LÆGEMIDDELSTYRELSEN
DANISH MEDICINES AGENCY

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21 April 2020
Case No.: 2020032081
Reference:
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A Phase 2b Multicentre, Randomized, Double-blind, Placebo-controlled, Parallel Group Dose Finding, Safety, Tolerability and Efficacy Study of PQ912 in Subjects with Mild Cognitive Impairment and Mild Dementia due to Alzheimer's Disease (The VIVIAD Trial)., protocol no./code PBD 01180, EudraCT no. 2019-003532-23

Decision:

The Danish Medicines Agency (DKMA) authorises the above-mentioned clinical trial on medicinal products. The authorisation is given pursuant to § 88(1) of the Danish Medicines Act.[1]

The authorisation is valid through **31 May 2023**

The trial covers the following investigational medicinal products:

- PQ912,
- Placebo

It is a condition for the authorisation that we are **notified** of any of the following events:

- Trial duration is extended beyond the date in authorisation letter
- Addition of new investigator sites (incl. an updated xml-file)
- Changes of principal/coordinating investigator (incl. an updated xml-file)
- Changes of CRO/applicant
- National end of trial

On the webpage http://laegemiddelstyrelsen.dk/en/topics/side-effects-and-trials/clinical-trials/trials-in-humans/guideline-for-applications-for-authorisa---in-humans/amendments-to-clinical-trials-.aspx you will find a summary of the changes that we consider substantial and therefore must be approved by us.

We have based our assessment on the following:

- Cover Letter, Signed 10 March 2020
- E-mail confirmation of EudraCT No. for study PBD-01180
- Clinical Trial Application form (pdf+xml), Signed 10 March 2020
- Study Protocol Version 1.0, dated 20 February 2020
- Danish Protokoltillæg Version 1.0, dated 27 February 2020
- Danish Protokolresumé Version 1.0, dated 27 February 2020
- List of CA submissions and opinions, dated 04 March 2020
- Investigator's Brochure Version 11.1, dated 05 March 2020
- Data Safety Monitoring Board Charter, Draft,
- Statement on active trials with PQ912, dated 23 January 2020

[1] Danish act no. 1180 of 12 December 2005 on medicinal products as amended by act no. 538 of 8 June 2006 and act no. 1557 of 20 December 2006

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- PQ912 IMPD: Intro, Drug substance and Placebo version 1.0, dated December 2019 and Drug product version 1.0, dated January 2020
- Certificates of Analysis
- Certificates of Compliance
- BSE/TSE Statement
- Manufacturer Authorisation/Importer Authorisation
- GMP Certificates
- Labels
- Instructions for Use
- Main Study ICF Version 1.0, dated 24 February 2020
- Power of Attorney
- Subject Card
- "Forsøgspersoners rettigheder ... " leaflet
- Recruitment Material (Subjects, Relatives)
- Geriatric Depression Scale - Short Form,
- MMSE, dated 06 Oct 2015
- Amsterdam IADL Questionnaire
- Winterlight test
- Cogstate Neuropsychological Tests
- Category Fluency Test
- Letter Fluency Test
- Test Supervisor Script
- Digit Symbol Substitution Test (WAIS-IV test)
- Letter of Grounds for Non-Acceptance, dated 07 April 2020
- Response to GNA, dated 17 April 2020

Prior to initiation, the trial has to be authorised by a research ethics committee.

We kindly refer to the enclosed extract of the Danish legislation.

If you have any questions, feel free to contact Lene Grejs Petersen

T: + 45 44 88 93 05 **E:lgp@dkma.dk**

Best Regards

Mette Andersen

Copy: Research Ethics Committee, The Capital Region of Denmark

Legal obligations related to the conduct of clinical trials on medicinal products

Good clinical practice (GCP)
Clinical trials on medicinal products must be conducted in accordance with good clinical practice, cf. section 88(2) of the Danish Medicines Act[2], and the Danish executive order on good clinical practice in clinical trials of medicinal products in humans[3].

Good manufacturing practice (GMP)
The medicinal products of clinical trials must comply with the current standards for good manufacturing practice, cf. section 92(1) of the Danish Medicines Act, and the Danish executive order on the manufacturing and import of medicinal products and intermediary products. Investigational medicinal products manufactured in or imported from a third country (a non EU/EEA country) must comply with good manufacturing standards (at least equivalent to EU GMP).
In order to ensure that the investigational products manufactured in a third country comply with EU GMP or similar requirements, it is the practice of the Danish Medicines Agency to require that documents in support thereof be made available on request. This could be in the form of a GMP certificate issued by an EU authority and/or an EU GMP audit report from a Qualified Person and/or other EU GMP report issued by a regulatory body. This also applies to sites that manufacture active biological substances. In the case of countries with mutual recognition agreements (Canada, Switzerland, Australia and new Zealand) the above documents may be replaced by a GMP certificate and/or manufacturing licence issued by a regulatory body in the concerned MRA country.

Good distribution practice (GDP)
Distribution of medicinal products to sites must be in accordance with GDP i.e. the Danish executive order on distribution of medicinal products. The Danish Medicines Agency must authorise wholesale or retail distribution of medicinal products, i.e. distribution of medicinal products, cf. section 39(1) of the Danish Medicines Act.

Free provision of test products
Investigational medicinal products and any devices used to administer investigational medicinal products must be supplied free of charge to trial subjects, cf. section 13 of the Danish executive order on good clinical practice in clinical trials of medicinal products in humans.

Amendments to clinical trials
Section 4 of the Danish executive order on clinical trials of medicinal products in humans establishes when amendments to a clinical trial require authorisation from the Danish Medicines Agency. Please also see 'Amendments to clinical trials' available on our website www.dkma.dk . Direct link: http://laegemiddelstyrelsen.dk/en/licensing/clinical-trials/trials-in-humans/guideline-for-applications-for-authorisation-of-clinical-trials-of-medicinal-products-in-humans/amendments-to-clinical-trials-

Reporting of adverse reactions occurring during the trial period
The sponsor must

- *immediately* inform the Danish Medicines Agency of any suspected unexpected serious adverse reactions that occur during the trial.
- once a year submit a list of all suspected serious adverse reactions that have occurred during the trial period as well as a report on the safety of the trial subjects, cf. section 89 (2) of the Danish Medicines Act.

Please notice that even though it is possible to select the Danish Medicines Agency as receiver of SUSARs in EVWeb, we are not able to process and acknowledge a case from a sender ID which is not configured as

[2] Danish act no. 1180 of 12 December 2005 on medicinal products as amended by act no. 538 of 8 June 2006 and act no. 1557 of 20 December 2006

[3] Danish executive order no. 744 of 29 June 2006 on good clinical practice in clinical trials of medicinal products in humans (Danish title: Bekendtgørelse nr. 744 af 29. juni 2006 om god klinisk praksis i forbindelse med kliniske forsøg med lægemidler på mennesker).

sender in the Danish Medicines Agency database. It is therefore advised to contact our colleagues handling E2B submissions and ask for configuration. They can be contacted at E2B@dkma.dk.

Termination of a trial

The sponsor must

- notify the Danish Medicines Agency when the trial has been completed no later than 90 days thereafter
- inform the Danish Medicines Agency (within 15 days) if a trial is discontinued earlier than planned. The reasons for stopping the trial must be given cf. 89 of the Danish Medicines Act.
- Please be reminded that a *Declaration of the End of a Clinical Trial* should be used, which can be found at: https://laegemiddelstyrelsen.dk/en/licensing/clinical-trials/trials-in-humans/guideline-for-applications-for-authorisation-of-clinical-trials-of-medicinal-products-in-humans/

Study results

- Results should be reported to the EudraCT database as soon as possible and no later than one year after end of trial according to http://ec.europa.eu/health/files/eudralex/vol-10/2012_302-03/2012_302-03_en.pdf.
- Please be reminded that results from clinical trials with children, sponsored by MAH, should be published in the EudraCT database no later than 6 months after end of trial in accordance with the EU guideline 1901/2006.
- The Danish Medicines Agency do not wish to be informed about this or receive the final study report. The Danish Medicines Agency will review the EudraCT database regarding study results.
- Please note that phase I trials (including FIH) in adults will not be made public at www.clinicaltrialsregister.eu. That is why evidence for the publication of the results should be separately submitted to DKMA in accordance with the Declaration of Helsinki, Article 30.

Please note that missing data/study results reporting to the Danish Medicines Agency is punishable by fine or imprisonment for up to four months in accordance with the Medicines Act §104 (1).