Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

Vazkepa 998 mg soft capsules

(icosapent ethyl)

PLGB 51241/0002

Amarin Pharmaceuticals Ireland Limited

LAY SUMMARY

Vazkepa 998 mg soft capsules (icosapent ethyl)

This is a summary of the Public Assessment Report (PAR) for Vazkepa 998 mg soft capsules. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Vazkepa in this lay summary for ease of reading.

For practical information about using Vazkepa, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Vazkepa and what is it used for?
This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA relied on a European Commission (EC) decision on 26 March 2021 (EMEA/H/C/005398/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP). This is known as the EC Decision Reliance Procedure.

This application is a full-dossier application. This means that the results of pharmaceutical, non-clinical and clinical tests have been submitted to show that this medicine is suitable for treating the specified indications.

Vazkepa lowers levels of triglycerides (types of fat) in the blood and it is used with a statin medicine (that lowers blood cholesterol) to prevent cardiovascular events, such as:
- heart attack
- stroke
- death from heart or vascular disease

Vazkepa is used in adults with high blood triglycerides who already have heart disease or have diabetes and other conditions that put them at a higher risk of cardiovascular events.

How does Vazkepa work?
Vazkepa contains the active substance icosapent ethyl, a highly purified omega-3 fatty acid from fish oil.

How is Vazkepa used?
The pharmaceutical form of this medicine is a soft capsule and the route of administration is oral (taken by mouth).

How much to take
The recommended dose is two capsules by mouth, twice a day, with or after a meal.
The patient should swallow the capsules whole; they should **not** break, crush, dissolve or chew the capsules.

Use in elderly
There is no need to change the dose in elderly patients. They can take the usual recommended dose.

For further information on how Vazkepa is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should always take the medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What are the possible side effects of Vazkepa?
For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on behalf of someone else they care for, directly via the Yellow Card scheme at www.mhra.gov.uk/yellowcard or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Why was Vazkepa approved?
It was concluded that Vazkepa has been shown to be effective in the following indications:

- Vazkepa lowers levels of triglycerides (types of fat) in the blood and it is used with a statin medicine (that lowers blood cholesterol) to prevent cardiovascular events, such as:
  - heart attack
  - stroke
  - death from heart or vascular disease

- Vazkepa is used in adults with high blood triglycerides who already have heart disease or have diabetes and other conditions that put them at a higher risk of cardiovascular events.

Furthermore, the side effects observed with use of this product are considered to be typical for this type of treatment. Therefore, the MHRA decided that the benefits are greater than the risks and recommended that this medicine can be approved for use.

What measures are being taken to ensure the safe and effective use of Vazkepa?
A Risk Management Plan (RMP) has been developed to ensure that Vazkepa is used as safely as possible. Based on this plan, safety information has been included in the SmPC and the PIL, 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 and reviewed continuously.

Other information about Vazkepa
A Marketing Authorisation was granted in Great Britain on 20 April 2021.

The full PAR for Vazkepa follows this summary.

This summary was last updated in June 2021.

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1. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Vazkepa 998 mg soft capsules (PLGB 51241/0002) could be approved.

The product is approved for the following indications:
To reduce the risk of cardiovascular events in adult statin-treated patients at high cardiovascular risk with elevated triglycerides (≥150 mg/dL) and

- established cardiovascular disease, or
- diabetes, and at least one other cardiovascular risk factor.

The active substance, icosapent ethyl, is a stable ethyl ester of the omega-3 fatty acid, eicosapentaenoic acid (EPA). The mechanisms of action contributing to reduction of cardiovascular events with icosapent ethyl are not completely understood. The mechanisms are likely multi-factorial including improved lipoprotein profile with reduction of triglyceride-rich lipoproteins, anti-inflammatory, and antioxidant effects, reduction of macrophage accumulation, improved endothelial function, increased fibrous cap thickness/stability, and antiplatelet effects. Each of these mechanisms can beneficially alter the development, progression, and stabilisation of atherosclerotic plaque, as well as the implications of plaque rupture, and preclinical and clinical studies support such benefits with EPA. Systemic and localised anti-inflammatory effects of EPA may result from displacement of pro-inflammatory arachidonic acid (AA), directing catabolism away from eicosanoids (2-series prostaglandins and thromboxanes, and 4-series leukotrienes) to non- or anti-inflammatory mediators. However, the direct clinical meaning of individual findings is not clear.

This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA relied on a European Commission (EC) decision on 26 March 2021 (EMEA/H/C/005398/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP).

For the scientific discussion of the quality, non-clinical and clinical assessment conducted by the European Medicines Agency (EMA), please refer to the European Public Assessment Report, available on the EMA website.

This application was submitted under Regulation 50 of the Human Medicines Regulations 2012, as amended (previously Article 8(3) of Directive 2001/83/EC, as amended), as a full dossier application.

In line with the legal requirements for children's medicines, the application included a licensing authority decision on the agreement of a full product specific waiver {EMEA-001300-PIP01-12}.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

A Marketing Authorisation was granted in Great Britain on 20 April 2021.

2. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION

SUMMARY OF PRODUCT CHARACTERITICS (SmPC)

The SmPC is in line with current guidelines and is satisfactory.

PATIENT INFORMATION LEAFLET (PIL)

The PIL is in line with current guidelines and is satisfactory.

LABEL

The labelling is in line with current guidelines and is satisfactory.

3. QUALITY ASPECTS

MHRA considered that the quality data submitted for this application is satisfactory.

The grant of a Marketing Authorisation is recommended.

4. NON-CLINICAL ASPECTS

MHRA considered that the non-clinical data submitted for this application is satisfactory.

The grant of a Marketing Authorisation are recommended.

5. CLINICAL ASPECTS

MHRA considered that the non-clinical data submitted for this application is satisfactory.

The grant of a Marketing Authorisation is recommended.

6. RISK MANAGEMENT PLAN (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulations 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

7. USER CONSULTATION

A full colour mock-up of the PIL has been provided with the application, in accordance with legal requirements.

The PIL has been evaluated via a user consultation study in accordance with legal requirements. The results show that the PIL meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

8. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The benefit/risk balance is, therefore, considered to be positive.

The SmPC, PIL and labelling are satisfactory.

In accordance with legal requirements, the current approved Great Britain versions of the SmPC and PIL for this product available on the MHRA website.

The following text is the currently approved label text. No label mock-ups have been provided for this product. In accordance with legal requirements, this product shall not be marketed until approval of the full-colour label mock-ups has been obtained.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

BOTTLE CARTON

1. NAME OF THE MEDICINAL PRODUCT

Vazkepa 998 mg soft capsules
icosapent ethyl

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 998 mg of icosapent ethyl.

3. LIST OF EXCIPIENTS

Contains maltitol (E965 ii), sorbitol (E420 ii) and soya lecithin.
See the package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Soft capsule

120 capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Swallow the capsules whole.
Do not break, crush, dissolve or chew the capsules.
Read the package leaflet before use.

Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Keep the bottle tightly closed in order to protect from moisture.

Store below 30 °C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amarin Pharmaceuticals Ireland Ltd.
88 Harcourt Street
Dublin 2
D02DK18
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

PLGB 51241/0002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

VAZKEPA

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

BOTTLE LABEL

1. NAME OF THE MEDICINAL PRODUCT

Vazkepa 998 mg soft capsules
icosapent ethyl

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 998 mg of icosapent ethyl.

3. LIST OF EXCIPIENTS

Contains maltitol (E965 ii), sorbitol (E420 ii) and soya lecithin.
See the package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Soft capsule

120 capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Swallow the capsules whole.
Do not break, crush, dissolve or chew the capsules.
Read the package leaflet before use.

Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Keep the bottle tightly closed in order to protect from moisture.

Store below 30 °C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amarin Pharmaceuticals Ireland Ltd.
88 Harcourt Street
Dublin 2
D02DK18
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

PLGB 51241/0002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

VAZKEPA

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON FOR UNIT DOSE BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

Vazkepa 998 mg soft capsules
icosapent ethyl

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 998 mg of icosapent ethyl.

3. LIST OF EXCIPIENTS

Contains maltitol (E965 ii), sorbitol (E420 ii) and soya lecithin.
See the package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Soft capsule

4x2 capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Swallow the capsules whole.
Do not break, crush, dissolve or chew the capsules.
Read the package leaflet before use.

Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.
Store below 30 °C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Amarin Pharmaceuticals Ireland Ltd.
88 Harcourt Street
Dublin 2
D02DK18
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

PLGB 51241/0002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY
POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

VAZKEPA

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

UNIT DOSE BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

Vazkepa 998 mg capsules
icosapent ethyl

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amarin Pharmaceuticals Ireland Ltd.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Day 1
Dose 1
Dose 2

Day 2
Dose 1
Dose 2

TABLE OF CONTENTS OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations, where significant changes are made, are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPCs and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**
Type IB	1. To update Section 4.2 of the SmPC to state the criteria applied for 'elevated triglycerides' in 'mmol/l' units, in addition to the presented units of 'mg/dl' units. 2. To introduce into the SmPC and PIL, the inclusion of black symbol and explanatory statement for medicinal products in the list of the medicinal products that are subject to additional monitoring.	SmPC PIL	06/10/2021	Approved	Y (Annex 1)

Annex 1

Reference: PLGB 51241/0002-0003

Product: Vazkepa 998 mg soft capsules

Type of Procedure: National

Submission category: Type IB Variation

Reason

1. To update Section 4.2 of the SmPC to state the criteria applied for 'elevated triglycerides' in 'mmol/l' units, in addition to the presented units of 'mg/dl' units.
2. To introduce into the SmPC and PIL, the inclusion of black symbol and explanatory statement for medicinal products in the list of the medicinal products that are subject to additional monitoring.

Supporting evidence
The Company has submitted an updated SmPC and PIL.

Evaluation
The updated documents are satisfactory.

Conclusion
The proposed changes are acceptable.

In accordance with legal requirements, the Summaries of Product Characteristics (SmPCs) and Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.

Decision: Grant

Date: 06 October 2021