Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Ilumetri 100 mg solution for injection in pre-filled pen

tildrakizumab

PLGB 16973/0047

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LAY SUMMARY

Ilumetri 100 mg solution for injection in pre-filled pen
tildrakizumab

This is a summary of the Public Assessment Report (PAR) for Ilumetri 100 mg solution for injection in pre-filled pen. 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 Ilumetri in this lay summary for ease of reading.

This product has been authorised by the Medicines and Healthcare products Regulatory Agency (MHRA) for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a Commission on Human Medicines Opinion on 26 January 2023 (EMEA/H/C/004514/II/0036), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP). This is known as the EC Decision Reliance Procedure.

Tildrakizumab is also authorised in a **pre-filled syringe** assembled with needle safety device. The product to which this report relates is a **pre-filled pen** presentation. The primary packaging, the route of administration and the pharmaceutical form (solution for injection) are unchanged, only the device intended to administer the medicinal product is modified.

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).

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

What is Ilumetri and what is it used for?
Ilumetri contains the active substance tildrakizumab. Tildrakizumab belongs to a group of medicines called interleukin (IL) inhibitors.

Ilumetri is used to treat a skin condition called plaque psoriasis, in adults with moderate to severe disease. The use Ilumetri will benefit a patient by improvements of skin clearance and reducing the symptoms of plaque psoriasis.

How does Ilumetri work?
This medicine works by blocking the activity of a protein called IL-23, a substance found in the body which is involved in normal inflammatory and immune responses and which is present at increased levels in diseases such as psoriasis.

How is Ilumetri used?
The pharmaceutical form of this medicine is solution for injection and the route of administration is subcutaneous use.

Ilumetri is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of psoriasis.

This medicine should always be used exactly in line with the instruction of the patient's doctor. The patient should check with their doctor or pharmacist if they are not sure about how to use this medicine. This medicine is for single use only.

The recommended dose of Ilumetri is 100 mg by subcutaneous injection at weeks 0, and 4 and every 12 weeks thereafter.

The patient's doctor may recommend a dose of 200 mg for patients with high disease burden or with a body weight above 90 kg. The doctor will decide for how long their patient needs to take Ilumetri.

For further information on how Ilumetri 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 Ilumetri have been shown in studies?
No additional studies were needed as Ilumetri contain(s) the same active substance as another product in the Ilumetri range, and satisfactory data to justify the differences have been provided.

What are the possible side effects of Ilumetri?
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 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 this medicine.

The most common side effect with Ilumetri (which may affect more than 1 in 10 people) is upper respiratory infections.

Why was Ilumetri approved?
MHRA decided that the benefits are greater than the risks and recommended that this medicine can be approved for use.

Ilumetri has been authorised with the condition to perform further studies see RMP section of in the main body of this report.

What measures are being taken to ensure the safe and effective use of Ilumetri?
As for all newly-authorised medicines, an Risk Management Plan (RMP) has been developed for Ilumetri. The RMP details the important risks of Ilumetri, how these risks can be minimised,

any uncertainties about Ilumetri (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Ilumetri:

Important identified risks	**None**
Important potential risks	Hypersensitivity Serious infections Malignancies Major adverse cardiac events Suicidal ideation behaviour (SIB) Inflammatory Bowel Disease (IBD)
Missing information	Safety in pregnant and lactating women Long-term safety Use after recent vaccination with live bacterial or live viral vaccines Use in immunosuppressed patients Use in patients with 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 Ilumetri are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

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

Other information about Ilumetri
A marketing authorisation was granted in Great Britain on 21 February 2024.

The full PAR for Ilumetri follows this summary.

This summary was last updated in March 2024.

TABLE OF CONTENTS

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 Ilumetri 100 mg solution for injection in pre-filled pen (PLGB 16973/0047) could be approved.

The product is approved for the following indications:
Ilumetri is indicated for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy.

Tildrakizumab is a humanised IgG1/k monoclonal antibody that specifically binds to the p19 protein subunit of the interleukin-23 (IL-23) cytokine without binding to IL-12 and inhibits its interaction with the IL-23 receptor.

IL-23 is a naturally occurring cytokine that is involved in inflammatory and immune responses. Tildrakizumab inhibits the release of proinflammatory cytokines and chemokines.

This product has 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 26 January 2023 (EMEA/H/C/004514/II/0036), 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).
This application is line extension; Tildrakizumab is also authorised in a pre-filled syringe assembled with needle safety device. The product to which this report relates is a pre-filled pen presentation. The primary packaging, the route of administration and the pharmaceutical form (solution for injection) are unchanged, only the device intended to administer the medicinal product is modified.

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-100525-PIP01-22-M01 (update).

At the time of the submission of the application 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 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 21 February 2024.

II. 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

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

The grant of a marketing authorisation was recommended.

IV. NON-CLINICAL ASPECTS

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

The grant of a marketing authorisation was recommended.

V. CLINICAL ASPECTS

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

The grant of a marketing authorisation was 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 activities have been proposed, this is acceptable:

Important potential risk: Hypersensitivity	
Evidence for linking the risk to the medicine	Treatment with monoclonal antibodies may lead to the development of serious anaphylactic or anaphylactoid hypersensitivity reactions, therefore hypersensitivity is considered as a potential risk in the RMP. The classification of hypersensitivity as a potential risk is based on evidence from literature the safety profile described for similar mAbs used for Psoriasis and form the tildrakizumab clinical development programme
Risk factors and risk groups	None identified
Risk minimisation measures	Routine risk minimisation measures • SmPC Sec. 4.3 • PL Sec. 2 • Pack size • Prescription only medicine

Additional pharmacovigilance activities	Additional pharmacovigilance activities • Review of safety data from long-term (4 years) extension studies • Post Authorisation Safety Study (PASS) in European Psoriasis Registries See Sec. II.C of this summary for an overview of the post-authorisation development plan.

Important potential risk: Serious infections	
Evidence for linking the risk to the medicine	The classification of serious infections as a potential risk is based on evidence from the clinical development programme and the safety profile described for similar MABs that acts in the same pathways used for Psoriasis Animal studies do not suggest that tildrakizumab produces a detrimental effect on the immune system. Tildrakizumab has an immunomodulatory mode of action, therefore serious infection is considered a potential risk in the RMP and will be monitored in the post-marketing setting.
Risk factors and risk groups	Patients with concomitant chronic debilitating conditions (such as haematological or lymphoreticular malignancies, organ transplanted patients, severe stages of rheumatoid arthritis or systemic lupus erythematosus) who require concomitant immunosuppressive therapies such as steroids at immunosuppressive doses, methotrexate, immunosuppressant or tumour necrosis factor α (TNFα) antagonists (Fica, 2014). A recent systemic review showed that there may be a small increased risk of overall infection related to the short-term use of TNFα antagonists in the treatment of psoriasis, the majority of infections were non-serious (97.6%) and were upper respiratory tract infections (Dommasch, 2011). It is well-recognised that serious infections including atypical infections like TB have been reported with the use of TNF-alpha inhibitors in psoriasis (Dommasch, 2011).
Risk minimisation measures	Routine risk minimisation measures • SmPC Sec. 4.3 and 4.4 • PL Sec. 2 • Pack size • Prescription only medicine
Additional pharmacovigilance activities	Additional pharmacovigilance activities • Review of safety data from long-term (4 years) extension studies • PASS in European Psoriasis Registries • US Observational Study See Sec. II.C of this summary for an overview of the post-authorisation development plan.

Important potential risk: Malignancies	
Evidence for linking the risk to the medicine	The classification of malignancies as a potential risk is based on the safety profile described for similar mAbs that acts in the same pathways used for Psoriasis and evidence from the clinical development programme. Animal studies for tildrakizumab have shown no increase in carcinogenic risk. Tildrakizumab has however an immunomodulatory

	mode of action, therefore malignancies is considered as a potential risk in the RMP and will be further assessed in the post-marketing setting.
Risk factors and risk groups	Cancer risk seems to be higher in patients with severe psoriasis (Beyaert, 2013). Patients with long standing psoriasis seem to be at an increased risk for colon, bladder and kidney cancer (Brauchli, 2009). Patients receiving high dose PUVA and methotrexate for psoriasis are at an increased risk of skin cancer. In a US prospective PUVA follow-up study of patients with severe psoriasis, more than 25% of patients exposed to high doses of PUVA developed squamous cell cancer (SCC): the relative risk of SCC for patients exposed to high dose PUVA was 5.9 (95% CI 4.0-8.7) compared to those exposed to low dose PUVA. High dose methotrexate was determined to be an independent risk factor for developing SCC with a relative risk of 2.1(95% CI 1.4-2.8) compared to low or no exposure to methotrexate (Stern, 1994).
Risk minimisation measures	Routine risk minimisation measures • SmPC Sec. 5.3 • Pack size • Prescription only medicine
Additional pharmacovigilance activities	Additional pharmacovigilance activities • Review of safety data from long-term (4 years) extension studies • PASS in European Psoriasis Registries • US Observational Study See Sec. II.C of this summary for an overview of the post-authorisation development plan.

Important potential risk: Major adverse cardiac events (MACE)	
Evidence for linking the risk to the medicine	Psoriasis patients have an increased risk of cardiovascular events due to overlapping mechanisms of systemic inflammation; therefore MACE is considered a potential risk in the RMP and will be further assessed in the post-marketing setting. The classification of MACE as a potential risk is based on evidence from the clinical development programme, the safety profile described for similar mAbs that acts in the same pathways used for Psoriasis.
Risk factors and risk groups	Patients with psoriasis are at increased risk of myocardial infarction (MI) and stroke (Armstrong, 2013) and of MACE (Parisi, 2015) and this risk appears to increase with severity of disease (Armstrong, 2013; Parisi, 2015; Mehta, 2011). The increased cardiovascular risk observed in psoriasis may result from a number of often related risk factors including: smoking, obesity, hypertension and alcohol misuse. In addition the use of dyslipidaemic therapies, such as corticosteroids, acitretin and ciclosporin and an associated unfavourable lipid profile with high triglycerides and low HDL cholesterol may contribute. Psoriasis itself is an independent risk factor for MACE (Mehta, 2011) and the overall increased risk may be related to a combination of these factors in the patient (Mrowietz, 2006).
Risk minimisation measures	Routine risk minimisation measures • Pack size • Prescription only medicine

Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Review of safety data from long-term (4 years) extension studies • PASS in European Psoriasis Registries • US Observational Study See Sec. II.C of this summary for an overview of the post-authorisation development plan.

Important potential risk: Suicidal ideation behaviour (SIB)	
Evidence for linking the risk to the medicine	The classification of SIB as a potential risk is based on the safety profile described for similar mAbs that acts in the same pathways used for Psoriasis and on evidence from the clinical development programme. Psoriasis patients have an increased risk of depression and suicidal ideation. SIB events have been observed with monoclonal antibodies used in psoriasis, therefore SIB is considered as a potential risk in the RMP and will be closely monitored in the post-marketing setting.
Risk factors and risk groups	Patients with psoriasis have an increased prevalence of the psychiatric disorders anxiety and depressive disorders (30% and 60% respectively). About 10% of psoriasis patients consider the possibility of suicide (Gupta, 1998). Patients with psoriasis are at a higher risk of depression, suicidal ideation, suicide attempt and completed suicide (Gupta, 1998; Kurd, 2010; Koo, 2017).
Risk minimisation measures	Routine risk minimisation measures • Pack size • Prescription only medicine
Additional pharmacovigilance activities	Additional pharmacovigilance activities • Review of safety data from long-term (4 years) extension studies • PASS in European Psoriasis Registries See Sec. II.C of this summary for an overview of the post-authorisation development plan.

Important potential risk: Inflammatory Bowel Disease (IBD)	
Evidence for linking the risk to the medicine	IBD events have been observed with other monoclonal antibodies (known as IL-17 inhibitors) used in psoriasis, therefore IBD is considered as a potential risk in the RMP and will be closely monitored in the post-marketing setting.
Risk factors and risk groups	IBD is considered a potential co-morbidity in patients with psoriasis. Patients with Crohn's Disease (CD) have a 7-times higher risk of developing psoriasis, and psoriasis patients have a 2.9-times higher risk of developing CD, when compared with the general population (Gulliver, 2008; Christophers, 2001;Vlachos, 2016).
Risk minimisation measures	Routine risk minimisation measures • Pack size • Prescription only medicine
Additional pharmacovigilance activities	Additional pharmacovigilance activities • Review of safety data from long-term (4 years) extension studies • PASS in European Psoriasis Registries

	See Sec. II.C of this summary for an overview of the post-authorisation development plan.

Missing information: Safety in pregnant and lactating women	
Risk minimisation measures	Routine risk minimisation measures • SmPC Sec. 4.6 and 5.3 • PL Sec. 2 • Pack size • Prescription only medicine
Additional pharmacovigilance activities	Additional pharmacovigilance activities • Pregnancy safety related studies (US). • PASS in European Psoriasis Registries

Missing information: Long-term safety	
Risk minimisation measures	Routine risk minimisation measures • Pack size • Prescription only medicine
Additional pharmacovigilance activities	Additional pharmacovigilance activities • Review of safety data from long-term (4 years) extension studies • PASS in European Psoriasis Registries • US Observational Study See Sec. II.C of this summary for an overview of the post-authorisation development plan.

Missing information: Use after recent vaccination with live bacterial or live viral vaccines	
Risk minimisation measures	Routine risk minimisation measures • SmPC Sec. 4.4 and 4.5 • PL Sec. 2 • Pack size • Prescription only medicine

Missing information: Use in immunosuppressed patients	
Risk minimisation measures	Routine risk minimisation measures • SmPC Sec. 4.5 • PL Sec. 2 • Pack size • Prescription only medicine

Missing information: Use in patients with severe hepatic impairment	
Risk minimisation measures	Routine risk minimisation measures • SmPC Sec. 4.2 and Sec 5.2 • Pack size • Prescription only medicine

Missing information: Use in patients with severe renal impairment	
Risk minimisation measures	Routine risk minimisation measures • SmPC Sec. 4.2 and Sec 5.2 • Pack size • Prescription only medicine

For table II.C please refer to the RMP on the EMA's website.

VII. USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) was provided with the application in accordance with legal requirements, including user consultation.

VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the product is acceptable, and no non-clinical or clinical safety concerns have been identified. Clinical experience with tildrakizumab is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.

The Summaries of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory.

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

IX. TABLE OF CONTENT 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**

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