



Public Assessment Report

National Procedure

QINLOCK 50 mg tablets
ripretinib

PLGB 55295/0004

Deciphera Pharmaceuticals (Netherlands) B.V.

LAY SUMMARY

QINLOCK 50 mg tablets ripretinib

This is a summary of the Public Assessment Report (PAR) for QINLOCK 50 mg tablets. 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 QINLOCK in this lay summary for ease of reading.

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

What is QINLOCK and what is it used for?

This product has been authorised by the MHRA for Great Britain (consisting of England, Scotland and Wales; GB). In coming to its decision, the MHRA has relied on a European Commission (EC) decision on 18 November 2021 (EMA/H/C/005614/0000), 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 indication.

QINLOCK is used to treat adults with gastrointestinal stromal tumour (GIST), a rare type of cancer of the digestive system including the stomach and bowel, that has:

- spread to other parts of the body or cannot be removed by surgery
- been treated with at least 3 previous cancer medicines, including imatinib.

How does QINLOCK work?

QINLOCK contains the active substance, ripretinib, which is a protein kinase inhibitor. Protein kinase inhibitors are used to treat cancer by stopping the activity of certain proteins that are involved in the growth and spread of cancer cells.

How is QINLOCK used?

The pharmaceutical form of this medicine is tablets and the route of administration is oral (taken by mouth).

The recommended daily dose is three 50 mg tablets (150 mg) once daily. The patient should take the tablets at the same time each day with or without food. The patient should swallow the tablets whole with a glass of water and not chew, split, or crush the tablets. They should not take any tablets that are broken, cracked, or otherwise damaged due to unknown effects of taking tablets that are not whole.

If the patient has to take certain other medicines at the same time as QINLOCK, their doctor may change their dose to three 50 mg tablets (150 mg) twice daily.

The patient will usually take QINLOCK as long as they are benefitting from it and not suffering unacceptable side effects (see section 4 of the PIL); however, their doctor may reduce their dose, or may decide to interrupt or stop the treatment temporarily or permanently if necessary.

If the patient has liver or kidney problems

While the patient is being treated with QINLOCK, their doctor will monitor their liver or kidney function more closely.

For further information on how QINLOCK 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 benefits of QINLOCK have been shown in studies?

QINLOCK was shown to be effective at treating GIST in a study involving 129 patients who had been previously treated with, or could not tolerate, at least three other cancer medicines. The study showed in patients treated with QINLOCK their disease did not get worse for 6.3 months, on average, compared with 1.0 month for patients given placebo (a dummy treatment).

What are the possible side effects of QINLOCK?

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 QINLOCK approved?

QINLOCK was shown to be effective at slowing down the progress of the disease in patients with GIST who had been treated with at least three other medicines. QINLOCK was shown to have a favourable safety profile with manageable side effects.

The MHRA therefore decided that the benefits are greater than the risks and recommended that this medicine can be approved for use,

QINLOCK 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, such as 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 QINLOCK?

As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for QINLOCK. The RMP details the important risks of QINLOCK, how these risks can be minimised, any uncertainties about QINLOCK (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for QINLOCK:

Summary of safety concerns	
Important identified risks	Palmar-plantar erythrodysesthesia syndrome Hypertension Cardiac failure Squamous cell carcinoma of skin
Important potential risks	Embryo-foetal toxicity Phototoxicity
Missing information	Use in patients with moderate or severe hepatic impairment Use in patients with severe renal impairment

The information included in the SmPC 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 QINLOCK 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 QINLOCK product information, to ensure the safe and effective use of QINLOCK, additional pharmacovigilance activity is proposed for the safety concern 'Missing information: Use in patients with moderate or severe hepatic impairment' in the form of a post authorisation study to investigate the impact of mild, moderate and severe hepatic impairment on ripretinib pharmacokinetics.

A RMP and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

Other information about QINLOCK

A Marketing Authorisation was granted in GB on 20 December 2021.

The full PAR for QINLOCK follows this summary.

This summary was last updated in February 2022.

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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 application for QINLOCK 50 mg tablets (PLGB 55295/0004) could be approved.

The product is approved for the following indication:

- the treatment of adult patients with advanced gastrointestinal stromal tumour (GIST) who have received prior treatment with three or more kinase inhibitors, including imatinib.

The active substance, ripretinib, is a novel tyrosine kinase inhibitor that inhibits proto-oncogene receptor tyrosine kinase (KIT) and Platelet Derived Growth Factor Receptor Alpha (PDGFRA) kinase, including wild type, primary, and secondary mutations. Ripretinib also inhibits other kinases *in vitro*, such as Platelet-Derived Growth Factor Receptor Beta (PDGFRB), Tunica interna endothelial kinase 2 (TIE2), Vascular endothelial growth factor receptor 2 (VEGFR2) and oncogene that Encodes the Protein B-Raf (BRAF).

This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales; GB). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 18 November 2021 (EMA/H/C/005614/0000), 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 approved under Regulation 50 of the Human Medicines Regulation 2012, as amended (previously Article 8.3 of Directive 2001/83/EC, as amended).

The application was evaluated for fulfilment of orphan designation criteria and the designation criteria were considered fulfilled. 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).

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

In line with the legal requirements for children's medicines, the application included a licensing authority decision on granting of a product specific waiver (P/0122/2020).

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 on 20 December 2021.

II. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION SUMMARY OF PRODUCT CHARACTERISTICS (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.

III. QUALITY ASPECTS

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

The grant of a Marketing Authorisation is recommended.

IV. NON-CLINICAL ASPECTS

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

The grant of a Marketing Authorisation is recommended.

V. CLINICAL ASPECTS

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

The grant of a Marketing Authorisation 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 Regulations 2012, as amended. In addition to routine pharmacovigilance and risk minimisation measures, additional pharmacovigilance activity is proposed in the form of a post authorisation safety study to investigate the impact of mild, moderate and severe hepatic impairment on ripretinib pharmacokinetics for the safety concern 'Missing information: Use in patients with moderate or severe hepatic impairment'.

This is acceptable.

VII. USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (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.

VIII. 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 GB versions of the SmPC and PIL for this product are available on the MHRA website.

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**OUTER CARTON****1. NAME OF THE MEDICINAL PRODUCT**

QINLOCK 50 mg tablets
ripretinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 50 mg of ripretinib.

3. LIST OF EXCIPIENTS

Contains lactose, see leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

30 tablets
90 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Read the package leaflet before 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 and keep bottle tightly closed in order to protect from light and moisture.

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

Deciphera Pharmaceuticals (Netherlands) B.V.
Atrium Building Floor 4th
Strawinskylaan 3051
1077ZX, Amsterdam
Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

PLGB 55295/0004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

QINLOCK 50 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**BOTTLE LABEL****1. NAME OF THE MEDICINAL PRODUCT**

QINLOCK 50 mg tablets
ripretinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 50 mg of ripretinib.

3. LIST OF EXCIPIENTS

Contains lactose, see leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

30 tablets
90 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Read the package leaflet before 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**

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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 SmPC 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

Product: QINLOCK 50 mg tablets
Active substance: Ripretinib
Orphan Designation Number: PLGB 55295/0004/OD1
Background:

This application was evaluated for fulfilment of orphan designation criteria and the designation criteria were considered fulfilled.

Evaluation:

Orphan condition

The orphan condition is gastrointestinal stromal tumour (GIST). This is acceptable and in line with the guidance on what constitutes a valid condition. GIST is a relatively rare form of soft tissue sarcoma that affects the stomach and small/large intestine. Most tumours arise due to activating mutations in protooncogenes (Proto-Oncogene Receptor Tyrosine Kinase (KIT) or Platelet-Derived Growth Factor Receptor Alpha (PDGFA)), although a small proportion are KIT/PDGFA wild-type (10-15%).

Symptoms of GIST vary depending on the location, size and aggressiveness of the tumour. The median age at diagnosis is 60- 65 years.

Orphan indication

The orphan indication is the treatment of adult patients with advanced gastrointestinal stromal tumour (GIST) who have received prior treatment with three or more kinase inhibitors, including imatinib.

Life threatening/ debilitating condition

The condition is debilitating and life-threatening. Larger tumours cause symptoms, most commonly gastrointestinal bleeding. There is also a high rate of relapse and progression resulting in poor survival.

Prevalence of the Condition in Great Britain (GB)

Suitable evidence has been provided that demonstrates that, at the time of orphan designation, the condition affects 2.1 in 10,000 people in GB. 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

Surgical resection is the only potentially curative treatment for GIST, but there is a 50% recurrence rate.

There are four tyrosine kinase inhibitors (TKIs) approved by the MHRA that are indicated to treat patients with GIST: imatinib (Glivec, first line), sunitinib (Sutent, second line), regorafenib (Stivarga, third line) and avapritinib (Ayvakyt, GIST carrying the PDGFA D842V mutation). Treatment with imatinib is the standard of care in high-risk patients with advanced/metastatic disease.

If patients experience progressive disease while on regorafenib, options in the fourth-line setting include TKI re-challenge, best supportive palliative care, or recruitment into clinical trials.

No authorised products exist for adult patients with advanced GIST who have received prior treatment with three or more kinase inhibitors, including imatinib. The indication for QINLOCK 50 mg tablets targets a different patient population than the indication of the authorised products.

Justification of significant benefit

Efficacy of QINLOCK 50 mg tablets was demonstrated in a Phase III study DCC-2618-03-001 (INVICTUS), that enrolled patients with unresectable and/or metastatic GIST who presented with disease progression after at least 3 approved lines of therapy.

As QINLOCK 50 mg tablets are intended for a patient population for whom no other satisfactory method is available, no justification of significant benefit is required.

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: 08 December 2021