Observational plan

Title	**ODA - Evaluation of effectiveness and therapeutic response to Preductal® OD 80 mg in daily practical use for chronic stable angina pectoris.**
Protocol number	**DIM-06795-001-RUS**
Trademark	Preductal® OD 80 mg
INN	Trimetazidine
Dosing	80 mg Once Daily
Pharmaceutical form	Prolonged-release hard capsule
National coordinator	Prof. Glezer Maria

Contents

1. Introduction and objectives

1.1. Introduction

Chronic angina is a common manifestation of ischaemic heart disease. Medical treatments are the main stay approach to reduce the occurrence of angina and improve patients' quality of life. Chronic stable angina is a common and progressive disease which has a major impact on patient quality of life and imposes a high financial and medical burden on society. Given the range of agents now available, optimal medical therapy - which according to International and National guidelines for CAD patients treatment is the preferred option in the majority of patients with that disease - offers the opportunity for effective control. However, recent studies suggest that management remains suboptimal in up to the third of patients and that physicians often underestimate the extent to which angina continues to limit patients' lives[i].

Approximately 50% of patients with cardiovascular disease and/or its major risk factors have poor adherence to their prescribed medications. Finding novel methods to help patients improve their adherence to existing evidence-based cardiovascular drug therapies has enormous potential to improve health outcomes while potentially reducing health care costs.[ii]

Interventions that may successfully improve adherence should include patient education and empowerment, patient reminders, frequent clinic visits, or telephone calls from staff or physicians. Every attempt should be made to simplify the patient's drug regimen by reducing the number of pills per day and by minimizing medication costs wherever possible.[iii] Simpler, less frequent dosing regimens resulted in better compliance across a variety of therapeutic classes[iv]

Preductal® OD 80 mg is a prolonged-release hard capsule containing 80 mg of trimetazidine, allowing a once-a-day dosage regimen. The rationale for developing a new modified release 80 mg intake is to improve patient's comfort and compliance, by offering the advantages of once a day formulation in comparison to the b.i.d. modified release 35 mg or t.i.d. immediate release 20 mg formulations registered in the treatment of stable angina pectoris.

The anti-ischemic and antianginal efficacy of trimetazidine was demonstrated in a range of randomised studies, controlled versus placebo or active comparator, including a total of 3,985 patients with chronic stable angina, treated with Trimetazidine 20 mg or Trimetazidine MR 35 mg for a duration ranging from 2 weeks to 6 months, in monotherapy or in combination with another antianginal treatment.[v],[vi],[vii] Based on its mechanism of action that directly targets the cardiac cell, trimetazidine provides robust antianginal efficacy, reduces the myocardial ischemic burden, and improves exercise capacity, and offers long-term cardioprotection in a range of clinical situations in the patients with angina, including those with a history of myocardial infarction, previous percutaneous coronary intervention, or with concomitant diabetes and/or left ventricular dysfunction.[viii], [ix], [x]. Moreover, data from clinical trials suggest that trimetazidine may offer long-term cardioprotection in a range of cardiovascular patients such as patients with a history of myocardial infarction[xi] or with ischemic heart failure[xii].

The positive benefit-risk balance of trimetazidine in stable angina was recently reaffirmed in an assessment of the European Medicines Agency in 2012, and recognized in the latest European guidelines for the treatment of stable CAD in 2013.[xiii]

1.2. Objectives

Aim of this non-interventional study (NIS) is to analyze effectiveness and tolerability of Preductal® OD 80 mg use in symptomatic patients with angina pectoris over a 3-month treatment under daily practice conditions.

It is of particular interest to collect data on anti-anginal effectiveness, symptomatic classification and compliance/adherence, as well as general tolerability in patients treated with Preductal® OD 80 mg in compliance with the summary of product characteristics.

Thereby the following questions shall be analyzed:

1) Effect of Preductal® OD 80 mg therapy on number of angina attacks

2) Effect of Preductal® OD 80 mg therapy on use of short-acting nitrates

3) Effect of Preductal® OD 80 mg therapy on symptomatic classification (CCS class) (see app. 1)

4) Effect of Preductal® OD 80 mg therapy on patients daily activity

5) Influence of Preductal® OD 80 mg therapy on patients' compliance/adherence (see app. 3)

6) General tolerance and adverse events (AE) / adverse drug reactions (ADR) under Preductal® OD 80 mg therapy

9) General assessment by physician of Preductal® OD 80 mg therapy in symptomatic patients with angina pectoris

2. Methods and documentation

2.1. Study type and rationale for choice of study type

ODA - is a non-interventional, multicentric, prospective study in which findings from patient treatment with medicinal products are analyzed by descriptive methods; in this context treatment, diagnosis and monitoring is not predefined by a fixed study protocol, but rather defined by practical use of the medicinal products, according to decisions of the attending physician.

To be able to evaluate the above defined topics with a sufficient number of patients, a multicentric, prospective non-interventional study is most appropriate. This allows analysis of Preductal® OD 80 mg therapy under "real-life" conditions without any further regulations or influences posed on the physician (e.g. study protocol). Special care has to be taken that inclusion of patients into the non-interventional study is exclusively determined by the decision of the physician regarding medical meaningfulness and necessity of treatment with Preductal® OD 80 mg.

2.2. Sample size

An overall population of 4000 patients is estimated to be necessary, under consideration of practicality of the study in daily routine use, to achieve a representative patient population within the given disease pattern.

2.3. Selection of physicians

This non-interventional study will involve 400 general practitioners, cardiologists based in outpatient clinics.

2.4. Selection of patients

Observation should take place in patients with chronic stable angina, which are considered to be eligible for Preductal® OD 80 mg treatment by their physician. Each participating physician should document 10 patients with chronic stable angina pectoris in an ambulatory setting.

2.4.1. Participant inclusion criteria

Patients with confirmed diagnosis of Chronic Coronary Artery Disease and stable angina will be included into the study. Special care has to be taken that inclusion of patients into the non-interventional study is exclusively determined by the decision of the physician regarding medical meaningfulness and necessity of treatment with Preductal® OD 80 mg. For participation in the study patient have to sign an informed consent form either.

2.4.2. Participant noninclusion criteria

- Age over 75 years or under 18 years

- Hypersensitivity to the active substance or to any of the excipients listed in Preductal® OD 80 mg SmPC
- Parkinson disease, parkinsonian symptoms, tremors, restlessleg syndrome, and other related movement disorders
- Severe renal impairment (creatinine clearance < 30ml/min)
- Moderate renal impairment (creatinine clearance [30-60] ml/min)
- Stable angina pectoris FC IV
- MI in the last 3 months before inclusion
- Stroke/TIA in the last 3 months before inclusion
- Uncontrolled HT (BP over 180/100 mm Hq) inspite of hypotensive therapy
- Pregnancy, breastfeeding

2.5. Treatment during the study

Doctor makes adjustments to the therapy in patients with persistent angina after the failure of previous treatment, according to his/her personal experience and current medical practice, as well as to indications and dosages stated in the instructions for use (SPCs) for the corresponding medication.

In case of therapy adjustment at the moment of inclusion doctor have to specify both treatments: before inclusion and modifications made at the moment of inclusion. There are necessary blocks in CRF.

2.5.1. Treatment with Preductal® OD 80 mg

Treatment with Preductal® OD 80 mg takes place according to usual therapeutic routine procedures of the attending physician and within the framework defined by the approved indication and the Summary of Product Characteristics (SPC).

Preductal® OD 80 mg is indicated in adults for long-time treatment of IHD: prevention of angina attacks as mono- or combined treatment.

The dose is one capsule of 80mg of trimetazidine once daily.

2.5.2. Concomitant medication

With regard to the non-interventional design of the study, every concomitant therapy and medication considered necessary by the attending physician is permitted. This will be appropriately documented in the study documents.

2.6. Duration of the non-interventional study

Patient recruitment for this non-interventional study (NIS) should be finalized within 1 month' time.

Observational follow-up time per patient will be approx. 3 months.

Start of patient recruitment will be 01/02/2017.

Patient recruitment is planned to be finished by 28/02/2017.

Study end is scheduled for 31/05/2017.

Filled CRFs collection is scheduled for 30/06/2017.

Statistical report is possible until 30/09/2017.

2.7. Documentation during the non-interventional study

2.7.1. Documentation folder

The documentation folder will be provided to each physician and will contain complete documents for 10 patients, i.e.:

- 1 Observation plan protocol
- patient documents for 10 patients (patient "informed consent" form, CRF forms) including 10 documentation forms for reporting of Adverse Events (AE)/ Adverse Drug Reactions (ADRs)/Special situations.

2.7.2. Time schedule for documentation

The exact schedule needs to be defined by the physician according to his routine practice.

Three points of examination are proposed:

1. Inclusion visit (V1): month 0
2. Control visit (V2): after approx. 1 month
3. Final visit (V3): after approx. 3 months or in case of Preductal® OD 80 mg withdrawal

2.7.3. Data collection

2.7.3.1. Overview of data to collect

In principle, all examinations in the context of this NIS just are to be performed if they take place in the framework of routine diagnostic and therapeutic procedures. Procedures that are out of the usual medical routine are prohibited.

To answer the most important scientific questions within this NIS, the following variables will be analyzed:

1) Data collection of number of angina attacks at each visit (V1-V2-V3)

2) Data collection on number of uses of short-acting nitrates at each visit (V1-V2-V3)

3) Evaluation of symptomatic status by physicians' assessment at each visit (V1-V2-V3)

4) Self – assesment of the patients daily activity at each visit (V1-V2-V3)

5) Patients' compliance/adherence at each visit (V1-V2-V3)

6) Collection of Adverse drug reaction/events ans special situations (see definitions in section 3) at visit V2 and V3

7) General assessment of Preductal® OD 80 mg therapy by physician at visit V3

Overview	Inclusion visit **V1**	Control visit (after appr. 1 month) **V2**	Final visit (after appr. 3 months) **V3**
Date of examination	√	√	√
Patient information and informed consent of patient	√		
Demographic data	√		
Risk factors and life-style	√		
Medical history	√		
Physical examination and vital signs	√	√	√
Current symptoms and use of short-acting nitrates	√	√	√
Most recent available measurements (biology, LVEF)	√		√
Data on current antianginal treatments	√	√	√
Data on other cardiovascular treatments	√		
Data on other medications	√		

Daily activity assessed by patient	√	√	√
Adherence to the current anti-anginal treatment	√	√	√
Treatment with Preductal® OD 80 mg	√	√	√
Adverse events/ reactions/ special situations		√	√
Phisician general assessment of Preductal® OD 80 mg therapy			√
Adherence to Preductal® OD 80 mg		√	√

Data collection in detail

(a) Data collection at inclusion visit (V1):

- Date of examination
- Signature of informed consent form
- Inclusion, exclusion criteria
- Demographic data: age, gender
- Risk factors and life-style : family history of premature CAD, treated hypertension, Type 2 diabetes, dyslipidemia, smoking status, physical activity
- Medical history: history of coronary artery disease, history of stable angina pectoris, history of myocardial infarction, PCI, CABG, peripherial arterial disease, internal cardiac defibrillator, pacemaker, stroke, TIA, atrial fibrillation, COPD, other.
- Physical examination and vital signs: body weight, height, sitting arterial blood preassure, resting heart rate
- Current symptoms: number of angina attacks and consumption of short acting nitrates during last week , CCS-classification (see app. 1), NYHA-classification (see app. 2)
- Most recent available measurements: total cholesterol, HDL, LDL, TGC, serum creatinine, fasting glucose, LVEF,
- Data on current antianginal treatment
- Data on other cardiovascular treatments
- Data on other medications
- Daily activity assessed by patient
- Adherence to the current anti-anginal treatment
    - Treatment with Preductal® OD 80 mg

(b) Data collection at control visit (V2):

- Date of examination
- Treatment with Preductal® OD 80 mg
- Physical examination and vital signs
- Data on ADRs/ AEs/Special situations (see section 3.1.1)
- Data on change other medication of chronic stable angina pectoris
- Current symptoms: number of angina attacks and consumption of short acting nitrates during last week , CCS-classification, NYHA-classification
- Daily activity assessed by patient
- Adherence to the current anti-anginal treatment
- Adherence to Preductal® OD 80 mg (see Questionnaire VII in CRF)

(c) Data collection at final visit (V3):

- Date of examination
- Treatment with Preductal® OD 80 mg

- Physical examination and vital signs
- Data on ADRs/ AEs/Special situations
- Data on change other medication of chronic stable angina pectoris
- Current symptoms: number of angina attacks and consumption of short acting nitrates during last week , CCS-classification, NYHA-classification
- Optional: Most recent available measurements: lab results, LVEF
- Daily activity assessed by patient
- Adherence to the current anti-anginal treatment
- Assessment of Preductal® OD 80 mg treatment by physician: efficacy, tolerability
- Adherence to Preductal® OD 80 mg (see Questionnaire VII in CRF)

2.7.3.2. Execution of the non-interventional study

The participating physician will receive the documentation folder and intructions by responsible field sales force employees of Servier.

The patient needs to be informed about his participation in this study and the transfer of his clinical data outside the investigational center to the responsible professional subcontractor for statistical analyses. The patient´s informed consent has to be obtained in written form. The informed consent declaration signed by the patient and the person responsible for collecting the informed consent has to be completed with the patient´s full name. The patient will receive a patient information sheet and a first original of his signed informed consent declaration. The second original informed consent declaration has to be archived by the physician.

The documentation sheets have to be filled in with a blue or black ball pen in a readable way. In case of corrections wrong data should be crossed out and be substituted by the correct data. Corrections should be documented with initials and date. No data should be deleted or erased.

To guarantee a high number of analyzable cases the documentation sheets always have to be filled in carefully and completely.

In case of occurrence of adverse drug reactions (ADRs). adverse events (AEs) or special situation, the participating physician must follow the requirements described in the section 3.2.2. "Responsibilities of the treating physician".

Please hand over fully completed documentation folders to your responsible Servier field sales force employee.

3. Pharmacovigilance management

3.1. DEFINITIONS

3.1.1. Pharmacovigilance information

Pharmacovigilance data include any unintended or adverse event associated with the use of a medicinal product in humans, whether or not considered drug related, including the following special situations (situations where no adverse event occurred but information needs to be collected):

- exposure during pregnancy or breastfeeding,
- overdose, abuse, misuse, off label uses, medication error, occupational exposure,
- lack of efficacy

3.1.2. Adverse Event (AE)

Adverse event (synonym adverse experience): any untoward medical occurrence in a patient or a clinical-trial subject administered a medicinal product and which does not necessarily have a causal relationship with this treatment.

An adverse event can therefore be any unfavourable and unintended sign (e.g. an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

3.1.3. Adverse (drug) reaction (ADR)

Adverse reaction (synonyms: Adverse drug reaction, Suspected adverse (drug) reaction, Adverse effect, Undesirable effect: a response to a medicinal product which is noxious and unintended.

Response in this context means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility.

Adverse reactions may arise from use of the product within or outside the terms of the marketing authorization or from occupational exposure. Conditions of use outside the marketing authorization include off-label use, overdose, misuse, abuse and medication errors.

3.1.4. Serious adverse (drug) reaction (SADR)

Serious adverse reaction: an adverse reaction which results in death, is life-threatening, requires in-patient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly/birth defect.

Life threatening in this context refers to a reaction in which the patient was at risk of death at the time of the reaction; it does not refer to a reaction that hypothetically might have caused death if more severe.

Medical and scientific judgement should be exercised in deciding whether other situations should be considered serious reactions, such as important medical events that might not be immediately life threatening or result in death or hospitalisation but might jeopardise the patient or might require intervention to prevent one of the other outcomes listed above.

Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalisation or development of dependency or abuse.

Any suspected transmission via a medicinal product of an infectious agent is also considered a serious adverse reaction.

3.2. RESPONSIBILITIES

3.2.1. Events to be reported

All available information about the following reported events occurring during the study will be recorded:

- All serious adverse drug reactions to Preductal® OD 80 mg
- All non-serious adverse drug reactions to Preductal® OD 80 mg
- Reports about special situations (see 3.1.1)
- All adverse events

Specific attention should be paid to:

- Parkinson's syndrome,

- Neurological symptoms/disorders (including disorientation, hallucination and convulsion) other than Parkinson syndrome

- Arterial hypotension, including ortostatic hypotension;

- Thrombocytopenia and agranulocytosis;

- Hepatic disorders

- Coagulation disorders (including haemorrhages and stroke)

3.2.2. Responsibilities of the treating physician

In prospective studies, at medical visits, the treating physician will ask the participating patient to indicate whether or not an adverse event (serious or not) has occurred.

The treating physician has to assess the causal relationship between an adverse event and the investigated drug intake, as well as the seriousness criteria and later on the outcome of the event.

In case of Adverse Events, Adverse Drug Reactions or special situations that occurs during the study (both serious and non-serious), the participating physician must complete the AE/ADR/Special situation form, without waiting for the clinical outcome or the results of additional investigations.

If the event is serious, it will be notified immediately (same or next working day at the latest) to Representative Office Les Laboratoires Servier in Russia via fax (495) 937 47 66 or via e-mail pv.mail@ru.netgrs.com. Any available and relevant laboratory findings, hospitalisation reports or other investigation results performed in connection with the adverse event should be attached to the form. All other events should be transmitted by the treating physician within 2 working days.

The same obligations will apply for follow-up reports. The treating physician must ensure that follow-up of the participant is appropriate to the nature of the event, and that it continues until resolution. She/he will continue to notify follow up data according to timeframes defined above.

If the follow-up of the participant is not done by the treating physician him/herself (hospitalisation, followed by a specialist or the participant's general practitioner,…), the treating physician will do every effort to establish/maintain contact with the person/department in charge of follow-up of the participant, so as to have additional information and report it.

3.2.3. Responsibilities of the Sponsor/Marketing Authorisation Holder

Independently of the regulatory obligations of the treating physician, the Sponsor/MAH must report the pharmacovigilance data to the appropriate Authorities (including Ethics Committees if applicable) according to Good Vigilance Practice Module VI and local regulations.

Cases are closed when an event has recovered or condition stabilised and the report is deemed sufficiently detailed for adequate medical assessment.

4. Data management, quality management, biometrics and reporting

4.1. Data management

Data collection in this study is performed by documentation sheets. Centralized data entry will be done by the responsible professional subcontractor for statistical analyses following receipt of the documentation sheets. Statistical analysis of data and creation of the final statistical study report will also be performed by responsible professional subcontractor for statistical analyses.

Consistency of ADR reporting data will be ensured by reconciliation of the project data base with the drug safety data base of Servier. Discrepancies will be solved by mutual coordination of the two parties (Servier and professional subcontractor for statistical analyses).

4.2. Biometrical analysis

According to the non-interventional setting of this study, statistical analysis will be conducted in a descriptive and explorative way. All the parameters will be analyzed using descriptive statistics methods. The number of patients, mean value, standard error, minimum and maximum value or proportion by categoty will be specified for each parameter. All compiled variables will be listed and also visualized by graphs and frequency/parameter tables.

For categorial variables a graphical counting of absolute and percental frequencies will be done. Only those patients will be included into the calculation of relative frequencies, for whom data on the respective variables is available.

All reports on adverse drug reactions (ADRs), adverse events (AEs) and Special situations will be encoded and results will be listed and classified by System-Organ-Class (SOC).

4.3. Reporting

Preparation of the final study report will be started after completion of biometrical analysis. Publication of core results is planned within 12 months after end of the study.

5. Ethical considerations

The study will be performed in accordance with the principles of the Declaration of Helsinki, as revised in Brazil in 2013.

The protocol must be reviewed and approved by independent ethics committees following submission by the coordinator or by the sponsor in accordance with local regulations, notably regarding data protection.

Patients will be fully informed, and written consent for participation in the study will be obtained. A record of the number of patients who refuse to participate will be kept. The physician must confirm in the case report form that informed consent was obtained and store the original of the signed

declaration of consent in the patient file. “Informed consent” also implies individual discussion with the patient in their national language about the nature of the interview and the examination to be conducted during the study.

Patient confidentiality

Investigators are obliged to keep confidential information about the patients who are included in the study. Confidential data have to contain enough information to contact the patient in case of emergency or if further follow-up is necessary.

The patient’s right to confidentiality is paramount. To protect the confidentiality of data and to preserve patient anonymity, their identity will be codified in the study documents. The patients will be identified by a unique number, age, and gender, which will be recorded on the CRF. To reveal the patient identity all investigators will keep a confidential patient identification list with patient names/addresses and assigned patient numbers. Thus, only the investigator will be capable of decoding the patient’s identity.

6. Appendices

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6.6. Appendix 6: Adverse event / Adverse drug reaction / Special situation* form

7. References

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Appendix 1: Canadian Cardiovascular Society (CCS) Classification of Symptoms of Angina

Class 1

"Ordinary activity does not cause angina"

Angina with strenuous or rapid or prolonged exertion only

Class 2

"Slight limitation of ordinary activity"

Angina on walking or climbing stairs rapidly, walking uphill or exertion after meals, in cold weather, when under emotional stress, or only during the first few hours after awakening

Class 3

"Marked limitation of ordinary physical activity"

Angina on walking one or two blocks (a) on the level or one flight of stairs at a normal pace under normal conditions

Class 4

"Inability to carry out any physical activity without discomfort"

or "angina at rest"

(a) Equivalent to 100-200 meters

From: Campeau L. Letter: grading of angina pectoris. Circulation 1976;54:522–-

Appendix 2. New York Heart Association (NYHA) Functional Classification

Class	Patient Symptoms
Class I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation (feeling heart beats), or dyspnea (shortness of breath).
Class II (Mild)	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnea.
Class III (Moderate)	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, palpitation, or dyspnea.
Class IV (Severe)	Unable to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency at rest. If any physical activity is undertaken, discomfort is increased.

Hurst Hurst JW, Morris DC, Alexander RW. The use of the New York Heart Association's classification of cardiovascular disease as part of the patient's complete Problem List. Clin Cardiol . JW, Morris DC, Alexander RW. L'utilisation de la New York Heart Association de classification du des maladies cardiovasculaires dans le cadre du patient compléter la liste des problèmes. Clin Cardiol. 1999 Jun ;22 (6):385-90.

Appendix 3. Evaluation of patients' adherence to the medical treatment

Question	YES	NO
This morning, did you forget to take your medication?		
Since the last consultation, have you run out of your medication?		
Have you ever taken your medication later than the usual time you take it?		
Have you ever not taken your medication because, on certain days, you forget?		
Have you ever not taken your medication because, on certain days, you feel the medication does more harm than good?		
Do you think that you have to take too many tablets?		

Responds "NO" to all questions: good adherence;

Responds "YES" to 1-2 questions: moderate adherence;

Responds "YES" to 3 or more questions: nonadherence

Girerd X, Radauceanu A, Achard JM, Fourcade J, Tournier B, Brillet G, Silhol F, Hanon O. [Evaluation of patient compliance among hypertensive patients treated by specialists]. [Article in French] Arch Mal Coeur Vaiss. 2001 Aug;94(8):839-42.

Appendix 4: Patient information

Dear _____,

Your doctor is taking part in an observational non-interventional program dedicated to the evaluation the effectiveness and therapeutic response to Preductal® OD 80 mg in daily practical use for chronic stable angina pectoris treatment.

This study will not alter the quality of your medical care and will not influence the doctor's decision regarding the treatment. You might be invited for participation only if your doctors decide that you need Preductal® OD 80 mg for your angina symptoms. Being involved into the observational program you will be asked to see your doctor 2 more times (after 1 and 3 months) in order to analyse the therapeutic response.

Your clinical information will be transmitted completely anonymously by your doctor to the responsible professional subcontractor for statistical analyses. Your name or any other information that could directly or indirectly be used to identify you, will not be disclosed.

You are absolutely free to accept or refuse (with no explanation necessary) that your clinical information be used in this study. Your decision will not influence the care you receive from your doctor in any way.

Should you require further information, please do not hesitate to ask your doctor.

Thank you for your cooperation.

Appendix 5: Patient consent form

NOTE: This signed declaration need to be signed in two copies and the one must remain in the patient's clinical records

ODA:

Evaluation of effectiveness and therapeutic response to Preductal® OD 80 mg in daily practical use for chronic stable angina pectoris

PATIENT DECLARATION

I, the undersigned, (indicate first and last name)

. . . . . .

Living at (indicate address)

. . . . . .

Freely agree to take part in the ODA study.

I have been given a full explanation by . . . . . who conducted the informed consent discussion of the nature, purpose, and duration of the study. I was able to ask him/her questions regarding all aspects of the study. I have been given the name of a person to contact if I have any questions during the study.

After due consideration, I agree to cooperate with the research doctor Prof/Dr . . . . . and all the designated persons from his/her team. I will inform them immediately of any abnormality observed.

I have noted that I am free to withdraw from the study at any time, if I so desire, and that my decision will in no way affect the standard of care I receive. I have noted that the research doctor will apply my rights of access and rectification, if necessary, to correct any of my personal data.

My identity will never be disclosed and any information collected will remain confidential. I agree that my medical records and other personal data generated during the study may be examined by representatives of the sponsor and by people working on behalf of the sponsor, members of the Ethic Committee, and by representatives of competent authorities. I agree that I will not seek to restrict the use to which the results of the study may be put.

Patient	Person responsible for collecting the informed consent

Date:	First and last name: . . . . .
Signature:	Date: . . . . .
	Signature:

Appendix 6:

Adverse event / Adverse drug reaction / Special situation* form

[DIM-06795-001-RUS]

Please print and fax/e-mail immediately to the Local Servier Representative (see the address in the Local Protocol)

Year of birth or **Age**	**Gender**	**Height**	**Weight**	**Patient number**
⌊⌊⌊⌊⌋ or ⌊⌊⌊⌋	M / F	⌊⌊⌊⌋	⌊⌊⌊⌋	⌊⌊⌊⌊⌊⌊⌊⌊⌊⌋

Observed adverse event:	**Date of onset**	**Until (if recovered)**
	⌊⌊ ⌊⌊ ⌊⌊⌊⌊	⌊⌊ ⌊⌊ ⌊⌊⌊⌊

Serious: ☐ No
☐ Yes, because: (please choose below)
- ☐ Fatal
- ☐ Life-threatening
- ☐ Hospitalisation or prolongation of hospitalisation
- ☐ Persistent or significant disability or incapacity
- ☐ Congenital anomaly/birth defect
- ☐ Medically significant

Outcome:
- ☐ Recovered
- ☐ Recovered with sequelae
- ☐ Recovering
- ☐ Not recovered
- ☐ Fatal
- ☐ Unknown

General disease(s) / Concomitant disease(s) (please indicate year of first diagnoses):

Course (please enclose relevant findings e.g. laboratory, hospital reports, histology, etc.):

Causal relationship with the studied drug:
☐ No ☐ Yes ☐ Not applicable

If yes, please specify dates of treatment with the studied drug in the table below on the first line:

If no or not applicable, please indicate whether the adverse event /special situation is related to a Servier medicinal product (as mentioned in the following table):
☐ No ☐ Yes *please specify which Servier medicinal product:* ……

Medication list	**Daily dosage / application**	**Administered from to**	**Indication**
		-	
		-	
		-	

Name of physician:
Speciality:
Address:
Phone:
Stamp
(stamp, if available)

Date:

Signature:

Special situations: situations where no adverse events occurred but information needs to be collected: exposure during pregnancy or breastfeeding, abuse, misuse, medication error, overdose, off label use, occupational exposure, lack of efficacy…*