - Yes
    - No **(SKIP to Q #9)**
    - I don't know (**If this response chosen, please skip to Q#9**)

8. How many prescription medicines for epilepsy do you take?
    - 1
    - 2
    - 3
    - 4 or more
    - None

9. How did you receive your first prescription for TROBALT?
    - From my neurologist
    - From another doctor or nurse other than my neurologist
    - Other (please specify)_ [FREE TEXT]

10. How do you obtain your repeat prescriptions for TROBALT? (Select all that apply)
    - From a pharmacy
    - From my neurologist's office
    - From a doctor or nurse other than my neurologist
    - By postal delivery
    - Through an internet order
    - Other (please specify)_ [FREE TEXT]

11. For how long have you been taking TROBALT?
    - Less than 1 month
    - 1 to 3 months
    - 4 to 6 months
    - 7 to 12 months
    - More than 1 year
    - I don't know

12. A Patient Information Leaflet comes with TROBALT. Have you read this leaflet?
    - Yes
    - No
    - I don't know

13. Which of these side effects are more likely to happen with TROBALT? Answer "yes," "no" or "I don't know" for each side effect.

	Yes	**No**	**I Don't know**

Cannot pass urine (urinary retention)	**X**	O	O
Diarrhea	O	**X**	O
Being confused	**X**	O	O
Fever	O	**X**	O
Seeing or hearing things that are not there (hallucinations)	**X**	O	O
Severe mental problems, such as being out of touch with reality (psychotic disorders)	**X**	O	O

14. You should call your doctor right away if you have which of these symptoms? Please answer “yes,” “no” or “I don’t know” for each one.

	Yes	**No**	**I Don’t Know**
Trouble starting to pass urine (urinary hesitation)	**X**	O	O
Headache	O	**X**	O
Thoughts of harming or killing yourself (suicidality)	**X**	O	O
Gaining weight	O	**X**	O
Constipation	O	**X**	O

15. How did you learn about the possible side effects of TROBALT? Please answer “yes,” “no” or “I don’t know” for each one.

	Yes	**No**	**I Don’t Know**
Neurologist told me	O	O	O
Family doctor or general practitioner (GP) told me	O	O	O
Online	O	O	O
Patient Information Leaflet	O	O	O
Patient Support Group	O	O	O

16. The Patient Information Leaflet says TROBALT can cause heart problems. Which one of the following heart conditions can TROBALT cause? (Select one answer)
    - Chest pain
    - **Making my heart beat too fast or too slow**
    - Heart attack
    - All of the above
    - None of the above

17. Which of the following raises the chance for effects on heart rhythm when you take TROBALT? Please answer "yes," "no" or "I don't know" for each one.

	Yes	**No**	**I Don't Know**
Taking other medicines	**X**	O	O
Smoking	O	**X**	O
Already having a heart problem	**X**	O	O
Having asthma	O	**X**	O
Being 65 years old or older	**X**	O	O

18. In what country do you live? (Will have drop-down menu of all countries in the survey).

19. What is your gender?
    - Male
    - Female

20. What is the highest level of education you have completed?
    - Some secondary school (EU equivalent) or less
    - Finished secondary school
    - Some university or technical/trade school
    - Graduated university
    - Post graduate studies
    - Prefer not to answer

[CLOSING] Thank you for completing the survey. The following are the correct answers to the survey questions about TROBALT.

The following are the correct answers to the survey questions about TROBALT.

Which side effects are more likely to happen with TROBALT?

- Cannot pass urine (urinary retention)
- Being confused
- Seeing or hearing things that are not there (hallucinations)
- Severe mental problems, such as being out of touch with reality (psychotic disorders)

You should call your doctor right away if you have which symptoms?

- Trouble starting to pass urine (urinary retention)
- Thoughts of harming or killing yourself (suicidality)

The Patient Information Leaflet says TROBALT can cause heart problems. Which heart condition can TROBALT cause?

- Making my heart beat too fast or too slow

Which factors raise the chance for effects on heart rhythm when you take TROBALT?

- Taking other medicines
- Already having a heart problem
- Being 65 years old or older

The information in this survey and the Patient Information Leaflet (PIL) should not take the place of talking with your health care professional. If you have any questions about your condition or treatment, or if you would like more information about TROBALT, talk to your health care professional. The Patient Information Leaflet can be obtained from the following website: http://www.gsk.com/products/prescription-medicines/trobalt.htm.

Thank You

Appendix 4 Health Care Provider Introduction to the Online Survey Regarding TROBALT

Introduction

GlaxoSmithKline, the maker of TROBALT™ (retigabine) is surveying health care professionals about TROBALT. The European Medicines Agency (EMA) has required that this research be conducted to assess health care professionals' knowledge of the prescribing information, as conveyed through the letter containing the wording from the Physician's Guide, for the safe use of TROBALT as part of the EMA's and GlaxoSmithKline's effort to ensure that the benefit of TROBALT remains greater than the risks. The questionnaire will take no more than 20 minutes to complete.

Disclaimer

This research is sponsored by a pharmaceutical company. The aim of this research is to assess knowledge about the prescribing information for TROBALT. Taking part in this survey is voluntary; you are under no obligation to participate. You may refuse to take the survey or stop taking the survey at any time. Your answers to the questions will not affect your ability to prescribe TROBALT.

How We Use Your Information

Your answers to the survey questions will be combined with those from other respondents and reported in anonymous form to GlaxoSmithKline. Your name will not be used in any report. If you are eligible to take the questionnaire, complete all the questions, and provide your contact information, you will receive [letter will be customized per country up to €75.] Your name and address will be used to send you the honorarium after you complete the survey.

How We Protect Your Privacy

We respect that the privacy of your personal information is important to you. All the information you provide will be kept strictly confidential. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. Your answers will be kept strictly confidential. Your privacy will be protected; however, research survey records may be inspected by the EMA or local country Ethics Committees. Your choice to allow GlaxoSmithKline to use your information is entirely voluntary but necessary to take part in this survey.

How to Learn More about the Online Survey

If you have questions about or problems with the survey, please contact the Help Desk at: [redacted] and your questions will be answered.

Appendix 5 Questionnaire for Neurologists who Prescribe AEDs and were Sent the TROBALT Letter Containing the Physician's Guide

Screening Questions:

1. Do you agree to take part in this survey?
    - **Yes**
    - No (Exclude)

2. When was the last time you prescribed an anti-epileptic drug for a patient?
    - Less than a month ago
    - Between 1 and 2 months ago
    - Between 2 and 3 months ago
    - More than 3 months ago (Exclude)

3. Have you ever prescribed TROBALT?
    - Yes
    - No
    - I don't know

4. In which country is your primary medical practice?
    - Germany
    - Denmark
    - United Kingdom
    - Switzerland
    - Sweden
    - Spain
    - Slovakia
    - Norway
    - Other (exclude)

[QUOTAS WILL BE ESTABLISHED FOR 200 NEUROLOGISTS FROM UK, SWEDEN, DENMARK, SWITZERLAND, SPAIN, SLOVAKIA, AND NORWAY; AT LEAST 75 SHOULD HAVE PRESCRIBED TORBALT. QUOTA OF 100 NEUROLOGISTS FROM GERMANY, OF WHICH AT LEAST 50 SHOULD HAVE PRESCRIBED TROBALT.]

5. Are you an employee of GlaxoSmithKline or [redacted] Corporation?
    - Yes (Exclude)
    - **No**

Questionnaire for Neurologists who Prescribe AEDs and Were Sent the TROBALT Letter Containing the Physician's Guide

[CORRECT ANSWERS ARE INDICATED IN BOLD]

6. For which of the following conditions is TROBALT approved for use?
   - Migraine
   - **Partial-onset seizures**
   - All types of seizures
   - All of the above
   - None of the above
   - I don't know

7. Is TROBALT indicated for use as monotherapy?
   - Yes
   - **No**
   - I don't know

8. What is the maximum recommended daily maintenance dose of TROBALT for most patients? (Please select the best response.)
- 600 mg
- 900 mg
- **1200 mg**
- 2000 mg
- None of the above
- I don't know

9. Which one of the following statements is true? (Please select the best response.)
- TROBALT should be taken once a day.
- TROBALT should be taken twice a day.
- **TROBALT should be taken three times a day.**
- TROBALT should be taken four times a day.
- None of the above
- I don't know

10. When increasing the dose, what is the maximum total daily dose at which TROBALT can be increased once every 7 days? (Please select the best response.)
- 50 mg
- **150 mg**
- 300 mg
- 600 mg
- None of the above

11. Which one of the following statements is true? (Please select the best response.)
- There are no lower age limits for TROBALT usage.
- The youngest age at which TROBALT can be used is 12.
- **The youngest age at which TROBALT can be used is 18.**
- I don't know

Please respond “true,” “false” or “I don’t know” to each of the following questions:

12. The quickest time by which the minimum maintenance dose of 600mg should be reached is the third week?
    - **True**
    - False
    - I don’t know

13. For the general population, the recommended total initial dosage should be 150mg per day for one week.
- True
- **False**
- I don’t know

14. People taking TROBALT had a higher chance of experiencing which of the following risks in clinical studies? (Please select all that apply)
- **Urinary retention**
- **Confusional state**
- **Hallucinations**
- **Psychotic disorders**
- Myocardial infarciton
- Renal carcinoma
- All of the above
- None of the above
- I don’t know

15. It is known from controlled studies that adverse events related to voiding dysfunction generally tend to be reported how soon after starting TROBALT?
    - Within the first week
    - **Within the first 8 weeks**
    - After 4 months
    - After 12 months
    - I don’t know

16. It is known from controlled studies that confusional state, hallucinations, and/or psychotic disorders generally tend to be reported how soon after starting TROBALT?
    - 4 weeks
    - **8 weeks**
    - 12 weeks
    - 16 weeks
    - I don’t know

17. Which of the following urinary symptoms, if any, should you specifically advise patients taking TROBALT to watch out for? (Please select the best response.)

- Pain when urinating
- Difficulty starting urination
- Slow stream
- Inability to pass urine
- **All of the above**
- None of the above
- I don't know

18. According to the TROBALT Physician's Guide, appropriate dose titration may minimize the risk of which of the following adverse events? (Please select the best response.)

- QT prolongation
- **CNS side effects such as hallucinations**
- Urinary retention
- All of the above
- None of the above
- I don't know

[DO NOT DISPLAY QUESTIONS 19 and 20 FOR RESPONDENTS FROM SWITZERLAND]

19. Using the Treatment Initiation Pack, by which week can the patient reach a dose of 600mg/day?

- 2 weeks
- **3 weeks**
- 4 weeks
- 5 weeks
- None of the above

20. At what dose has TROBALT been shown to produce a possible QT prolonging effect?

- 600 mg
- 900 mg
- **1200mg**
- 1800 mg
- I don't know

21. For which patients is it recommended that an ECG is recorded before initiating TROBALT? (Please select all that apply.)

    - Patients with hypertension
    - **Patients with congestive heart failure**
    - **Patients with ventricular hypertrophy**

- **Patients with hypokalemia**
- All of the above
- None of the above
- I don't know

22. What should you do in a patient with a QTc of more than 440ms before starting TROBALT? (Please select the best response)

- Recheck the ECG 1 week after the first dose
- Recheck the ECG at monthly intervals
- **Recheck the ECG after reaching the maintenance dose**
- I don't know

23. Which new cardiac effects in particular should you warn your patients about after prescribing TROBALT? (Please select all that apply)

- Syncope
- Palpitations
- Any other symptoms of arrhythmia
- **All of above**
- None of the above

24. How would you classify your primary medical specialty?

- Neurology
- Neurosurgery
- Epileptology
- Other (specify) _____ [FREE TEXT]
-

25. Have you read the TROBALT information letter that was sent at the launch of TROBALT?

- Yes
- No
- I don't know

26. From which of the following sources have you learned about the risks associated with use of TROBALT? (Please select all that apply)

- TROBALT launch letter
- GlaxoSmithKline medical information
- Other health care professionals
- GlaxoSmithKline promotional materials
- GlaxoSmithKline sales representatives
- Journal article
- GlaxoSmithKline-sponsored educational meeting
- None of the above

27. What is your gender?
- Male
- Female

28. For how many years have you been in medical practice?
- Less than 3 years
- 3-5 years
- 6-10 years
- 11-15 years
- 16-20 years
- More than 20 years
- Prefer not to answer

29. Do you agree to provide your name and address so that we can issue a payment for your time in completing this survey?
    - Yes (Record name and address)
    - No

Name _____

Address _____

[CLOSING] That ends the survey. Thank you again for your help. The correct answers to the questions about TROBALT follow.

The following are the correct answers to the survey questions about TROBALT.

For which condition is TROBALT approved for use?

- **Partial-onset seizures**

Is TROBALT indicated for use as monotherapy?

- **No**

What is the maximum recommended daily maintenance dose of TROBALT for most patients?

- **1200 mg**

Which one of the following statements is true? (Please select the best response.)

- TROBALT should be taken once a day.
- TROBALT should be taken twice a day.
- **TROBALT should be taken three times a day. [CORRECT RESPONSE]**
- TROBALT should be taken four times a day.

When increasing the dose, what is the maximum total daily dose at which TROBALT can be increased once every 7 days?

- **150 mg**

Which one of the following statements is true?

- There are no lower age limits for TROBALT usage.
- The youngest age at which TROBALT can be used is 12.
- **The youngest age at which TROBALT can be used is 18. [CORRECT RESPONSE]**

The quickest time by which the minimum maintenance dose of 600mg should be reached is the third week?

- **True**

For the general population, the recommended total initial dosage should be 150mg per day for one week.

- **False**
  The starting dose is 300 mg/day

People taking TROBALT had a higher chance of experiencing which of the following risks in clinical studies?

- Urinary retention
- Confusional state
- Hallucinations
- Psychotic disorders

It is known from controlled studies that adverse events related to voiding dysfunction generally tend to be reported how soon after starting TROBALT?

- **Within the first 8 weeks**

It is known from controlled studies that confusional state, hallucinations, and/or psychotic disorders generally tend to be reported how soon after starting TROBALT?

- **8 weeks**

Which of the following urinary symptoms, if any, should you specifically advise patients taking TROBALT to watch out for?

- Pain when urinating
- Difficulty starting urination
- Slow stream
- Inability to pass urine
- **All of the above**

According to the TROBALT Physician's Guide, appropriate dose titration may minimize the risk of which of the following adverse events?

- **CNS side effects such as hallucinations**

[DO NOT DISPLAY THE FOLLOWING TWO QUESTIONS FOR RESPONDENTS FROM SWITZERLAND]

Using the Treatment Initiation Pack, by which week can the patient reach a dose of 600mg/day?

- **3 weeks**

At what dose has TROBALT been shown to produce a possible QT prolonging effect?

- **1200mg**

For which patient is it recommended that an ECG is recorded before initiating TROBALT?

- Patients with congestive heart failure
- Patients with ventricular hypertrophy
- Patients with hypokalemia

What should you do in a patient with a QTc of less than 440ms before starting TROBALT?

- **Recheck the ECG after reaching the maintenance dose**

Which new cardiac effects in particular should you warn your patients about after prescribing TROBALT?

- Syncope
- Palpitations
- Any other symptoms of arrhythmia
- **All of above**

Please refer to the Physician's Guide and the TROBALT Prescribing Information for further details.

THANK YOU

Appendix 6 GlaxoSmithKline Adverse Drug Reaction Form- Revised Nov 30, 2009

Global Adverse Event Report Reporting Form for Marketing Research

To be completed by Market Research Agency – this form applies to both patients and HCPs.
This form is to be used for AEs mentioned worldwide in market research commissioned by GSK global.
Minimum criteria - A Reporter, at least one patient detail, suspect drug and adverse event
Please complete with as much detail as possible and forward within one business day (24 hours) to your Pharmaceutical company contact via fax to:

For drugs	GSK Case Management Group	Reports from Americas: +1 919 483 5404 (US fax #) Reports outside of Americas: +44 208 754 7821 (UK fax #)
For vaccines	GSK Biologicals Case Management Group	Reports from US & Canada: +1 919 483 5404 (US fax #) Reports outside US & Canada: +32 2 656 8009 (Belgium fax #)

Market Research Agency:	**Date aware of the adverse event/product complaint:** ***Month: Date: Year:***
Agency Address (include country):	**Project Title and Agency Reference/Project No:**
Agency Telephone No:	**Researchers Name:**
Agency Fax No:	**Researchers Signature:**

Drug(s)/ Vaccine(s) and Event(s) Details

Drug/ Vaccines Name(s):	**Adverse Event(s)/Product Complaint details:**
Indication (condition for which the drug(s)/ vaccine(s) has been prescribed): Unknown ☐ **Was the patient pregnant?** Yes ☐ No ☐ Unknown ☐	**Reported to the local regulatory agency?** Yes ☐ No ☐ Unknown ☐ **Lot/Batch number:** Unknown ☐
Dose: **Unknown** ☐	**Did the HCP/patient consider that the event was possibly related to the drug/ vaccine?** Yes ☐ No ☐ Unknown ☐

Patient Details (At least one of these patient details MUST be completed)	
Age:	**Other (approx. age of patient)**
Sex: Male ☐ Female ☐	

Respondent Details **If consent not given to disclose personal details, just complete the type of reporter (i.e., Dr., nurse, patient, pharm.)**	
Respondent name:	**Doctor** ☐
Address:	**Nurse** ☐ **Patient** ☐
Telephone No:	**Pharmacist** ☐
Email:	
Is respondent willing for the Pharmaceutical company's safety team to contact them or their doctor to discuss further? Yes ☐ No ☐	**Respondent Signature:**