Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

Pyrukynd 5 mg film-coated tablets
Pyrukynd 20 mg film-coated tablets
Pyrukynd 50 mg film-coated tablets
Pyrukynd 20 mg film-coated tablets + 5 mg film-coated tablets
Pyrukynd 50 mg film-coated tablets + 20 mg film-coated tablets

(mitapivat)

PLGB 52779/0001-0005

Agios Netherlands B.V.

LAY SUMMARY

Pyrukynd 5 mg film-coated tablets
Pyrukynd 20 mg film-coated tablets
Pyrukynd 50 mg film-coated tablets
Pyrukynd 20 mg film-coated tablets + 5 mg film-coated tablets
Pyrukynd 50 mg film-coated tablets + 20 mg film-coated tablets
(mitapivat)

This is a summary of the Public Assessment Report (PAR) for Pyrukynd 5 mg, 20 mg and 50 mg film-coated tablets. It explains how these products were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use these products.

These products will be referred to as Pyrukynd in this lay summary for ease of reading.

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

What is Pyrukynd and what is it used for?
These products have been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 9 November 2022 (EMEA/H/C/005540), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP). This is known as the EC Decision Reliance Procedure.

These applications are full-dossier applications. This means that the results of pharmaceutical, non-clinical and clinical tests have been submitted to show that these medicines are suitable for treating the specified indication

Pyrukynd is used to treat adults with an inherited condition called pyruvate kinase deficiency. Patients with pyruvate kinase deficiency have changes to an enzyme in their red blood cells called pyruvate kinase, which result in it not working properly. This leads to the red blood cells being broken down too fast, a process known as haemolytic anaemia.

The patient should talk to their doctor, pharmacist or nurse if they have any questions about why this medicine has been prescribed for them.

How does Pyrukynd work?
Pyrukynd contains the active substance mitapivat (as mitapivat sulfate). Mitapivat helps the pyruvate kinase enzyme to work better. It increases the energy in the red blood cells and stops them from being broken down too fast.

How is Pyrukynd used?
The pharmaceutical form of these medicines is a film-coated tablet and the route of administration is oral (taken by mouth).

How much to take
The recommended starting dose of Pyrukynd is one 5 mg tablet taken twice a day. The patient's doctor may gradually increase the dose every few weeks based on the results of the

blood tests (haemoglobin levels) and how well the patient's condition responds, up to a maximum of one 50 mg tablet taken twice a day.

The patient should keep taking the medicine unless their doctor tells them to stop.

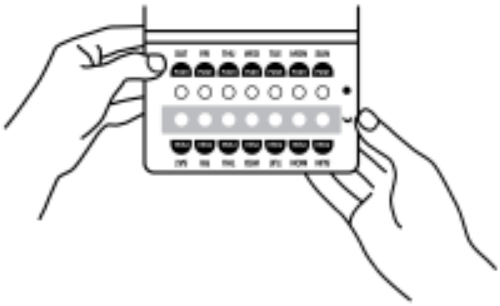
How to take
The patient:
• should swallow the tablet whole.
• can take it with or without food.
• should not split, crush, chew or dissolve the tablets.

Elderly
Pyrukynd has been used in a limited number of patients aged 65 years and older. There is no evidence to suggest that elderly patients need a different dose compared to younger adults.

Instructions for opening the blisters
The following pictures show how to take the tablet out of the blister.

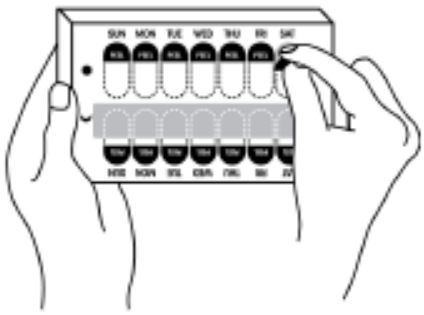
Find the correct blister pocket indicated by the day of the week and, if applicable, time of the day(morning or evening dose, as shown on the blister by sun and moon symbols). At the corresponding
tab:

1. Use thumb to PUSH.



The image above shows the inside of the blister wallet.

2. Turn package over, PEEL the raised tab on the back.



The image above shows the back of the blister wallet.

3. Push tablet through the foil.

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

These medicines can only be obtained with a prescription.

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

What benefits of Pyrukynd have been shown in studies?
The benefits of Pyrukynd were evaluated in two main studies. In the first study, involving 80 patients with pyruvate kinase deficiency (PK Deficiency) who were not regularly receiving blood transfusions, Pyrukynd was compared with placebo (dummy treatment). In this study, 40% of patients treated with Pyrukynd had an increase of their haemoglobin levels of 1.5 g/dL, which was maintained at 2 or more check-ups carried out after 16, 20 and 24 weeks of treatment, compared with none of the patients treated with placebo.

In the second study, involving 27 patients who were regularly receiving blood transfusions, Pyrukynd was not compared with placebo or any other medicines. In this study, the volume of red blood cells received in transfusions was reduced by more than a third in 37% of patients.

What are the possible side effects of Pyrukynd?
The most common side effects with Pyrukynd (which may affect more than 1 in 10 people) are:
• difficulty sleeping (insomnia)
• decreased levels of the hormone oestrone - seen in blood tests in men
• nausea

For the full list of all side effects reported with these medicines, see Section 4 of the PIL or the SmPCs 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 medicines. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of these medicines.

Why was Pyrukynd approved?
There are limited treatment options for patients with PKD as management of the disease is restricted to supportive treatments to improve the symptoms and complications associated with haemolytic anaemia. Although there were some limitations associated with the main studies, Pyrukynd has been shown to provide clinically meaningful benefits to some patients with PKD, by increasing haemoglobin levels and reducing the need for transfusions. It was therefore considered that Pyrukynd addressed an unmet medical need in these patients.

Furthermore, the side effects of Pyrukynd are considered manageable. The MHRA decided that the benefits are greater than the risks and recommended that these medicines can be approved for use.

Pyrukynd has been authorised with the condition to perform further studies to minimise the risk. See section below "What measures are being taken to ensure the safe and effective use of Pyrukynd?"

Pyrukynd has been authorised as a GB Orphan medicine. Orphan medicines are intended for use against rare conditions that are life-threatening or chronically debilitating. To qualify as an orphan medicine, certain criteria, for example concerning the rarity of the disease and the lack of currently available treatments, must be fulfilled.

What measures are being taken to ensure the safe and effective use of Pyrukynd?
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Pyrukynd. The RMP details the important risks of Pyrukynd, how these risks can be minimised, any uncertainties about Pyrukynd (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Pyrukynd:

Summary of Safety Concerns	
Important identified risks	Acute hemolysis
Important potential risks	Embryo-fetal toxicity
Missing information	Use in patients with hepatic impairment Long-term use

The information included in the SmPCs and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Pyrukynd are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

In addition to the safety information provided in the Pyrukynd product information, the Marketing Authorisation Holder (MAH) has committed to additional pharmacovigilance activities through the provision of effectiveness and safety data derived from pharmacovigilance and post-authorisation studies to further evaluate the long-term effectiveness and safety of Pyrukynd.

An RMP and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

Other information about Pyrukynd
Marketing authorisations were granted in Great Britain on 20 December 2022.

The full PAR for Pyrukynd follows this summary.

This summary was last updated in March 2023.

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I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the applications for Pyrukynd 5 mg, 20 mg, 50 mg, 20 mg + 5 mg, and 50 mg + 20 mg film-coated tablets (PLGB 52779/0001-0005) could be approved.

The products are approved for the following indication:

- the treatment of pyruvate kinase deficiency (PK deficiency) in adult patients (see section 4.4 of the Summary of Product Characteristics (SmPC)).

The active substance, mitapivat (as mitapivat sulfate), is a pyruvate kinase activator and acts by directly binding to the pyruvate kinase tetramer. The red blood cell (RBC) form of pyruvate kinase (PKR) is mutated in PK deficiency, which leads to reduced adenosine triphosphate (ATP) levels, shortened RBC lifespan and chronic haemolysis. Mitapivat improves RBC energy homeostasis by increasing PKR activity.

These products have been authorised by MHRA for Great Britain (GB; consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 9 November 2022 (EMEA/H/C/005540), 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.

These applications were approved under Regulation 50 of the Human Medicines Regulation 2012, as amended (previously Article 8.3 of Directive 2001/83/EC, as amended).

These applications were evaluated for fulfilment of orphan designation criteria and were examined by the Commission on Human Medicines (CHM) in November 2022 of CHM discussion. It was concluded that fulfilment of the criteria for approval as an orphan medicinal product was satisfactorily demonstrated. Please see Annex 1 for a summary of the orphan approval.

In line with the legal requirements for children's medicines, the application included a licensing authority decision on the agreement of a paediatric investigation plan (PIP) (MHRA-100608-PIP01-22-M01).

At the time of the submission of the applications the PIP was not yet completed as some measures were deferred.

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

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

Marketing authorisations were granted on 20 December 2022.

II. PRODUCT INFORMATION

SUMMARY OF PRODUCT CHARACTERITICS (SmPC)

The SmPCs are in line with current guidelines and are 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.

III. QUALITY ASPECTS

The MHRA considered that the quality data submitted for these applications is satisfactory.

The grant of marketing authorisations is recommended.

IV. NON-CLINICAL ASPECTS

The MHRA considered that the non-clinical data submitted for these applications is satisfactory.

The grant of marketing authorisations is recommended.

V. CLINICAL ASPECTS

The MHRA considered that the clinical data submitted for these applications is satisfactory.

The grant of marketing authorisations is recommended.

VI. RISK MANAGEMENT PLAN (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. In addition to routine pharmacovigilance and risk minimisation measures, the following additional pharmacovigilance measures have been proposed:

Summary Table of Pharmacovigilance Activities and Risk Minimization Activities by Safety Concern

Safety Concern	Risk Minimization Measures	Pharmacovigilance Activities
Acute hemolysis	Routine risk minimization measures: • *Acute haemolysis is listed as a special warnings and precautions for use in the Summary of Product Characteristics (SmPC) Section 4.4* • *Acute haemolysis is described as a selected adverse reaction in the SmPC Section 4.8* • *Acute haemolysis is listed as a warning and precaution in Package Leaflet (PL) Section 2* • *Acute haemolysis, after abrupt interruption or discontinuation of Pyrukynd, is described in PL Section 4* • *Warning and precaution that acute haemolysis with subsequent anaemia has been observed following abrupt interruption or discontinuation of Pyrukynd in SmPC Section 4.4*	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: • *None* Additional pharmacovigilance activities: • *Long-term safety and tolerability study AG348-C-011; final study report available 30 November 2025.*
	• *Warning that to minimize the risk of acute haemolysis, avoid abrupt interruption or discontinuation of Pyrukynd in SmPC Sections 4.2 and 4.4* • *Advice on the dose taper schedule to be followed when discontinuing Pyrukynd in SmPC Section 4.2* • *Warning to monitor patients for signs of acute haemolysis with worsening of anaemia if discontinuing treatment in SmPC Sections 4.2 and 4.4* • *Warning and precaution for the patient to talk to their doctor if they develop symptoms of acute haemolysis in PL Section 4* • *Pack size: Dose taper blister packs, that follow the dose taper schedule, when discontinuing Pyrukynd* • *Description of the dose taper blister packs in SmPC Section 6.5 and PL Section 6* Additional risk minimization measures: • *None*	

Summary Table of Pharmacovigilance Activities and Risk Minimization Activities by Safety Concern

Safety Concern	Risk Minimization Measures	Pharmacovigilance Activities
Embryo-fetal toxicity	Routine risk minimization measures: • *Information on nonclinical findings in SmPC Section 5.3* • *Advice that Pyrukynd is not recommended during pregnancy and in women of childbearing potential not using contraception in SmPC Section 4.6* • *Advice that contraception should be used by women of childbearing potential during treatment and for at least 1 month after the last dose in SmPC Section 4.6* • *Advice that mitapivat may decrease systemic exposure of hormonal contraceptives that are sensitive substrates of CYP3A4 in SmPC Sections 4.4, 4.5 and 4.6* • *Advice that women of childbearing potential should be counselled regarding the use of additional or alternative contraception methods in SmPC Section 4.4* • *Advice that Pyrukynd should be avoided during pregnancy and women of childbearing potential must use reliable contraception and for at least 1 month after the last dose in PL Section 2* • *Advice that birth control medicines containing hormones may not work as well as expected and pregnancy may occur so a patient should discuss contraception methods with their doctor in PL Section 2* Additional risk minimization measures: • *None*	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: • *Pregnancy-, lactation-, embryo-fetal toxicity-follow up form* Additional pharmacovigilance activities: • *None*

Summary Table of Pharmacovigilance Activities and Risk Minimization Activities by Safety Concern

Safety Concern	Risk Minimization Measures	Pharmacovigilance Activities
Use in patients with hepatic impairment	Routine risk minimization measures: • *Information that the pharmacokinetics of mitapivat in patients with mild, moderate, or severe hepatic impairment have not been studied in SmPC Section 5.2* • *Advice that Pyrukynd has not been studied in patients with hepatic impairment and no dose recommendations can be made in SmPC Sections 4.2 and 5.2* Additional risk minimization measures: • *None*	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: • *None* Additional pharmacovigilance activities: • *Hepatic impairment Study AG348-C-0HEP; final study report available: 31 March 2024*
Long-term Use	Routine risk minimization measures: • *Information that the median duration of treatment with Pyrukynd was 24.1 weeks in AG348-C-006 and median duration of treatment in AG348-C-007 was 40.3 weeks in SmPC Section 5.1* • *Advice that treatment with Pyrukynd is intended to be long-term and should be discontinued if there is no improvement of haemolytic anaemia at the maximum recommended dose, based on the totality of laboratory results and clinical status of the patient, unless there is another explanation for response failure in SmPC Section 4.2.* Additional risk minimization measures: • *None*	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: • *None* Additional pharmacovigilance activities: • *Long-term safety and tolerability study AG348-C-011; final study report available 30 November 2025.* • *Longitudinal observational study AG348-C-008 (Peak Registry); final study report for patients that received mitapivat available 30 September 2028.*

This is acceptable.

VII. USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) has been provided with the applications, 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.

VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the products 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 SmPCs, PIL and labelling text are satisfactory.

In accordance with legal requirements, the current approved UK versions of the SmPCs and PIL for these products are available on the MHRA website.

The following **representative text** is the currently approved label text for Pyrukynd 5 mg film-coated tablets.

No label mock-ups have been provided for these products. In accordance with legal requirements, these products shall not be marketed until approval of the full-colour label mock-ups has been obtained.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (pack of 56 × 5 mg film-coated tablets)

1. NAME OF THE MEDICINAL PRODUCT

Pyrukynd 5 mg film-coated tablets
mitapivat

2. STATEMENT OF ACTIVE SUBSTANCE

Each film-coated tablet contains 5 mg mitapivat (as sulfate).

3. LIST OF EXCIPIENTS

Also contains lactose.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Film-coated tablet
56 film-coated tablets

5. METHOD AND ROUTE OF ADMINISTRATION

Do not split, crush, chew, or dissolve the tablets.
Read the package leaflet before use.
For 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 below 25°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

Agios Netherlands B.V.
Zuidplein 36
Regus Amsterdam WTC
1077XV Amsterdam
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

PLGB 52779/0001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Pyrukynd 5 mg

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

BLISTER WALLET (pack of 56 × 5 mg film-coated tablets)

1. NAME OF THE MEDICINAL PRODUCT

Pyrukynd 5 mg film-coated tablets
mitapivat

2. STATEMENT OF ACTIVE SUBSTANCE

Each film-coated tablet contains 5 mg mitapivat (as sulfate).

3. LIST OF EXCIPIENTS

Also contains lactose.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

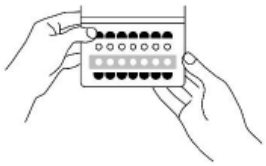
Film-coated tablet
14 film-coated tablets

5. METHOD AND ROUTE OF ADMINISTRATION

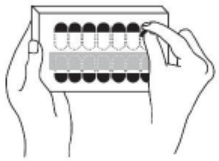
Do not split, crush, chew, or dissolve the tablets.
Read the package leaflet before use.
For oral use.

OPENING INSTRUCTIONS

1. Use thumb to PUSH



2. Turn package over, PEEL the raised tab on the back



3. Push tablet through the foil
PUSH
PEEL

SUN
MON
TUE
WED
THU
FRI
SAT

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 below 25°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

Agios Netherlands B.V.
Zuidplein 36, Regus Amsterdam WTC

1077XV Amsterdam, The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

PLGB 52779/0001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Pyrukynd 5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (taper pack of 7 × 5 mg film-coated tablets)

1. NAME OF THE MEDICINAL PRODUCT

Pyrukynd 5 mg film-coated tablets
mitapivat

2. STATEMENT OF ACTIVE SUBSTANCE

Each 5 mg film-coated tablet contains 5 mg mitapivat (as sulfate).

3. LIST OF EXCIPIENTS

Also contains lactose.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Film-coated tablet
7 film-coated tablets

5. METHOD AND ROUTE OF ADMINISTRATION

Do not split, crush, chew, or dissolve the tablets.
Read the package leaflet before use.
For 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 below 25°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

Agios Netherlands B.V.
Zuidplein 36
Regus Amsterdam WTC
1077XV Amsterdam
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

PLGB 52779/0001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Pyrukynd 5 mg

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

BLISTERS (5 mg film-coated tablets)

1. NAME OF THE MEDICINAL PRODUCT

Pyrukynd 5 mg
mitapivat

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Agios Netherlands B.V.
Zuidplein 36
Regus Amsterdam WTC
1077XV Amsterdam
The Netherlands

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

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**

Annex 1
Summary of fulfilment of the criteria for orphan drug designation

Products:	Pyrukynd 5 mg film-coated tablets Pyrukynd 20 mg film-coated tablets Pyrukynd 50 mg film-coated tablets Pyrukynd 20 mg + 5 mg film-coated tablets Pyrukynd 50 mg + 20 mg film-coated tablets
Active substance:	Mitapivat (as mitapivat sulfate)
Orphan Designation Number:	PLGB 52779/0001-0005 OD1

Background:

These applications were evaluated for fulfilment of orphan designation criteria by the Commission on Human Medicines (CHM) and the designation criteria were considered fulfilled.

Evaluation:

Orphan condition
The orphan condition is pyruvate kinase deficiency.

Orphan indication
The orphan indication is "the treatment of pyruvate kinase deficiency (PK deficiency) in adult patients".

Life threatening/ debilitating condition
The condition is chronically debilitating and life-threatening due to symptoms of chronic haemolytic anaemia and sequelae of periodic red blood cell transfusions, comprising fatigue, shortness of breath, splenomegaly, cholecystolithiasis, heart failure, as well as compromised immune function and thromboembolic complications after splenectomy.

The condition is also life-threatening due to aggravation of haemolytic anaemia during pregnancy and aplastic crisis during viral infections, as well as hydrops fetalis and perinatal death.

Prevalence of the Condition in Great Britain (GB)
Suitable evidence has been provided that demonstrates that, at the time of orphan designation, the point prevalence of the condition in GB is estimated to be 0.05 in 10,000 people. This does not exceed the upper limit of prevalence for orphan designation, which is 5 in 10,000 people in GB.

Existing methods of treatment
There are no existing authorised methods of treatment of the orphan condition in GB.

The current standard clinical care of patients with PK deficiency is mainly supportive and involves the treatment and management of symptoms and complications of PK deficiency. This includes red blood cell transfusions, splenectomy, iron chelation, cholecystectomy and jaundice therapies. Haematopoietic stem cell transplant has been pursued in a small number of patients with mixed outcomes.

Justification of significant benefit
There are no licensed methods of treatment available in GB for the treatment of the orphan condition.

The currently proposed clinical development is sufficient to demonstrate significant benefit; this is acceptable.

Conclusion:

Conclusion on acceptability of orphan designation
The applicant has demonstrated fulfilment of the criteria for approval as an orphan medicinal product.

All medicines that gain an orphan marketing authorisation from the UK Licensing Authority are listed on its publicly available Orphan Register until the end of the market exclusivity period. The authorised orphan indication defines the scope of orphan market exclusivity.

Decision: Grant

Date: 20 December 2022