Public Assessment Report

UK PAR

Amiodarone 200 mg Tablets

(Amiodarone hydrochloride)

UK Licence No: PL 44041/0001

Noumed Life Sciences Limited
LAY SUMMARY
Amiodarone 200 mg Tablets
(Amiodarone hydrochloride)

This is a summary of the Public Assessment Report (PAR) for Amiodarone 200 mg Tablets
(PL 44041/0001). It explains how the application for Amiodarone 200 mg Tablets was assessed and its
authorisation recommended, as well as the conditions of use. It is not intended to provide practical
advice on how to use Amiodarone 200 mg Tablets.

For practical information about using Amiodarone 200 mg Tablets, patients should read the package
leaflet or contact their doctor or pharmacist.

Amiodarone 200 mg Tablets may be referred to as ‘Amiodarone Tablets’ in this Lay Summary.

What are Amiodarone Tablets and what are they used for?
This medicine is the same as Amiodarone 200 mg tablets (PL 21880/0096; Medreich plc), which are
already authorised in the UK. The licence holder (Medreich plc, UK) for Amiodarone 200 mg tablets
(PL 21880/0096) has agreed that its own scientific data can be used as a basis for the grant of an
identical licence for Amiodarone 200 mg Tablets (PL 44041/0001; Medreich plc) (informed consent).

Amiodarone Tablets can be used to treat:
• uneven heartbeats where other medicines either have not worked or cannot be used
• an illness called Wolff-Parkinson-White Syndrome. This is where the heart beats unusually fast.
• other types of fast or uneven heartbeats known as “atrial flutter” or “atrial fibrillation”. Amiodarone
  Tablets are used only when other medicines cannot be used.
• fast heartbeats which may happen suddenly and may be uneven. Amiodarone Tablets are used only
  when other medicines cannot be used.

Amiodarone Tablets are only used for severe disorders that do not respond to other therapies or when
other treatments cannot be used. Therapy should only be initiated and monitored under hospital or
specialist supervision.

How do Amiodarone Tablets work?
Amiodarone Tablets contain the active substance, amiodarone (as amiodarone hydrochloride).
Amiodarone belongs to a group of drugs known as antiarrhythmics. It is used to control an irregular or
rapid heart rate (called arrhythmias).

How are Amiodarone Tablets used?
Amiodarone Tablets are taken by mouth. The tablets should be swallowed whole; the tablets should not
be crushed or chewed.

Amiodarone Tablets can only be obtained with a prescription. The tablets should be taken exactly as
instructed by the prescribing doctor. The patient should check with the doctor or pharmacist if not sure.

Please read section 3 of the package leaflet for detailed information on dosing recommendations and the
duration of treatment.
What benefits of Amiodarone Tablets have been shown in studies?
The application for Amiodarone Tablets (PL 44041/0001) is considered to be identical to the previously authorised licence for Amiodarone 200 mg Tablets (PL 21880/0096; Medreich plc), with the same benefits and risks. So, no new studies have been provided for Amiodarone Tablets (PL 44041/0001). However, reference is made to the studies for Amiodarone Tablets (PL 21880/0096; Medreich plc).

What are the possible side effects of Amiodarone Tablets?
Like all medicines, Amiodarone Tablets can cause side effects, although not everybody gets them.

For the full list of all side effects reported with Amiodarone Tablets, see section 4 of the package leaflet.
For the full list of restrictions, see the package leaflet.

Why are Amiodarone Tablets approved?
No new or unexpected safety concerns arose from this application. The MHRA, therefore, considered that the benefits of Amiodarone Tablets outweigh their risks; and the grant of Marketing Authorisation was recommended.

What measures are being taken to ensure the safe and effective use of Amiodarone Tablets?
A Risk Management Plan has been developed to ensure that Amiodarone Tablets are used as safely as possible. Based on this plan, safety information has been included in the Summary of Product Characteristics and the package leaflet for Amiodarone Tablets, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored/reviewed continuously.

Other information about Amiodarone Tablets
A Marketing Authorisation was granted in the UK to Noumed Life Sciences Limited on 10 March 2017.

The full PAR for Amiodarone Tablets follows this summary.

For more information about treatment with Amiodarone Tablets read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in April 2017.
Amiodarone 200 mg Tablets
(Amiodarone hydrochloride)

PL 44041/0001

SCIENTIFIC DISCUSSION

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I. INTRODUCTION
The Medicines and Healthcare products Regulatory Agency (MHRA) granted Noumed Life Sciences Limited a Marketing Authorisation for the medicinal product Amiodarone 200 mg Tablets (PL 44041/0001) on 10 March 2017. The product is a Prescription Only Medicine (POM) indicated for the treatment of severe rhythm disorders not responding to other therapies or when other treatments cannot be used. Treatment should be initiated and normally monitored only under hospital or specialist supervision.

Amiodarone 200 mg Tablets are indicated for the treatment of the following conditions:
• tachyarrhythmias associated with Wolff-Parkinson-White Syndrome.
• atrial flutter and fibrillation when other drugs cannot be used.
• all types of tachyarrhythmias of paroxysmal nature including: supraventricular, nodal and ventricular tachycardias, ventricular fibrillation; when other drugs cannot be used.

Amiodarone 200 mg Tablets are used for stabilisation and long-term treatment.

The application was submitted as a simple abridged (informed consent) application according to Article 10c of Directive 2001/83/EC, as amended. The application for Amiodarone 200 mg tablets (PL 44041/0001) cross-refers to Amiodarone 200 mg tablets (PL 21880/0096; Medreich plc), which was authorised in the UK through a Change of Ownership application (COA) procedure of Amyben 200 mg Tablets/Amiodarone hydrochloride 200mg Tablets (PL 15184/0163; Lexon UK Limited) on 19 August 2010. The application for Amyben 200 mg Tablets/Amiodarone hydrochloride 200 mg Tablets (PL15184/0163; Lexon UK Limited) cross-refer to Cordarone X 100 mg tablets/Amiodarone hydrochloride 100 mg Tablets (PL 11723/0012; Sanofi-Synthelabo Limited), which were approved following a COA procedure on 14 October 1993. The original product, Cordarone X 100 mg tablets/Amiodarone hydrochloride 100 mg Tablets (PL 00623/0017; Sanofi Winthrop Limited), was approved on 19 January 1984.

The active substance, amiodarone hydrochloride, is a class III antiarrhythmic drug.

No new data were submitted nor were they required for this application, as the product is identical to that of the previously granted cross-reference product.

II. QUALITY ASPECTS
II.1 INTRODUCTION
This is an informed consent application for Amiodarone 200 mg Tablets (PL 44041/0001), submitted under Article 10c of Directive 2001/83/EC, as amended.

The application for Amiodarone 200 mg Tablets (PL 44041/0001) cross-refers to the medical product Amiodarone 200 mg tablets (PL 21880/0096; Medreich plc), which was authorised in the UK through a Change of Ownership application (COA) procedure of Amyben 200 mg Tablets/Amiodarone hydrochloride 200mg Tablets (PL 15184/0163; Lexon UK Limited) on 19 August 2010. Amyben 200 mg Tablets/Amiodarone hydrochloride 200 mg Tablets (PL 15184/0163; Lexon UK Limited) cross-refer to Cordarone X 100 mg tablets/Amiodarone hydrochloride 100 mg Tablets (PL 11723/0012; Sanofi-Synthelabo Limited), which were approved following a COA procedure on 14 October 1993. The original product, Cordarone X 100 mg tablets/Amiodarone hydrochloride 100 mg Tablets (PL 00623/0017; Sanofi Winthrop Limited), was approved on 19 January 1984. The application is considered valid.
II.2 Drug substance
The proposed drug substance specification is consistent with the details registered for the cross reference product.

II.3 Medicinal Product
Name
The proposed name of the product is Amiodarone 200 mg Tablets. The product has been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes
Each tablet contains 200 mg of amiodarone hydrochloride, as the active substance. The tablets are taken orally (by mouth).

The product is packaged in blisters, in a pack size of 28 tablets.

The proposed shelf life for the products is 36 months, with the special storage conditions “Do not store above 25ºC. Store in the original package.”

The packaging, proposed shelf-life and storage conditions are consistent with the details registered for the cross-reference product.

Legal status
The product is available as a Prescription Only Medicine (POM).

Marketing Authorisation Holder/Contact Persons/Company
Noumed Life Sciences, 5 Cattle Market, Hexham, Northumberland, NE46 1NJ, United Kingdom.

The Qualified Person (QP) responsible for pharmacovigilance is stated and a satisfactory CV has been provided.

Manufacturers
The proposed manufacturing sites are consistent with those registered for the cross-reference products and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the cross-reference product.

Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

Finished product/shelf-life specification
The proposed finished product specification is consistent with the details registered for the cross-reference product.

TSE Compliance
With the exception of lactose monohydrate, none of the excipients contains materials of animal or human origin. The suppliers of lactose monohydrate have confirmed that the milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that intended for human consumption. In addition, the suppliers have confirmed that no ruminant material, other than calf
rennet, is used during the production of lactose monohydrate. This is consistent with the cross-reference product.

This is consistent with the cross-reference product.

**Bioequivalence**

No bioequivalence data are required to support this simple abridged application because the proposed product are manufactured to the same formula and utilises the same processes as the reference product Amiodarone 200 mg tablets (PL 21880/0096; Medreich plc).

**Product Name and Appearance**

See Section II.3 ‘Medicinal Product, Name’ for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

**Summary of Product Characteristics (SmPC)**

The proposed SmPC is consistent with the details registered for the cross-reference product.

**Patient Information Leaflet (PIL) and Labelling**

PIL

The PIL has been prepared in line with the details registered for the cross-reference product.

**Carton and label**

The proposed artwork is consistent with the artwork registered for the cross-reference product and complies with statutory requirements. In line with current legislation, the applicant has also included the name of the product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

II.4  **Discussion on chemical, pharmaceutical and biological aspects**

The data submitted with the application are acceptable. The grant of a Marketing Authorisation is recommended.

**III. NON-CLINICAL ASPECTS**

**Introduction**

As this is an informed consent application submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data have been supplied and none are required.

**Ecotoxicity/Environmental Risk Assessment (ERA)**

Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the application is an identical version of an already authorised product, it is not expected that environmental exposure will increase following approval of the Marketing Authorisation for the proposed product.

**Discussion on the non-clinical aspects**

The grant of a Marketing Authorisation is recommended.
IV. CLINICAL ASPECTS

Introduction
As this informed consent application submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

Pharmacovigilance and Risk Management Plan (RMP)
The Marketing Authorisation Holder has provided details of a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that they have the services of a qualified person responsible for pharmacovigilance, and have the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

An acceptable Risk Management Plan (RMP) has been submitted. A summary of safety concerns is listed in the following table.

<table>
<thead>
<tr>
<th>Summary of safety concerns</th>
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<tbody>
<tr>
<td>Important identified risks</td>
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<tr>
<td>Cardiac disorders (including bradycardia, torsade depooints conduction disorders and arrhythmia)</td>
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<tr>
<td>Hypo- or hyperthyroidism</td>
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<td>Optic neuropathy and/or optic neuritis</td>
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<td>Peripheral sensorimotor neuropathy and/or myopathy</td>
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<td>Pulmonary toxicity (incl. pneumonitis, pleuritis, and fibrosis)</td>
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<td>Liver disorders (incl. hepatitis, cirrhosis and hepatic failure)</td>
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<tr>
<td>Blood dyscrasia (incl. aplastic anaemia, haemolytic anaemia and thrombocytopenia)</td>
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<td>Phototoxic skin reactions</td>
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<td>Blue skin pigmentation</td>
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<tr>
<td>Hypersensitivity reaction with vasculitis, renal involvement or thrombocytopenia</td>
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<tr>
<td>Use during pregnancy and breastfeeding</td>
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<tr>
<td>Drug interactions with CYP3A4 substrates and inhibitors, CYP2D6 substrates, CYP2C8 inhibitors, CYP2C9 substrates, and PgP substrates</td>
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<tr>
<td>Important potential risks</td>
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<tr>
<td>Bone marrow granulomas</td>
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<tr>
<td>Missing information</td>
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<td>Safety and efficacy in children</td>
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Routine pharmacovigilance and routine risk minimisation are proposed for all safety concerns.

Discussion on the clinical aspects
The grant of a Marketing Authorisation is recommended.

V. USER CONSULTATION
A user consultation with target patient groups on the Patient Information Leaflet (PIL) has been performed on the basis of a bridging report making reference to the PIL for Amiodarone 200 mg tablets (PL 21880/0096; Medreich plc). The bridging report has been found to be acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

QUALITY
The data for this application is consistent with those previously assessed for the cross-reference product and as such have been judged to be satisfactory.
NON-CLINICAL
No new non-clinical data were submitted and none are required for this type of application.

EFFICACY
No new efficacy data were supplied or required for this application. Amiodarone hydrochloride has a well-established efficacy profile. The product is identical to the previously granted licence for Amiodarone 200 mg tablets (PL 21880/0096; Medreich plc).

SAFETY
No new safety data were supplied or required for this application. Amiodarone has a well-established safety profile. This product is identical to the previously authorised Amiodarone 200 mg tablets (PL 21880/0096; Medreich plc).

PRODUCT LITERATURE
The SmPC and package leaflet are satisfactory, and consistent with those for the respective cross-reference product. The labelling text complies with statutory requirements and is satisfactory.

BENEFIT/RISK ASSESSMENT
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant’s product is identical to the cross-reference product. Extensive clinical experience with amiodarone hydrochloride is considered to have demonstrated the therapeutic value of the compound. The benefit/risk assessment is, therefore, considered to be positive.
In accordance with Directive 2010/84/EU, the current version of the SmPCs and PILs is available on the MHRA website. The current labelling is presented below:
Amiodarone 200 mg Tablets

(Amiodarone hydrochloride)

PL 44041/0001

### STEPS TAKEN AFTER AUTHORISATION - SUMMARY

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<thead>
<tr>
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<th>Application type</th>
<th>Scope</th>
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