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LAY SUMMARY

Nefopam Hydrochloride 30 mg Tablets

This is a summary of the Public Assessment Report (PAR) for Nefopam Hydrochloride 30 mg Tablets (PL 15142/0268). It explains how the application for Nefopam Hydrochloride 30 mg Tablets 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 Nefopam Hydrochloride 30 mg Tablets.

For practical information about using Nefopam Hydrochloride 30 mg Tablets, patients should read the package leaflet or contact their doctor or pharmacist.

The product may be referred to as ‘Nefopam Hydrochloride Tablets’ in this report.

What are Nefopam Hydrochloride Tablets and what are they used for?
This medicine is the same as Acupan 30 mg Tablets (PL 15142/0109; Meda Pharmaceuticals Limited), which are already authorised in the UK. The licence holder (Meda Pharmaceuticals Limited) for Acupan 30 mg Tablets (15142/0109) has agreed that its own scientific data can be used as a basis for the grant of an identical licence for Nefopam Hydrochloride Tablets (informed consent).

Nefopam Hydrochloride Tablets are used to relieve of acute and chronic pain (for example pain after an operation, dental pain, joint or muscle pain, pain after an injury, or pain caused by cancer). Nefopam Hydrochloride Tablets should not be used to treat the pain from a heart attack.

How do Nefopam Hydrochloride Tablets work?
The active ingredient, nefopam hydrochloride, belongs to a group of medicines called analgesics, commonly known as pain killers or pain relievers. Nefopam hydrochloride interrupts the pain messages being sent to the brain, and it also acts in the brain to stop pain messages being felt. This means that Nefopam Hydrochloride Tablets do not stop the pain from happening, but the patient will not be able to feel the pain as much.

How are Nefopam Hydrochloride Tablets used?
Nefopam Hydrochloride Tablets are taken by mouth; the tablets should be swallowed with water. The patient should always take this medicine exactly as advised by his/her doctor or pharmacist. The patient should check with his/her doctor or pharmacist if unsure about how many tablets to take or when to take them or if he/she thinks the effect of the tablets is too strong or weak.

Dosage for adults
The dosage may range from 1 to 3 tablets three times a day.

The usual initial recommended dose is two tablets taken three times a day. The patient’s doctor may increase this dose up to a maximum of three tablets taken three times a day according to the patient’s needs.

Use in children and adolescents:
Over 12 years – as per above.

Under 12 years – Nefopam Hydrochloride Tablets should not be taken by children under 12.

Use in older patients:
In older patients the doctor may reduce the number of tablets that are taken.
Use in patients with kidney and/or liver problems:
The patient’s doctor may adjust the dose of Nefopam Hydrochloride Tablets depending upon the patient’s condition.

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

Nefopam Hydrochloride Tablets can only be obtained with a prescription.

What benefits of Nefopam Hydrochloride Tablet have been shown in studies?
The application for Nefopam Hydrochloride Tablets is considered to be identical to the previously authorised licence for Acupan 30 mg Tablets (PL 15142/0109; Meda Pharmaceuticals Limited), with the same benefits and risks. So, no new studies have been provided for Nefopam Hydrochloride Tablets. However, reference is made to the studies for Acupan 30 mg Tablets (PL 15142/0109; Meda Pharmaceuticals Limited).

What are the possible side effects from Nefopam Hydrochloride Tablets?
Like all medicines, Nefopam Hydrochloride Tablets can cause side effects, although not everybody gets them.

For the full list of all side effects reported with Nefopam Hydrochloride Tablets, see section 4 of the package leaflet.

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

Why are Nefopam Hydrochloride Tablets approved?
No new or unexpected safety concerns arose from this application. The MHRA, therefore, considered that the benefits of Nefopam Hydrochloride Tablets outweigh their risks; and the grant of a Marketing Authorisation was recommended.

What measures are being taken to ensure the safe and effective use of Nefopam Hydrochloride Tablets?
A Risk Management Plan has been developed to ensure that Nefopam Hydrochloride Tablets are 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 Nefopam Hydrochloride Tablets, 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 Nefopam Hydrochloride Tablets
A Marketing Authorisation was granted in the UK on 29 September 2015.

The full PAR for Nefopam Hydrochloride Tablets follows this summary.

For more information about treatment with Nefopam Hydrochloride Tablets, read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in November 2015.
Nefopam Hydrochloride 30 mg Tablets

PL 15142/0268

SCIENTIFIC DISCUSSION

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INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Meda Pharmaceuticals Limited (trading as Beechmere Pharmaceuticals) a Marketing Authorisation for the medicinal product Nefopam Hydrochloride 30 mg Tablets (PL 15142/0268) on 29 September 2015. The product is a prescription-only medicine (POM) indicated for the relief of acute and chronic pain, including post-operative pain, dental pain, musculo-skeletal pain, acute traumatic pain and cancer pain.

The application was submitted as a simple abridged (informed consent) application according to Article 10c of Directive 2001/83/EC, as amended. Nefopam Hydrochloride 30 mg Tablets cross-refers to Acupan 30 mg Tablets (PL 15142/0109; Meda Pharmaceuticals Limited), which was granted in February 2010 following a change of ownership from Valeant Pharmaceuticals Ltd. Acupan Tablets (PL 19166/0088; Valeant Pharmaceuticals Ltd) was granted in October 2007, following a change of ownership from 3M Health Care Limited (PL 00068/0061). Acupan Tablets (PL 00068/0061; 3M Health Care Limited) was authorised as a new active substance national application in March 1978.

Nefopam Hydrochloride 30 mg Tablets contain the active ingredient, nefopam hydrochloride, which is a potent and rapidly-acting analgesic. It is totally distinct from other centrally-acting analgesics such as morphine, codeine, pentazocine and propoxyphene.

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

LICENCE NO: PL 15142/0268
PROPRIETARY NAME(S): Nefopam Hydrochloride 30 mg Tablets
ACTIVE(S): Nefopam hydrochloride
COMPANY NAME: Meda Pharmaceuticals Limited (trading as Beechmere Pharmaceuticals)
E.C. ARTICLE: Article 10c of Directive 2001/83/EC, as amended
LEGAL STATUS: POM

1. INTRODUCTION
This is an informed consent application for Nefopam Hydrochloride 30 mg Tablets (PL 15142/0268) submitted under Article 10c of Directive 2001/83/EC, as amended.

The application cross-refers to Acupan 30 mg Tablets (PL 15142/0109; Meda Pharmaceuticals Limited), which was granted after a series of Change of Ownership (COA) procedures of the originator product Acupan Tablets (PL 00068/0061; 3M Health Care Limited), which was authorised in March 1978. The application is considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM
2.1. Name
The proposed name of the product is Nefopam Hydrochloride 30 mg Tablets. The product has been named in line with current requirements.

2.2. Strength, pharmaceutical form, route of administration, container and pack sizes
Each tablet contains 30 mg of nefopam hydrochloride. The product is packaged in 20 micron aluminium foil/250 micron unplasticised polyvinylchloride blisters, in a pack size of 90 tablets.

The proposed shelf life for the product is 5 years, with the special storage conditions ‘Store below 30°C.’

The packaging, proposed shelf-life and storage conditions are consistent with the details registered for the cross-reference product.

2.3. Legal status
The product is available as a Prescription Only Medicine (POM).

2.4. Marketing Authorisation Holder/Contact Persons/Company
Meda Pharmaceuticals Ltd, Skyway House, Parsonage Road, Takeley, Bishop's Stortford, CM22 6PU, United Kingdom (trading as Beechmere Pharmaceuticals, Merlin Place, Milton Road, Cambridge, CB4 0DP UK).

The Qualified Person (QP) responsible for pharmacovigilance is stated and a satisfactory CV has been provided.

2.5 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.
2.6. Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the cross-reference product.

2.7. Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

2.8. Finished product/shelf-life specification
The proposed finished product specification is consistent with the details registered for the cross-reference product.

2.9. Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference product.

2.10. TSE Compliance
None of the excipients contain materials of animal or human origin. This is consistent with the cross-reference product.

2.11. Bioequivalence
No bioequivalence data are required to support this simple abridged application because the proposed product is manufactured to the same formula and utilises the same processes as the reference product Acupan 30 mg Tablets (PL 15142/0109; Meda Pharmaceuticals Limited).

3. EXPERT REPORT
The applicant cross-refers to the data for Acupan 30 mg Tablets (PL 15142/0109; Meda Pharmaceuticals Limited) to which this application is claimed to be identical. This is acceptable.

4. PRODUCT NAME & APPEARANCE
See Section 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The proposed SmPC is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET (PIL) AND LABELLING
   PIL
   The PIL has been prepared in line with the details registered for the cross-reference product.

   User-testing of the PIL for Nefopam Hydrochloride 30 mg Tablets (PL 15142/0268) has been accepted based on the bridging report provided by the applicant making reference to the successful user-testing of the PIL for Acupan 30 mg Tablets (PL 15142/0109; Meda Pharmaceuticals Limited) as the ‘parent PIL’.

   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 names of the product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.
7. CONCLUSION
The data submitted with the application is acceptable. The grant of a Marketing Authorisation is recommended.
NON-CLINICAL ASSESSMENT

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.

Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the application is an identical version of an already authorised product, it is not expected that environmental exposure will increase following approval of the Marketing Authorisation for the proposed product.

The grant of a Marketing Authorisation is recommended.
CLINICAL ASSESSMENT

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.

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. A summary of safety concerns is listed in the following table.

<table>
<thead>
<tr>
<th>Table 1. Summary of safety concerns</th>
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<tr>
<td><strong>Summary of safety concerns</strong></td>
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<tr>
<td>Important identified risks</td>
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<tr>
<td>• Increased risk of CNS side effects in elderly patients.</td>
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<tr>
<td>• Drug-drug interactions between nefopam hydrochloride and MAO inhibitors.</td>
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<tr>
<td>• Drug-drug interactions between nefopam hydrochloride and anticholinergics, sympathomimetics and tricyclic antidepressants.</td>
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<tr>
<td>• Allergic reaction to product ingredients.</td>
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<td>• Interference of metabolism or excretion of product in patients with hepatic impairment causing increased exposure to drug which may result in aggravated side effects of hepatic impairment.</td>
</tr>
<tr>
<td>• Interference of metabolism or excretion of product in patients with renal impairment causing increased exposure to drug which may result in side effects such as convulsions, hallucinations, agitation and tachycardia and increased urinary retention, with symptoms of hesitancy, poor stream or dribbling.</td>
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<tr>
<td>Important potential risks</td>
</tr>
<tr>
<td>• False positive results during screening tests for benzodiazepines and opioids.</td>
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<td>• Overdose.</td>
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<td>• Medication errors.</td>
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<td>• Off-label use.</td>
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<tr>
<td>Missing information</td>
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<td>• Paediatric use (under 12 years of age).</td>
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<td>• Use during pregnancy and breast feeding.</td>
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<td>• Use in patients with myocardial infarction.</td>
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Routine risk minimisation is provided through the Summary of Product Characteristics and the Patient Information Leaflet and this is sufficient.

The grant of a Marketing Authorisation is recommended.
OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The data for this application is 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 this type of application.

EFFICACY
This application is identical to the previously granted licence for Acupan 30 mg Tablets (PL 15142/0109; Meda Pharmaceuticals Limited).

SAFETY
No new safety data were supplied or required for this application. Nefopam hydrochloride 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 nefopam hydrochloride is considered to have demonstrated the therapeutic value of the compound. The benefit/risk assessment is, therefore, considered to be positive.
SUMMARY OF PRODUCT CHARACTERISTICS

In accordance with Directive 2010/84/EU, the Summaries of Product Characteristics (SmPCs) for products granted Marketing Authorisations at a national level are available on the MHRA website.
PATIENT INFORMATION LEAFLET

In accordance with Directive 2010/84/EU, the Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.
LABELLING

Each tablet contains Nefopam hydrochloride 30 mg, microcrystalline cellulose, pregelatinised maize starch.

Dosage
The recommended starting dosage is two tablets three times daily. Dosage may range from one to three tablets three times daily depending on response.

Read the package leaflet before use.

It is strongly recommended that the starting dose for the elderly does not exceed one tablet three times daily.

Store below 30 °C.

Keep out of the sight and reach of children.

Beechmere

Nefopam Hydrochloride 30 mg Tablets

For the relief of pain
For oral administration

90 tablets