A 6-month, open label, prospective, multicenter, international, exploratory study of a transition to flexibly dosed paliperidone palmitate in patients with schizophrenia previously unsuccessfully treated with oral or long-acting injectable antipsychotics.

Published: 21-09-2010
Last updated: 04-05-2024

Primary ObjectivesThe primary objective is to explore the tolerability, safety and treatment response (maintained/improved efficacy), based on total Positive and Negative Syndrome Scale (PANSS) score, of a transition to flexibly dosed paliperidone...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Schizophrenia and other psychotic disorders
Study type	Interventional

Summary

ID

NL-OMON36637

Source
ToetsingOnline

Brief title
PALMFlexS

Condition

- Schizophrenia and other psychotic disorders

Synonym
psychosis., Split personality

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: Janssen-Cilag

Intervention

Keyword: Psychiatry, Schizophrenia

Outcome measures

Primary outcome

STATISTICAL METHODS

A total of approximately 1,000 subjects will be included in this study.

For the group of non-acute subjects switching from oral antipsychotics (group A) the primary objective is driven by the reason for switching of antipsychotic medication. For subjects switching for reason lack of efficacy, the primary objective is to investigate improved efficacy, based on total Positive and Negative Syndrome Scale (PANSS) score. The expected percentage of subjects with at least 20% improvement in total PANSS is 30%. When the sample size is 81, a two-sided 95.0% confidence interval for a single proportion using the large sample normal approximation will extend 10% from the observed proportion for an expected proportion of 30%.

For subjects switching for other reasons, i.e., lack of tolerability or lack of compliance or patient*s wish, the primary objective is to investigate maintained efficacy. A difference of 5 points in change versus baseline on the total PANSS is considered to be a minimum clinically relevant difference. With a standard deviation of 17, a power of 90% and a (one-sided) significance level

of 0.025, 124 subjects are needed to test the hypothesis that paliperidone palmitate is not inferior in efficacy to the previous antipsychotic treatment (by means of Schuirmann's test).

Preferably, the above grouping on reason for switching will be evaluated within each of the two diagnostic groups (recently diagnosed versus not recently diagnosed), but only if the subgroup size is sufficiently large, i.e. meeting the respective sample size criterion.

For the group of non-acute subjects switching from long acting injectable antipsychotics (group B) the objective is to descriptively explore tolerability, safety and treatment response of switching from each individual LAI antipsychotic to paliperidone palmitate. Five different long acting injectable antipsychotics will be studied, each with a target of approximately 40 subjects.

For the group of acute subjects (group C) the primary objective is to investigate improved efficacy, based on total PANSS score. The expected percentage of subjects with at least 30% improvement in total PANSS is 40%. When the sample size is 93, a two-sided 95.0% confidence interval for a single proportion using the large sample normal approximation will extend 10% from the observed proportion for an expected proportion of 40%.

Assuming that in 4% of the subjects the primary parameter (based on the PANSS) cannot be evaluated, the minimum (sub)group size will be 85 (group A switching for lack of efficacy or group C) or 130 (group A - switching for other reasons, i.e., lack of tolerability or lack of compliance or patient*s wish) or 97 (group C). To be able to explore certain additional subgroups (e.g., prior

treatment with oral risperidone, prior treatment with olanzapine, prior treatment with other oral atypical antipsychotics, prior treatment with oral conventional antipsychotic medication), the sample size of group A has been increased to 600.

Recruitment of subjects into the 4 subgroups of group A and group C and the 5 subgroups in group B will be monitored regularly. Once a subgroup has reached the intended number of subjects, investigators will be notified and asked not to include that specific type of subjects anymore in the study.

The statistical analysis will be done by or under the supervision of Janssen-Cilag EMEA.

All subjects who receive paliperidone palmitate at least once will be included in the analysis of demographic and baseline characteristic data. This is the intent-to-treat analysis set.

All subjects who receive paliperidone palmitate at least once and provide * 1 post-baseline efficacy measurement will be included in efficacy data analyses. This is the intent-to-treat analysis set for efficacy.

All subjects who receive paliperidone palmitate at least once and provide any post-baseline information will be included in safety data analyses. This is the intent-to-treat analysis set for safety.

Changes from baseline (if appropriate) and observed values for continuous/ordinal efficacy variables will be summarized descriptively at each assessment time point and at the subject's last efficacy evaluation (endpoint).

Safety analyses include descriptive summaries of incidence of adverse event and changes in vital signs, body weight/BMI and ESRS from baseline.

The extension phase of the trial is focused at exposure and safety and will be

analyzed descriptively.

Secondary outcome

See primary study parameters/outcome of the study.

Study description

Background summary

Paliperidone palmitate (R092670) is the palmitate ester prodrug of paliperidone (9 hydroxy risperidone, R076477), a selective, monoaminergic antagonist that exhibits the characteristic dopamine type 2 (D2) and serotonin (5 hydroxytryptamine [5-HT]) type 2A (5HT2A) antagonism of the newer, or second generation, antipsychotic drugs. Paliperidone is the major active metabolite of risperidone and is a racemic mixture of the enantiomers R078543(+) and R078544(-). Paliperidone palmitate is being developed as a long-acting (LAI) intramuscular (i.m.) injectable aqueous suspension formulation for the treatment of schizophrenia. Paliperidone palmitate enables the slow release of the drug from the injection site, and thus a single dose may enable therapeutic plasma concentrations for 1 or 3 months depending on the particle size of the formulation.

Study objective

Primary Objectives
The primary objective is to explore the tolerability, safety and treatment response (maintained/improved efficacy), based on total Positive and Negative Syndrome Scale (PANSS) score, of a transition to flexibly dosed paliperidone palmitate in subjects with schizophrenia previously unsuccessfully treated with oral or long-acting injectable (LAI) antipsychotics. Subjects may present either acute or non-acute symptoms of schizophrenia.
Improved efficacy (i.e., at least 20% improvement in total PANSS score at endpoint versus baseline) will be the primary endpoint for non-acute subjects transitioned from oral antipsychotics to paliperidone palmitate due to lack of efficacy of the previous oral antipsychotic treatment.
Improved efficacy (i.e., at least 30% improvement in total PANSS score at endpoint versus baseline) will be the primary endpoint for acute subjects transitioned from oral antipsychotics to paliperidone palmitate.
Maintained efficacy will be the primary endpoint for non-acute subjects transitioned to paliperidone palmitate due to lack of tolerability of or lack of compliance with the previous oral antipsychotic treatment and for non-acute

subjects transitioned to paliperidone palmitate due to patient*s wish.
For the group of non-acute subjects switching from LAI antipsychotics, the primary objective is to descriptively explore tolerability, safety and treatment response of switching from each individual LAI antipsychotic to paliperidone palmitate. Five different long-acting injectable antipsychotics will be studied, each with a target of approximately 40 subjects.
Secondary Objectives
To collect data in order to develop recommendations for use of and transition to paliperidone palmitate from previous oral and LAI antipsychotic medications. This will be done by assessing:
• PANSS subscores and Marder factors;
• General measures of disease severity (Clinical Global Impression-Severity Scale [CGI-S], Clinical Global Impression-Change Scale [CGI-C]);
• Personal and social functioning (Personal and Social Performance Scale [PSP]);
• Health status (Self-reported health status questionnaire [SF-36]);
• Measure of Health Outcome (EQ-5D);
• Patient well-being (Subjective Well-Being under Neuroleptics Scale [SWN-S]);
• Hospitalizations during the 6 months before and after enrollment in the study (e.g., number of stays, number of days,*);
• Extrapyramidal symptoms (Extrapyramidal Symptom Rating Scale [ESRS]);
• Quality of sleep and daytime drowsiness (11-point categorical rating scales);
• Patient satisfaction with medication (Treatment Satisfaction Questionnaire for Medication [TSQM]);
• Physician treatment satisfaction (7-point categorical scale);
• Caregiver burden (Involvement Evaluation Questionnaire [IEQ]; in limited number of countries depending on availability of the scale in local languages);

Additional Objectives
• Assessment of activity or capacity limitations and participation restrictions in psychological and mental disorders (Mini International Classification of Functionality, Disability and Health Rating for Activity and Participation Disorders in Psychological Illnesses [Mini-ICF-APP]);
• Measures of alcohol and substance use (Clinician Rating Alcohol Use Scale [CRAUS], Clinician Rating Substance Use Scale [CRSUS]);
• Medical Resource Utilization (MRU through the Healthcare Resource Use Questionnaire [HRUQ]);
• Clear Thinking Scale [CTS] will be explored in a limited number of countries depending on availability of the scale in local languages.

Overall safety will be assessed.

Study design

OVERVIEW OF STUDY DESIGN
This is a non-randomized, single arm, multicenter, 6-month study that is aiming to explore the tolerability, safety and treatment response of flexibly dosed

paliperidone palmitate in approximately 1,000 subjects with schizophrenia previously unsuccessfully treated with an oral or LAI antipsychotic medication. Approximately 1,000 subjects of both genders and of minimally 18 years of age, who have a Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) diagnosis of schizophrenia (acute and non-acute) will be enrolled. Subjects can be either in- or outpatients. A transition period of preferably a maximum of 4 weeks will be allowed for the previous oral antipsychotic. When switching subjects from previous LAI antipsychotics, paliperidone palmitate will be initiated in place of the next scheduled injection. Anticholinergic medication may continue up to four weeks and should then be tapered off at the discretion of the investigator.
Subjects transitioning from oral antipsychotics will receive a first injection of 150 mg eq. of paliperidone palmitate at Day 1, followed by a second injection of 100 mg eq. at Day 8, both in the deltoid muscle. Subjects transitioning from previous LAI antipsychotics will receive their first injection with paliperidone palmitate in place of the next scheduled injection in the deltoid muscle. The paliperidone palmitate starting dose (Day 1) in subjects previously unsuccessfully treated with conventional depots should be guided both by the previous depot dose and the clinical status of the subject, and should be within the range of 50 to 150 mg eq. The paliperidone palmitate starting dose (Day 1) in subjects previously unsuccessfully treated with risperidone LAI (RLAI) should be guided both by the previous RLAI dose and the clinical status of the subject. Subjects previously on 25 mg RLAI every 2 weeks can attain similar steady state exposure to paliperidone with 50 mg eq. paliperidone palmitate once monthly. Subjects previously on 37.5 mg RLAI every 2 weeks can attain similar steady state exposure to paliperidone with 75 mg eq. paliperidone palmitate once monthly. Subjects previously on 50 mg RLAI every 2 weeks can attain similar steady state exposure to paliperidone with 100 mg eq. paliperidone palmitate once monthly. In exceptional cases, depending on the clinical situation of the subject, a starting dose of 150 mg eq. may be allowed. Subjects transitioning from a LAI antipsychotic treatment will not need a second injection on Day 8. Subsequent once monthly injections will then be administered in either the deltoid or gluteal muscle during the duration of the study. The recommended maintenance dose is 75 mg eq. monthly but flexible dosing in the range of 50 to 150 mg eq. monthly will be allowed. Flexible dosing will allow investigators to individually adjust the dosage of each subject.
Subjects who successfully complete the 6-month core treatment phase and would like to continue treatment with paliperidone palmitate may be enrolled in an extension phase until paliperidone palmitate is available in their respective country or until a maximum duration of 12 months (per subject) whichever comes first. Subjects will receive without cost paliperidone palmitate.

Intervention

DOSAGE AND ADMINISTRATION
Paliperidone palmitate will be administered once-monthly after the first 2

injections that are given one week apart (Day 1 and Day 8). In subjects transitioning from oral antipsychotics, the first dose of paliperidone palmitate will be 150 mg eq. given at Day 1 of the 6-month core treatment phase (Visit 2). The second dose of paliperidone palmitate will be 100 mg eq. given at Day 8 (* 2 days) of the 6-month core treatment phase (Visit 2b). The 3rd dose of paliperidone palmitate will be given at Day 38 of the 6-month core treatment phase (Visit 3). Subsequent doses of paliperidone palmitate will be given within the range of 50 to 150 mg eq. every 30 (* 7) days.
Subjects transitioning from previous LAI antipsychotics will receive their first injection with paliperidone palmitate in place of the next scheduled injection in the deltoid muscle. The paliperidone palmitate starting dose (Day 1) in subjects previously unsuccessfully treated with conventional depots should be guided both by the previous depot dose and the clinical status of the subject, and should be within the range of 50 to 150 mg eq. The paliperidone palmitate starting dose (Day 1) in subjects previously unsuccessfully treated with risperidone LAI (RLAI) should be guided both by the previous RLAI dose and the clinical status of the subject. Subjects previously on 25 mg RLAI every 2 weeks can attain similar steady state exposure to paliperidone with 50 mg eq. paliperidone palmitate once monthly. Subjects previously on 37.5 mg RLAI every 2 weeks can attain similar steady state exposure to paliperidone with 75 mg eq. paliperidone palmitate once monthly. Subjects previously on 50 mg RLAI every 2 weeks can attain similar steady state exposure to paliperidone with 100 mg eq. paliperidone palmitate once monthly. In exceptional cases, depending on the clinical situation of the subject, a starting dose of 150 mg eq. may be allowed. For subjects transitioned from previous LAI antipsychotic treatment, the injection at Day 8 (Visit 2b) will not be required (see Switching Guidelines below for details). Their 2nd dose of paliperidone palmitate will be given at Day 31 of the 6-month core treatment phase (Visit 3) and will be guided both by the previous LAI dose and the clinical status of the subject (within the range of 50 to 150 mg eq.). Subsequent doses of paliperidone palmitate will be given within the range of 50 to 150 mg eq. every 30 (* 7) days.
In subjects switching from oral antipsychotics, the doses on Day 1 and Day 8 will be administered through a deltoid injection on alternating arms, subsequent injections can be given either in the deltoid or the gluteal muscle. In subjects switching from LAI antipsychotics, the dose on Day 1 is given in the deltoid muscle. Subsequent once monthly injections will then be administered in either the deltoid or gluteal muscle for the duration of the study in both groups of subjects.
The recommended maintenance dose is 75 mg eq. monthly (every 30 * 7 days) but flexible dosing in the range of 50 to 150 mg eq. monthly will be allowed. The investigator may flexibly increase or decrease the dose preferably by one dosing level according to the subjects* clinical needs. Subjects will continue to return to the study site once monthly for injections and, if scheduled, study evaluations.

Study burden and risks

TREATMENT PHASE
The subject will be in the study for about 6 months and will be visiting your study doctor on day 1 (day of first injection with paliperidone palmitate; Visit 2) and 1 week later (Visit 2b). If the subject is changing from a long-acting inject able treatment, the visit 1 week after the first injection with paliperidone palmitate is not required. During the rest of the study, subject will visit the doctor monthly for 6 months (i.e., Visits 3 to 8). During these visits, subject will receive the injection with paliperidone palmitate. Inject able paliperidone palmitate must be administered by the study doctor. The first injection will be given into one of the arms and the second injection (1 week later) into the other arm. The subsequent injections will be given once monthly either in the arms or in the buttock.
A urine sample will be collected for a pregnancy test if the subject is a woman capable of becoming pregnant to make sure that she is not pregnant at Visit 8. Subject should not take any over the counter medicine (including vitamins and herbal remedies) that subject purchase without a prescription, unless the study doctor approves its use.
After subject have completed the 6-month treatment period, subject will be eligible to take part in an *extension phase* until paliperidone palmitate is available in the country or for a maximum of 12 additional months, whichever comes first. During that extension phase subject can continue receiving treatment with paliperidone palmitate monthly. The study doctor will discuss this with the subject. If subjects are eligible to participate and choose to participate in the extension part of the study, subject will be expected to see the study doctor every three months. At these visits subject will also be asked about possible side effects he/she suffered from since the previous visit and the doctor will measure the body weight.
To test the study drug paliperidone, some of the medicines subject now take may have to be stopped. Stopping these medicines may cause a return of some symptoms that were under control. For example, stopping antipsychotics may cause insomnia (difficulty sleeping), or the appearance of abnormal muscle movements. The study doctor may be able to give medicine to help control these symptoms.
One of the best known side effects of Paliperidone is a group of movement disorders known under the name of extrapyramidal disorder. Symptoms may include abnormal muscle movements, abnormal movements of the mouth, tongue or jaw, jaw spasms, drooling, slow or persistent muscle spasms, stiff muscles allowing the subject jerking movements, slow, shuffling gait, muscle cramps, tremors (shaking), abnormal eye movements, involuntary muscle contractions, prolonged contraction of the neck muscles to face an unnatural attitude, slow movements, or restlessness. Sometimes these reactions can be treated with another medicine while the subject continues to use Paliperidone.
The most common side effects subject might have when he/she take paliperidone (the study medication) are: headache and insomnia (difficulty falling or

staying asleep). These side effects are experienced at some point during treatment by at least 1 out of every 10 patients taking the drug.
One of the most well-known side effects of paliperidone is a group of movement problems known as extra pyramidal disorder. Symptoms may include: restlessness, slow or sustained involuntary contraction of muscles, abnormal movements of the eyes, mouth, tongue or jaw, repetitive, spastic or writhing movements, sensation of stiffness or tightness of the muscles, a slow shuffling walk, and a loss of expression on the face. Sometimes these side effects can be treated with another medicine while you continue on paliperidone.

There may be risks with the use of paliperidone palmitate or paliperidone that are not yet known. Sometimes, during the course of a study, we may learn new information about the treatment or study drug that might change whether or not you want to continue in the study. If this happens, your study doctor will tell you about it in a timely manner.

Contacts

Public
Janssen-Cilag

Dr. Paul Janssenweg 150
5026 RH Tilburg
NL
Scientific
Janssen-Cilag

Dr. Paul Janssenweg 150
5026 RH Tilburg
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

•Man or woman of minimally 18 years of age:
•Subjects who meet the DSM-IV criteria for schizophrenia;
•A) Subject is currently non-acute, i.e. on the same antipsychotic medication used for the treatment of schizophrenia given in an adequate dose and a CGI-S change < or = in the past 4 weeks before enrollment. Subject has been given an adequate dose of either an appropriate oral antipsychotic, or one of the following LAI antipsychotics: haloperidol decanoate, flupentixol decanoate, fluphenazine decanoate, zuclopenthixol or LAI risperidone, for an adequate period of time prior to enrollment, but current treatment is considered unsuccessful due to one or more of the following reasons:
- Lack of efficacy, or
- Lack of tolerability or safety, or
- Lack of compliance, or
- Patient*s wish
Lack of efficacy is defined as subjects with a baseline total PANSS score >= 70 or >= 2 items scoring >= 4 in the PANSS positive or negative subscale or >= 3 items scoring >= 4 in the PANSS general psychopathology subscale, as judged by the investigator.

Lack of tolerability is defined as the presence of clinically relevant (i.e., either clinically relevant according to the investigator and/or intolerable to the subject) side effects with the current antipsychotic medication.;OR,;B) Subjects with acute symptoms of schizophrenia, previously treated with an oral antipsychotic, having a baseline total PANSS score >= 80 and a baseline CGI-S score >= 4;
•The subjects may benefit from a switch of antipsychotic medication to paliperidone palmitate at the discretion of the investigator;
•In the opinion of the investigator, subject is otherwise healthy on the basis of a physical examination, medical history and vital signs performed at screening. If there are abnormalities, they must be consistent with the underlying illness in the study population;
•Subjects must have signed an informed consent document indicating that they understand the purpose of and procedures required for the study and are willing to participate in the study;
•Women must be:
-postmenopausal for at least 1 year,
-surgically sterile (have had a hysterectomy or bilateral oophorectomy, tubal ligation, or otherwise be incapable of pregnancy),
-abstinent (at the discretion of the investigator/per local regulations), or
-if sexually active, be practicing a highly effective method of birth control (e.g. prescription oral contraceptives, contraceptive injections, contraceptive patch, intrauterine device, double-barrier method [e.g. condoms, diaphragm, or cervical cap, with spermicidal foam, cream, or gel], male partner sterilization) as local regulations permit,
before entry, and must agree to continue to use the same method of contraception throughout the study. Prescription hormonal contraceptives (the *pill*) should not contain

less than 20 ug of estrogen and should not be used as the only method of birth control. Women using oral contraceptives should agree to use an additional birth control method.
•Women of childbearing potential must have a negative urine pregnancy test at screening;
•Subjects must be willing and able to fill out self-administered questionnaires;
•Willing/able to adhere to the prohibitions and restrictions specified in this protocol;
•The subject is cooperative and reliable, and agrees to receive regular injections and complete all aspects of the protocol;
•Men must agree to use a double barrier method of birth control and to not donate sperm during the study and for 3 months after receiving the last dose of study drug.

Exclusion criteria

•The subject*s psychiatric diagnosis is due to direct pharmacological effects of a substance (e.g., a drug of abuse or medication) or a general medical condition (e.g., clinically notable hypothyroidism);
•First antipsychotic treatment ever, i.e., subject has never been treated with antipsychotics before and antipsychotic treatment given in this study will be the first antipsychotic treatment that the subject will have ever received;
•On clozapine during the last 3 months;
•Subjects who remain at imminent risk of suicide even after clinical intervention;
•Serious unstable medical condition, including recent and present clinically relevant laboratory abnormalities;
•History or current symptoms of tardive dyskinesia;
•History of neuroleptic malignant syndrome;
•Subject received an investigational drug or used an investigational medical device within 3 months before the planned start of treatment, or has participated in more than one investigational drug trial in the past 12 months, or has planned use of other investigational drugs during the time frame of the trial, or is currently enrolled in an investigational study;
•Pregnant or breast-feeding female;
•Known allergies, hypersensitivity, or intolerance to risperidone or paliperidone or its excipients (refer to Section 14.1, Physical Description of Study Drug(s);
•Any condition that, in the opinion of the investigator, would compromise the well-being of the subject or the study or prevent the subjects from meeting or performing study requirements;
•Subjects who have evidence of alcohol or drug dependence (except for nicotine and caffeine) according to DSM-IV Axis 1 criteria within 6 months prior to entry. However, subjects with current substance use or abuse, with the exception of intravenous drug use, will be eligible for enrolment;
• Employees of the investigator or study center, with direct involvement in the proposed study or other studies under the direction of that investigator or study center, as well as family members of the employees or the investigator.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-02-2011
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Paliperidone Sustenna
Generic name:	Paliperidone Palmitate

Ethics review

Approved WMO

Date:	21-09-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	26-11-2010
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	17-12-2010
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-01-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-03-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-03-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-03-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-04-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-07-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-12-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	21-12-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-12-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2009-018022-30-NL
CCMO	NL33246.060.10