



Clinical trial results:

A multi-centre clinical trial evaluating patients' ability to independently and safely use the medicinal product indicated in the treatment of erectile dysfunction

Summary

EudraCT number	2018-002597-41
Trial protocol	PL
Global end of trial date	26 April 2019

Results information

Result version number	v1 (current)
This version publication date	10 May 2020
First version publication date	10 May 2020

Trial information

Trial identification

Sponsor protocol code	O321
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Adamed Pharma S.A.
Sponsor organisation address	Pieńków, ul. Mariana Adamkiewicza 6A, Czosnów, Poland, 05-152
Public contact	Coordinating Investigator, Roland Dadej, 48 501516005, urologia@vp.pl
Scientific contact	Coordinating Investigator, Roland Dadej, 48 501516005, urologia@vp.pl

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 April 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 April 2019
Global end of trial reached?	Yes
Global end of trial date	26 April 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to assess whether patients using specially designed diagnostic tool can independently make safe decision about whether it is appropriate for them to use or not use sildenafil in dose of 50 mg.

Protection of trial subjects:

IMP used in the study has Marketing Authorization and is used according to approved SmPC. The only additional diagnostic procedures performed according to study protocol are laboratory blood test and cardiac stress test.

Background therapy:

Routine care

Evidence for comparator:

Not applicable - the comparator has not been used.

Actual start date of recruitment	07 December 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 403
Worldwide total number of subjects	403
EEA total number of subjects	403

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	292
From 65 to 84 years	108

85 years and over	3
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Subject disposition

Recruitment

Recruitment details:

Patients recruitment took place from 07 Dec 2018 until 26 Apr 2019. Patients were recruited in clinical sites in Poland.

Pre-assignment

Screening details:

No screening procedures applied. Patients who signed informed consent, met all inclusion criteria and none of the exclusion criteria were enrolled into the study.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not applicable.

Arms

Are arms mutually exclusive?	No
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Arm title	Sildenafil 50 mg
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Arm description:

Each patient was given a package with 2 tablets of IMP, containing 50 mg sildenafil citrate as an active substance (Visit 1). Patients were instructed to use no more than 1 tablet a day and to return for Visit 2 - scheduled within 3 weeks from Visit 1. During visit 2 it was verified: whether patient had used the medication; the patients' perception on efficacy of used medication; whether and what adverse drug reactions had occurred.

Arm type	Experimental
Investigational medicinal product name	Maxon, 50 mg, film-coated tablets
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Not more than one tablet a day.

Arm title	Diagnostic tool
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Arm description:

All patients enrolled into the study were given diagnostic tool at Visit 1. Each patient was instructed to use diagnostic tool without consulting the physician. The patient's final decision was not revealed to the physician - diagnostic tool was returned in a sealed envelope.

After that, the physician performed subjective and objective examination to decide whether it is appropriate for the patient to use sildenafil in dose of 50 mg. Each patient was directed to perform laboratory blood testing. Additionally patients with cardiac disorders were directed to perform cardiac stress test.

These procedures were used to further assess coherence of answers given by the patients on selected questions contained in the diagnostic tool with the findings implied by results of these tests.

Arm type	Observational
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No investigational medicinal product assigned in this arm

Number of subjects in period 1	Sildenafil 50 mg	Diagnostic tool
Started	20	403
Completed	20	403

Baseline characteristics

Reporting groups

Reporting group title	overall trial
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Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	403	403	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	292	292	
From 65-84 years	108	108	
85 years and over	3	3	
Gender categorical			
Units: Subjects			
Female	0	0	
Male	403	403	

End points

End points reporting groups

Reporting group title	Sildenafil 50 mg
Reporting group description:	
Each patient was given a package with 2 tablets of IMP, containing 50 mg sildenafil citrate as an active substance (Visit 1). Patients were instructed to use no more than 1 tablet a day and to return for Visit 2 - scheduled within 3 weeks from Visit 1. During visit 2 it was verified: whether patient had used the medication; the patients' perception on efficacy of used medication; whether and what adverse drug reactions had occurred.	
Reporting group title	Diagnostic tool
Reporting group description:	
All patients enrolled into the study were given diagnostic tool at Visit 1. Each patient was instructed to use diagnostic tool without consulting the physician. The patient's final decision was not revealed to the physician - diagnostic tool was returned in a sealed envelope. After that, the physician performed subjective and objective examination to decide whether it is appropriate for the patient to use sildenafil in dose of 50 mg. Each patient was directed to perform laboratory blood testing. Additionally patients with cardiac disorders were directed to perform cardiac stress test. These procedures were used to further assess coherence of answers given by the patients on selected questions contained in the diagnostic tool with the findings implied by results of these tests.	

Primary: The proportion of patients who will independently make a safe decision on the possibility of taking sildenafil in dose 50 mg.

End point title	The proportion of patients who will independently make a safe decision on the possibility of taking sildenafil in dose 50 mg. ^{[1][2]}
End point description:	
In the study 97.2 % (379) of patients included in the analysis (390) of primary endpoint had made safe decision based on diagnostic tool. Taking into consideration the confidence interval (95% CI was in the range of 95.0% - 98.4%), the proportion of safe answers was fairly higher than the minimal value specified in the study protocol (i.e. the lower end of CI >80%).	
End point type	Primary
End point timeframe:	
Visit 1 (after the patient used the diagnostic tool and both patient and investigator made independent decision on patient's possibility of taking sildenafil).	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: For the primary endpoint the confidence interval for proportion has been calculated. According to study protocol, the lower end of CI should be over 80%. There was no comparison group. The system requires that for statistical analysis at least 2 Comparison groups are chosen. Otherwise, the full data set cannot be validated positively. Thus, section related to statistical analysis has not been filled. The results of the endpoint have been described in "end point description" and "end point values

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Both arms are analysed independently. There is no comparison between the groups. Therefore, this endpoint refers only to Arm: Diagnostic tool.

The section related to statistical analysis has not been filled. The results of the endpoint have been described in "end point description" and "end point values".

End point values	Diagnostic tool			
Subject group type	Reporting group			
Number of subjects analysed	390			
Units: Percentage of patients				
number (confidence interval 95%)	97.2 (95.0 to 98.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: The proportion of patients whose decision to take sildenafil in 25 mg or 50 mg dose is coherent with the Investigator's opinion

End point title	The proportion of patients whose decision to take sildenafil in 25 mg or 50 mg dose is coherent with the Investigator's opinion ^[3]
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End point description:

In the study 60% (234) of patients included in the analysis of this endpoint (390) have made decision coherent with decision of investigator (95% CI was within 55.1% - 64.7%). In case of 156 patients (40%) who have given different answer in most cases these answers were safe (even though doctor decided that patient is allowed to take sildenafil, patient based on the diagnostic tool decided either not to take the drug or to take lower dose than is feasible according to physician).

End point type	Secondary
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End point timeframe:

Visit 1.

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Both arms are analysed independently. There is no comparison between the groups. Therefore, this endpoint refers only to Arm: Diagnostic tool. As for primary endpoint, the section related to statistical analysis has not been filled. The results of the endpoint have been described in "end point description" and "end point values".

End point values	Diagnostic tool			
Subject group type	Reporting group			
Number of subjects analysed	390			
Units: Percentage of patients				
number (confidence interval 95%)	60.0 (55.1 to 64.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: The proportion of patients who will make a decision coherent with the decision indicated by the answers given when using the diagnostic tool.

End point title	The proportion of patients who will make a decision coherent with the decision indicated by the answers given when using the diagnostic tool. ^[4]
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End point description:

In the study 83.4% (317) of patients taken to the analysis of this endpoint (380) made decision, that

was in line with decision indicated by diagnostic tool (95% CI was within 79.4% - 86.8%). Age, education, previous experience with PDE5 inhibitors or whether patient has medical occupation does not seem to affect patient's compliance with diagnostic tool.

End point type	Secondary
End point timeframe:	
Visit 1	

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Both arms are analysed independently. There is no comparison between the groups.

Therefore, this endpoint refers only to Arm: Diagnostic tool.

As for primary endpoint, the section related to statistical analysis has not been filled. The results of the endpoint have been described in "end point description" and "end point values".

End point values	Diagnostic tool			
Subject group type	Reporting group			
Number of subjects analysed	380			
Units: Percentage of patients				
number (confidence interval 95%)	83.4 (79.4 to 86.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: For a selected group of patients with cardiac disorders who will receive the IMP, a descriptive analysis will be carried out.

End point title	For a selected group of patients with cardiac disorders who will receive the IMP, a descriptive analysis will be carried out. ^[5]
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End point description:

20 patients with cardiac disorders were given two tablets of medicinal product. Among them 18 patients used both tablets, while 2 patients used only one of given tablets - one of patients due to health concerns related to arrhythmia, second due to lack of efficacy. Finally 17 patients were analysed.

End point type	Secondary
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End point timeframe:

From Visit 1 until Visit 2

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Both arms are analysed independently. There is no comparison between the groups.

Therefore, this endpoint refers only to Arm: Sildenafil 50 mg.

As for primary endpoint, the section related to statistical analysis has not been filled. The results of the endpoint have been described in details in the field "end point description".

End point values	Sildenafil 50 mg			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Number of patients	17			

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Information regarding AEs were collected throughout the study i.e. from 07 Dec 2018 until 26 Apr 2019. For individual patient - time from Visit 1 until Visit 2 (the actual maximum time between Visit 1 and Visit 2 was 12 weeks).

Adverse event reporting additional description:

Safety analysis set included all patients who were given study treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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Reporting groups

Reporting group title	Sildenafil 50 mg
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Reporting group description: -

Serious adverse events	Sildenafil 50 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 20 (5.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Sildenafil 50 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 20 (15.00%)		
General disorders and administration site conditions			
Drug ineffective			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported