A 12-MONTH OPEN-LABEL STUDY TO EVALUATE THE SAFETY AND TOLERABILITY OF PREGABALIN AS ADJUNCTIVE THERAPY IN PEDIATRIC SUBJECTS 1 MONTH TO 16 YEARS OF AGE WITH PARTIAL ONSET SEIZURES AND PEDIATRIC AND ADULT SUBJECTS 5 TO 65 YEARS OF AGE WITH PRIMARY GENERALIZED TONIC-CLONIC SEIZURES

Published: 17-04-2012
Last updated: 26-04-2024

To evaluate the long-term safety and tolerability of pregabalin in pediatric subjects 1 month through 16 years of age with partial onset seizures and pediatric and adult subjects 5 to 65 years of age with (PGTC) seizures.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Seizures (incl subtypes)
Study type	Interventional

Summary

ID

NL-OMON44084

Source
ToetsingOnline

Brief title
A0081106 Epilepsy open label extension study

Condition

- Seizures (incl subtypes)

Synonym
Epilepsy with partial onset seizures

Research involving
Human

Sponsors and support

Primary sponsor: Pfizer
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Epilepsy, Open-label extension study, Partial Seizures, Pregabalin

Outcome measures

Primary outcome

Safety Endpoints:

* Adverse event (AE) data (occurrence, nature, intensity, and relationship to

study drug).

* Physical and neurological examinations.

* Vital signs.

* Growth and development parameters (height, weight, Tanner stage).

* Clinical laboratory data (hematology, chemistry, urinalysis).

* Electrocardiograms (ECGs).

* 28-day seizure rate (number of seizures per 28 day period).

* Suicidality assessments.

* Cognitive assessment battery (POS pediatric subjects 4-16 years of age only).

Secondary outcome

not applicable

Study description

Background summary

Epilepsy is a common disorder in childhood affecting 4 to 5 of every 1000 children. Although epilepsy is often well controlled with existing antiepileptic drug (AED) therapy, more than 25% of pediatric patients have seizures that are uncontrolled by currently available agents, or have adverse effects related to AEDs that complicate their seizure control. In addition, children with epilepsy often suffer from impaired academic performance and have a higher likelihood of developing behavioral difficulties, which may persist into adulthood. Early age of onset and a higher number of total lifetime seizures are the strongest correlates of academic underachievement. Therefore, the availability of a new AED that has been shown to improve seizure control and that is generally well tolerated is needed.

Pregabalin is approved in more than 100 countries, for different indications for the United States (US), European Union (EU), and Japan.

Pregabalin has not yet been studied in large numbers of pediatric patients. This study will enroll those subjects who have participated in Studies A0081041, A0081042, and A0081105 and in whom pregabalin shows acceptable safety and tolerability in those studies. In addition to subjects who have participated in Studies A0081041, A0081042 and A0081105, pediatric subjects (1 month to 16 years of age) with partial onset seizures will also be considered for direct enrollment into Study A0081106 from selected sites that are not participating in Studies A0081041, A0081042, or A0081105.
This study is one of several studies that will be conducted to assess the safety and efficacy of pregabalin in pediatric subjects with epilepsy and to address post approval commitments to US and EU regulatory authorities.
Complete information for pregabalin may be found in the Single Reference Safety document which for this study is the Investigator Brochure.

Study objective

To evaluate the long-term safety and tolerability of pregabalin in pediatric subjects 1 month through 16 years of age with partial onset seizures and pediatric and adult subjects 5 to 65 years of age with (PGTC) seizures.

Study design

Study A0081106 is a 12 month, open-label, flexible dose, multicenter study to

evaluate the tolerability and safety of pregabalin administered BID as adjunctive therapy in pediatric subjects 1 month to 16 years of age with partial onset seizures and pediatric and adult subjects 5 to 65 years of age with (PGTC) seizures. Subjects who have completed the studies A0081041, A0081042, or A0081105 will be eligible for screening for this study.
For subjects who have participated in, but did not complete Studies A0081041, A0081042, or A0081105, eligibility for Study A0081106 will be considered on a case by case basis. A minimum of 4 weeks in the double-blind treatment phase of either Study A0081041 or Study A0081105 will be required for consideration of enrollment into Study A0081106. Selected sites that are not participating in studies A0081041 or A0081042 may screen and enroll pediatric subjects (1 month to 16 years of age) with partial onset seizures directly into Study A0081106 provided they meet the study inclusion/exclusion criteria. When subject enrollment for Studies A0081041 and A0081042 is complete, sites that were enrolling subjects in Studies A0081041 or A0081042 may screen and enroll pediatric subjects (1 month to 16 years of age) with partial onset seizures directly into Study A0081106 until enrollment into Study A0081106 is closed by Pfizer.

Intervention

The day of the last visit (completion of taper phase) of Studies A0081041, A0081042, and A0081105 is designated as Day 1 (Visit 1A) of this study. Baseline values for analysis of change in safety endpoints will be the assessments made prior to initiating double-blind dosing at Visit 1 of Studies A0081041, A0081042, or A0081105. For subjects directly entering Study A0081106 without participation in one of the studies above, baseline values for analysis of change in safety endpoints will be the assessments made at the first visit (Screening Visit 1B) of this study.
For pediatric subjects, pregabalin dosing will initiate at the daily dose of 2.5 mg/kg/day (subjects *30 kg) or 3.5 mg/kg/day (subjects <30 kg) at this visit. Adult subjects who enroll in this study following participation in Study A0081105 will initiate dosing at 150 mg/day.
All seizures experienced will be self-recorded by the subject or recorded by their parents/legally acceptable representative as appropriate, in a daily seizure diary beginning at Visit 1 and subsequently throughout the entire study. Subjects will return for the designated assessments of safety, tolerability, and drug accountability at Week 1 (Visit 2), Month 1 (Visit 3), Month 2 (Visit 4), Month 4 (Visit 5), Month 6 (Visit 6), Month 9 (Visit 7), Month 12/Early Termination (Visit 8), and Follow-up (Visit 9). Investigator site staff will contact the subject and/or parent/caregiver by telephone at least monthly between visits, to address questions, assess safety and adverse events, and ensure compliance with study directives.
At Visit 2 and subsequent visits thereafter, the investigator or designee will review seizure diary data and tolerability with the subject and may adjust the dose at his/her discretion. For pediatric subjects (1 month to 16 years of age) doses may remain the same or be adjusted upward in increments of no more than

2.5 mg/kg/day to daily dose levels of 5.0, 7.5, or 10.0 mg/kg/day. For pediatric subjects with body weight <30 kg, doses may be adjusted in increments of no more than 3.5 mg/kg/day to daily dose levels of 7.0, 10.5, or 14.0 mg/kg/day. For adult subjects (17 to 65 years of age) doses may be adjusted in increments of 150 mg/day to daily dose levels of 300, 450, or 600 mg/day.

Study burden and risks

The most common side effects reported in subjects who took pregabalin in past studies are:
* dizziness
* sleepiness

Contacts

Public
Pfizer

East 42nd Street, 235
New York 10017
US
Scientific
Pfizer

East 42nd Street, 235
New York 10017
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

Inclusion Criteria for Subjects who have Participated in Studies A0081041, A0081042, or A0081105 - Subject eligibility should be reviewed and documented by an appropriately qualified member of investigator*s study team before subjects are included in study. Subjects must meet all of the following inclusion criteria to be eligible for enrollment into the study: ;1. Evidence of a personally signed and dated informed consent document indicating that the subject (or a legally acceptable representative) has been informed of all pertinent aspects of Study A0081106. When there are 2 parents or 2 legally acceptable representatives, consent should be obtained from both of the child*s parents/legal representatives if present at the meeting where the informed consent document is signed. Subject to local regulations whenever the minor is able to give assent, the minor*s assent must be obtained. ;2. Subjects and/or parents/legally acceptable representative who are willing and able to comply with scheduled visits, treatment plan, laboratory tests, and other study procedures. ;3. Male and female subjects who have participated in and completed, or participated in Studies A0081041, A0081042, or A0081105. For subjects who have participated in, but did not complete Studies A0081041, A0081042, or A0081105, eligibility for Study A0081106 will be reviewed with a member of the Pfizer study team to determine further eligibility. Subjects are required to have completed a minimum of 4 weeks of double blind treatment in Studies A0081041 or A0081105 to be considered potentially eligible for Study A0081106. ;4. Male and female epilepsy subjects who have participated in either Study A0081041 or Study A0081042, 1 month to 16 years of age inclusive on the date of the Screening Visit with diagnosis of epilepsy with seizures classified as simple partial, complex partial or partial becoming secondarily generalized, according to the International League Against Epilepsy (ILAE 2010) Diagnosis must be established by: Subject*s history (eg, description of seizures excluding confounding disorders such as pseudoseizures, syncopes etc) family history and neurological exam; Subjects must have had a contrast enhanced computed tomography (CT) or magnetic resonance imaging (MRI) scan of the brain and EEG testing prior to Study A0081041 or Study A0081042. Results must have been consistent with the diagnosis of focal onset epilepsy and must have demonstrated that no abnormality was likely to be progressive. ;5. Male and female subjects 5 65 years of age who have participated in Study A0081105 with a diagnosis of epilepsy (ILAE 2010) with PGTC seizures and who continue to satisfy seizure related inclusion criteria for that study (see Protocol A0081105). ;6. Currently receiving 1 to 3 antiepileptic drugs at Visit 1. Benzodiazepine medication used on a regular basis will be considered 1 of the concurrent antiepileptic treatments. The vagus nerve stimulator (VNS) is allowed and considered 1 of the 3 antiepileptic treatments. ;7. A 12 lead ECG at (the last visit of Studies A0081041, A0081042, A0081105) without significant abnormal findings.;Inclusion Criteria for Directly Enrolling Subjects (i.e., partial onset seizure subjects who have not participated in either Studies A0081041 or A0081042) ;1. Evidence of a personally signed and dated informed consent document and willing and able to complete study related visits and procedures as indicated in Inclusion Criteria 1 and 2 above.;2. Male and female epilepsy subjects, 1 month to 16 years of age inclusive on the date of the Screening Visit with diagnosis of epilepsy with seizures classified as simple partial, complex partial or partial becoming secondarily generalized, according to the International League Against Epilepsy (ILAE 20103) Diagnosis must be established by: Subject*s history (eg, description of seizures excluding confounding disorders such as pseudoseizures, syncopes

etc.) family history and neurological exam; Subjects must have had a contrast enhanced computed tomography (CT) or magnetic resonance imaging (MRI) scan of the brain and EEG testing within 2 years of Study A0081106 Visit 1. Results must be consistent with the diagnosis of focal onset epilepsy and must demonstrate that no abnormality is likely to be progressive; Subjects must have had an average of at least 3 seizures per month in the 3 months prior to screening.;3. Currently receiving a stable dose of 1 to 3 antiepileptic drugs (stable within 28 days prior to screening). Benzodiazepine medication used on a regular basis at a stable dosage will be considered 1 of the concurrent antiepileptic treatments. The vagus nerve stimulator (VNS) is allowed and considered 1 of the 3 antiepileptic treatments.;4. A 12 lead ECG at screening without clinically significant abnormal findings as determined by the investigator.

Exclusion criteria

1. Lennox Gastaut syndrome, Infantile Spasms, Absence seizures, BECT (Benign epilepsy with centrotemporal spikes) and Dravet syndrome. A current diagnosis of febrile seizures, or seizures related to an ongoing acute medical illness. Any febrile seizures within 1 year of screening. ;2. Status epilepticus within 1 year prior to Visit 1 of this study. ;3. Seizures related to drugs, alcohol, or acute medical illness.;4. Progressive structural CNS lesion or a progressive encephalopathy. Progressive inborn errors of metabolism.;5. Known or suspected chronic hematologic, hepatic or renal disease (AST and ALT above 3 times the upper limit of normal; or bilirubin, BUN, or creatinine above 2 times the upper limit of normal within the previous 6 months for infants, children and adolescents aged 6 months or more, or at any postnatal period for infants younger than 6 months). Estimated creatinine clearance (CLcr) <60 mL/min for subjects *17 yr and <80 mL/min/1.73m2 (using age appropriate equations) for subjects <17 years of age. ;6. Other severe acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or investigational product administration or may interfere with the interpretation of results and, in the judgment of the investigator, would make the subject inappropriate for entry into this study.;7. Pregnant or nursing females (females who are menarchal must have a negative urine pregnancy test); menarchal females of childbearing potential who are unwilling or unable to use an acceptable method of contraception, as outlined in the protocol, until completion of follow-up procedures.;8. Taking any non antiepileptic (non AED) medication that could alter the effectiveness of the subject*s medication, response, seizure frequency or characteristics. Medications for Attention Deficit/Hyperactivity Disorder will be permitted if medication doses are stable and remain so throughout the duration of the study. A ketogenic diet will also be allowed given that the diet is adhered to for the duration of the study. ;9. Taking or have taken any other investigational drug (aside from participation in Studies A0081041, A0081042 or A0081105) within the last 30 days prior to screening. ;10. The concomitant use of gabapentin is prohibited.;11. Use of cocaine, phencyclidine (PCP), or other illegal or illicit drugs is prohibited. Use of amphetamines, barbiturates, opiates, or benzodiazepines without a valid current prescription is prohibited.;12. Unwilling or unable to comply with the Life Style Guidelines.;13. Subjects not reasonably expected to complete the study.;14. Any subjects considered at risk of suicide based on the MINI KID and C SSRS Lifetime (subjects *6 years of age) or CBCL (subjects <6 years of age) or likely to self harm

based on clinical judgment. Based on the judgment of the investigator, a subject should be excluded or a risk assessment should be done by a qualified mental health professional based on responses to suicidality assessments and if the subject has had suicidal ideation in the last 6 months prior to screening, suicidal behaviors or attempts in the past year, or current major psychiatric disorders that are not explicitly permitted in the inclusion/exclusion criteria. A risk assessment should also be performed in any child <6 years of age who has ever exhibited any potentially self injurious or high risk behaviors such as hurting himself or herself, or unusual behaviors such as running into traffic or using items as weapons (eg, knife, bat).;15. For subjects who have not participated in Studies A0081041, A0081042, or A0081105 and enrolling directly into Study A0081106, treatment with pregabalin for any reason within 60 days prior to screening, or prior participation in a pregabalin clinical study is prohibited.;16. Known allergy or intolerance to pregabalin or other *2* ligands (eg, gabapentin).;17. Subjects, or subjects whose parents/legally acceptable representatives are investigational site staff members; and subjects, or subjects whose parents/legally acceptable representative are Pfizer employees directly involved in the conduct of the study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	8
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Lyrica
Generic name:	Pregabalin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	17-04-2012
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	03-10-2012
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	27-11-2012
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	04-12-2012
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	28-08-2013
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	22-10-2013
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	30-10-2013
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	16-05-2014
Application type:	Amendment
Review commission:	METOPP: Medisch Ethische Toetsing Onderzoek bij Patienten en Proefpersonen (Tilburg)

Approved WMO

Date:	10-06-2014
Application type:	Amendment
Review commission:	METOPP: Medisch Ethische Toetsing Onderzoek bij Patienten en Proefpersonen (Tilburg)
Approved WMO Date:	08-08-2014
Application type:	Amendment
Review commission:	METOPP: Medisch Ethische Toetsing Onderzoek bij Patienten en Proefpersonen (Tilburg)
Approved WMO Date:	27-08-2014
Application type:	Amendment
Review commission:	METOPP: Medisch Ethische Toetsing Onderzoek bij Patienten en Proefpersonen (Tilburg)
Approved WMO Date:	08-12-2016
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	EUCTR2011-001412-65-NL
ClinicalTrials.gov	NCT01463306
CCMO	NL38823.028.12