Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

Public Assessment Report

UK PAR

Butec 15 microgram/hour transdermal patch

(Buprenorphine)

UK Licence No: PL 40431/0027

Qdem Pharmaceuticals Limited

LAY SUMMARY

Butec 15 microgram/hour transdermal patch

(buprenorphine)

This is a summary of the Public Assessment Report (PAR) for Butec 15 microgram/hour transdermal patch (PL 40431/0027). It explains how the application for Butec 15 microgram/hour transdermal patch 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 Butec 15 microgram/hour transdermal patch.

For practical information about using Butec 15 microgram/hour transdermal patch, patients should read the package leaflet or contact their doctor or pharmacist.

The product may be referred to as 'Butec Transdermal Patch' or 'Butec Transdermal Patches' in this report.

What is Butec Transdermal Patch and what is it used for?

This medicine is the same as BuTrans 15 microgram/hour transdermal patch (PL 16950/0349; Napp Pharmaceuticals Limited), which is already authorised in the UK. The licence holder (Napp Pharmaceuticals Limited) for BuTrans 15 microgram/hour transdermal patch (PL 16950/0349) has agreed that its own scientific data can be used as a basis for the grant of an identical licence for Butec Transdermal Patch (informed consent).

Butec Transdermal Patch is used to relieve moderate, long-lasting pain that requires the use of a strong painkiller. Butec Transdermal Patches should not be used to relieve acute pain.

How does Butec Transdermal Patch work?

Butec Transdermal Patch contains the active ingredient, buprenorphine, which belongs to a group of medicines called strong analgesics or strong 'painkillers'. Butec Transdermal Patch acts through the skin. After application, buprenorphine passes through the skin into the blood. Each patch lasts for seven days.

How is Butec Transdermal Patch used?

Butec Transdermal Patch is applied to the skin on the upper outer arm, upper chest, upper back or side of the chest.

Each 18.75 cm^2 transdermal patch contains 15 mg of buprenorphine and releases about 15 micrograms of buprenorphine per hour (over a period of 7 days).

The patient should always use the Butec Transdermal Patch exactly as advised by the doctor and should check with the doctor or pharmacist if not sure.

Different strengths of Butec transdermal patches are available. The prescribing doctor will decide which strength of Butec Transdermal Patch will best suit the patient. During treatment, the doctor may change the patch used to a smaller or larger one if necessary. The patient should not apply more than two patches at the same time, regardless of the patch strength.

Adults and elderly patients
Unless the doctor has advised differently, one Butec Transdermal Patch should be applied (as described in the package leaflet) and changed every seventh day, preferably at the same time of day. The patient's doctor may wish to adjust the dose after 3-7 days until the correct level of pain control has been found. If the doctor has advised that other painkillers in addition to the patch should be taken, the doctor's instructions should be strictly followed, otherwise the patient will not fully benefit from treatment with the Butec Transdermal Patch. The patch should be worn for 3 full days before increasing the dose; this is when the maximum effect of a given dose is established.

Patients under 18 years of age
Butec Transdermal Patches should not be used in patients below the age of 18 years.

Patients with kidney disease/ dialysis patients
In patients with kidney disease, no change in dose is necessary.

Patients with liver disease
In patients with liver disease, the effects and period of action of the Butec Transdermal Patch may be affected and the doctor will therefore check more closely on the patient.

Please read section 3 of the package leaflet for detailed information on dosing recommendations, the route of administration, and the duration of treatment.

Butec Transdermal Patch can only be obtained with a prescription.

What benefits of Butec Transdermal Patch have been shown in studies?

The application for Butec Transdermal Patch is considered to be identical to the previously authorised licence for BuTrans 15 microgram/hour transdermal patch (Napp Pharmaceuticals Limited), with the same benefits and risks. So, no new studies have been provided for Butec Transdermal Patch. However, reference is made to the studies for BuTrans 15 microgram/hour transdermal patch (Napp Pharmaceuticals Limited).

What are the possible side effects from Butec Transdermal Patch?

Like all medicines, Butec Transdermal Patch can cause side effects, although not everybody gets them.

For the full list of all side effects reported with Butec Transdermal Patch, see section 4 of the package leaflet.

For the full list of restrictions, see the package leaflet.

Why is Butec Transdermal Patch approved?

No new or unexpected safety concerns arose from this application. The MHRA, therefore, considered that the benefits of Butec Transdermal Patch outweigh their risks; and the grant of Marketing Authorisations was recommended.

What measures are being taken to ensure the safe and effective use of Butec Transdermal Patch?

A Risk Management Plan has been developed to ensure that Butec Transdermal Patch is 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 Butec Transdermal Patch, 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 Butec Transdermal Patch

A Marketing Authorisation was granted for Butec 15 microgram/hour transdermal Patch to Qdem Pharmaceuticals Limited on 14 July 2016.

The full PAR for Butec Transdermal Patch follows this summary.

For more information about treatment with Butec Transdermal Patch, read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in July 2016.

Butec 15 microgram/hour transdermal patch

(buprenorphine)

PL 40431/0027

SCIENTIFIC DISCUSSION

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I. INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Qdem Pharmaceuticals Limited a Marketing Authorisation for the medicinal product Butec 15 microgram/hour transdermal patch (PL 40431/0027) on 14 July 2016. This is a Prescription Only Medicine (POM) that is indicated for the treatment of non-malignant pain of moderate intensity when an opioid is necessary for obtaining adequate analgesia. Butec Transdermal patches are not suitable for the treatment of acute pain.

The application was submitted as an informed consent application according to Article 10c of Directive 2001/83/EC, as amended, cross-referring to BuTrans 15microgram/hour transdermal patch (PL 16950/0349, Napp Pharmaceuticals Limited), which was authorised on 21 July 2015 as a hybrid application, following incoming Mutual Recognition Procedure DK/H/718/004/MR, with Denmark as Reference Member State and the UK as a Concerned Member State.

Butec Transdermal Patch contains the active ingredient buprenorphine. Buprenorphine is a partial opioid agonist, acting at the mu opioid receptor. It also has antagonistic activity at the kappa opioid receptor.

No new data were submitted nor were necessary to be submitted for this application, as the data are identical to that of the previously granted cross-reference product

II. QUALITY ASPECTS

II.1 Introduction

This is an informed consent application for the product Butec 15 microgram/hour transdermal patch (PL 40431/0027) submitted under Article 10c of Directive 2001/83/EC, as amended.

The application cross-refers to BuTrans 15microgram/hour transdermal patch (PL 16950/0349, Napp Pharmaceuticals Limited), which was granted a Marketing Authorisation in the UK on 21 July 2015. The application is considered valid.

II.2 Drug substance

Drug substance specification

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 Butec 15 microgram/hour transdermal patch. The product has been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes

Each Butec 15 microgram/hour transdermal patch contains 15 mg of buprenorphine in a patch size of 18.75 cm^2 and releases 15 micrograms of buprenorphine per hour (over a period of 7 days).

The product is packaged in sealed sachets, composed of: identical top and bottom layers of heat-sealable laminate, comprising (from outside to inside) of:

1. paper, low-density polyethylene, aluminium and poly(acrylic acid-co-ethylene), or
2. paper, polyethylene terephthalate, polyethylene, aluminium and poly(acrylic acid-co-ethylene).

The product is available in pack sizes of 1, 2, 3, 4, 5, 8, 10 and 12 transdermal patches.

Not all pack sizes may be marketed.

The proposed shelf life for the product is 2 years, with the special storage conditions 'Do not store above 25°C'. The packaging, proposed shelf-life and storage conditions are consistent with the details registered for the cross-reference product.

Legal status
On approval, the product will be available as a Prescription Only Medicine (POM).

Marketing Authorisation Holder/Contact Persons/Company
Qdem Pharmaceuticals Limited, Cambridge Science Park, Milton Road, Cambridge, CB4 0AB, 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 product 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 processes are 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
None of the excipients contain materials of animal or human origin. This is consistent with the cross-reference product.

Bioequivalence
No bioequivalence data are required to support this informed consent application because the proposed product is manufactured to the same formulae and utilises the same processes as the reference product, BuTrans 15 microgram/hour transdermal patch (PL 16950/0349; Napp Pharmaceuticals Limited).

Product Name and Appearance
See Section 'Medicinal Product, Name' above 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 is 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 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 is an 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. Please see below a table of the summary of safety concerns.

Summary of safety concerns	
Important identified risks	Respiratory depression Accidental overdose Drug withdrawal syndrome and physical dependence
Important potential risks	Drug abuse Medication error Psychological dependence Off-label use (Cutting of BTDS patch to achieve an intermediate dose)
Important missing information	Use in pregnant or breastfeeding women Paediatric use

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 BuTrans 15 microgram/hour transdermal patch (PL 16950/0349; Napp Pharmaceuticals Limited). The bridging report has been found to be acceptable.

VI. OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

QUALITY
The data for the application are 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 an application of this type.

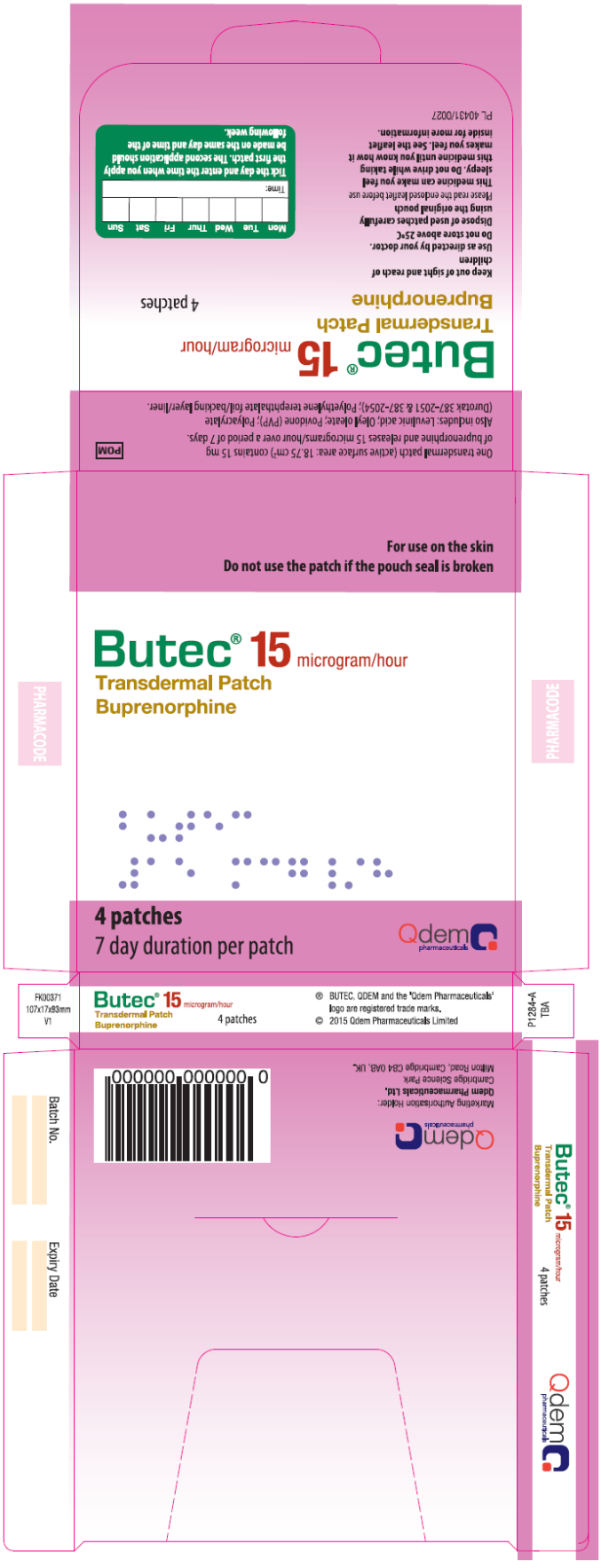
EFFICACY
The application is identical to the previously granted licence for BuTrans 15 microgram/hour transdermal patch (PL 16950/0349; Napp Pharmaceuticals Limited).

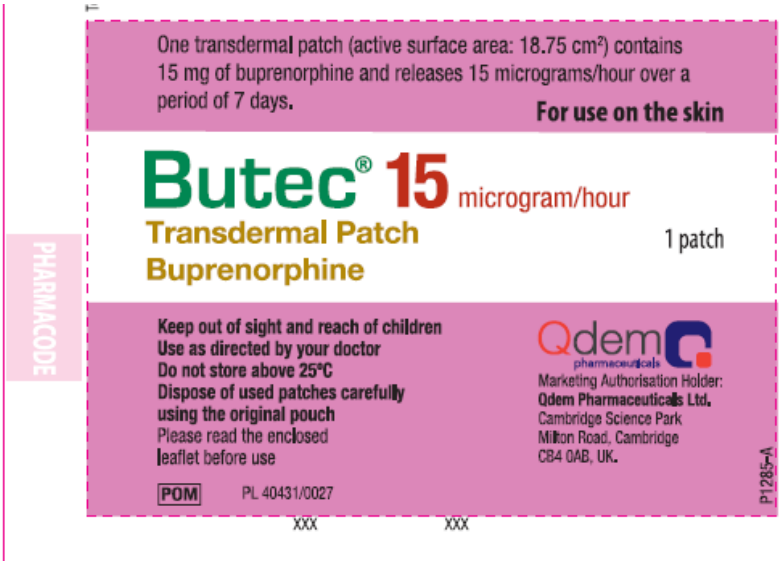
SAFETY
No new safety data were supplied or required for this application. Buprenorphine has a well-established safety profile. No new or unexpected safety concerns arose from this application.

PRODUCT LITERATURE
The SmPC and PIL are satisfactory, and consistent with those for the 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 buprenorphine 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 SmPC and PIL is available on the MHRA website. The current labelling is presented below:




PHARMACODE
One transdermal patch (active surface area: 18.75 cm²) contains 15 mg of buprenorphine and releases 15 micrograms/hour over a period of 7 days.
For use on the skin
Butec® 15 microgram/hour
Transdermal Patch
Buprenorphine
1 patch
Keep out of sight and reach of children
Use as directed by your doctor
Do not store above 25°C
Dispose of used patches carefully using the original pouch
Please read the enclosed leaflet before use
POM
PL 40431/0027
Qdem pharmaceuticals
Marketing Authorisation Holder:
Qdem Pharmaceuticals Ltd.
Cambridge Science Park
Milton Road, Cambridge
CB4 0AB, UK.
P1285-A
XXX
XXX

Butec 15 microgram/hour transdermal patch

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STEPS TAKEN AFTER AUTHORISATION - SUMMARY

Date submitted	Application type	Scope	Outcome