PARA-SUPPS PARACETAMOL 125 MG SUPPOSITORIES
PARA-SUPPS PARACETAMOL 250 MG SUPPOSITORIES
PARA-SUPPS PARACETAMOL 500 MG SUPPOSITORIES

(Paracetamol)

PL 19255/0001-0003

UKPAR

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Lay Summary

On 27 February 2013, the Medicines and Healthcare products Regulatory Agency (MHRA) granted Amdeepcha Limited Marketing Authorisations (licences) for the medicinal products Para-Supps Paracetamol 125 mg, 250 mg and 500 mg Suppositories (PL 19255/0001-0003). These are pharmacy (P) medicines.

Para-Supps Paracetamol 125 mg, 250 mg and 500 mg Suppositories contain the active ingredient paracetamol, which belongs to a group of medicines called anti-inflammatory painkillers (analgesics).

A suppository is a small, torpedo-shaped medicine which is inserted into the back passage (rectum). These may be useful in people who find it difficult to take tablets or syrup.

Para-Supps Paracetamol 125 mg Suppositories are used to relieve mild to moderate pain and fever in children from 1 to 5 years of age.

Para-Supps Paracetamol 250 mg Suppositories can be used to relieve mild to moderate pain and fever in children from 6 to 12 years of age.

Para-Supps Paracetamol 500 mg Suppositories can be used to relieve mild to moderate pain and fever in children over 12 years of age and adults.

No new or unexpected safety concerns arose from these applications and it was, therefore, judged that the benefits of using Para-Supps Paracetamol 125 mg, 250 mg and 500 mg Suppositories outweigh the risks; hence Marketing Authorisations have been granted.
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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted Amdeepcha Limited Marketing Authorisations for the medicinal products Para-Supps Paracetamol 125 mg, 250 mg and 500 mg Suppositories (PL 19255/0001-0003) on 27 February 2013. These are pharmacy (P) medicines for the treatment of mild to moderate pain and fever in children aged from 1 to 5 years (125 mg strength); 6 to 12 years old (250 mg strength) and children over 12 years old and adults (500 mg strength only).

These applications were submitted according to Article 10a of Directive 2001/83/EC, as amended, claiming to be applications for a product containing an active substance of well-established use.

Para-Supps Paracetamol 125 mg, 250 mg and 500 mg Suppositories contain the active ingredient paracetamol. Paracetamol is an aniline derivative (ATC code N02B E01) with analgesic and antipyretic actions similar to those of aspirin but with no demonstrable anti-inflammatory activity. Paracetamol is less of an irritant to the stomach than aspirin. It does not affect thrombocyte aggregation or bleeding time. Paracetamol is generally well tolerated by patients hypersensitive to acetylsalicylic acid.

No new non-clinical or clinical studies were conducted for these applications, which is acceptable given that these are bibliographic applications for a product containing an active of well-established use.

No new or unexpected safety concerns were raised during the assessment of these applications and it was, therefore, judged that the benefits of using Para-Supps Paracetamol 125 mg, 250 mg and 500 mg Suppositories outweigh the risks; hence Marketing Authorisations have been granted.
PHARMACEUTICAL ASSESSMENT

ACTIVE SUBSTANCE:
INN: Paracetamol
Chemical name: N-(4-hydroxyphenyl)acetamide
Structure:

Molecular formula: C₈H₉NO₂
Molecular weight: 151.2 g/mol
Appearance: White or almost white, crystalline powder.
Solubility: Paracetamol is sparingly soluble in water, freely soluble in alcohol and very slightly soluble in methylene chloride.

Paracetamol is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance paracetamol are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

Appropriate stability data have been generated to support a suitable retest period when stored in the proposed packaging.

MEDICINAL PRODUCT
Other Ingredients
The other ingredient contained in these products is the pharmaceutical excipient, hard fat. In addition, the 500 mg strength also contains soya lecithin.

All excipients comply with their respective European Pharmacopoeia monograph with the exception of soya lecithin which is compliant with the United States Pharmacopoeia and The National Formulary (USP-NF). Satisfactory Certificates of Analysis have been provided for all excipients.

None of the excipients contain materials of animal or human origin. No genetically modified organisms (GMO) have been used in the preparation of these excipients.

Pharmaceutical Development
The objective of the development programme was to formulate safe, efficacious, stable suppository products containing 125 mg, 250 mg or 500 mg of the active ingredient paracetamol.

Suitable pharmaceutical development data has been provided for these applications.

Manufacturing Process
A description and flow-chart of the manufacturing method have been provided.
In-process controls are satisfactory based on process validation data and controls on the finished product. The manufacturing process has been validated at commercial scale and has shown satisfactory results.

**Finished Product Specification**
The finished product specification proposed is satisfactory. Test methods have been described and have been adequately validated. Batch data have been provided and comply with the release specifications.

**Container Closure System**
All strengths of finished product are packaged in low density polyethylene (LDPE)-coated aluminium foil blister strips in pack sizes of 10 suppositories.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current European regulations concerning materials in contact with food.

**Stability of the Product**
Stability studies were performed in accordance with current guidelines on batches of finished product packed in the packaging proposed for marketing. The data from these studies support a shelf-life of 4 years, with the storage conditions, “Do not store above 25°C. Keep in the outer carton”

**Bioequivalence/Bioavailability**
Satisfactory certificates of analysis have been provided for the test and reference batches used in the bioequivalence studies.

**Summaries of Product Characteristics (SmPC), Product Information Leaflets (PILs) and Labelling**
The SmPCs, PILs and labelling are satisfactory.

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC, as amended. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

**MAA Form**
The MAA forms are satisfactory.

**Expert Report**
The pharmaceutical expert report is written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

**Conclusion**
The grant of Marketing Authorisations is recommended.
NON-CLINICAL ASSESSMENT

PHARMACODYNAMICS, PHARMACOKINETICS AND TOXICOLOGY
No new non-clinical data were submitted, which is acceptable given that these are bibliographic applications for products containing an active substance of well-established use.

NON-CLINICAL EXPERT REPORT
The non-clinical expert report has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the non-clinical aspects of the dossier.

CONCLUSION
The grant of Marketing Authorisations is recommended.
CLINICAL ASSESSMENT

CLINICAL PHARMACOLOGY
The clinical pharmacology of paracetamol is well-known. No new pharmacodynamic or pharmacokinetic data are provided or required for this application.

EFFICACY
No new efficacy data were submitted and none were required for these applications.

SAFETY
No new safety data were submitted or required for these applications. The applicant has provided an acceptable safety review from the literature. No new safety issues have been raised from these applications.

PHARMACOVIGILANCE SYSTEM AND RISK MANAGEMENT PLAN
The Pharmacovigilance System, as described by the applicant, fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance, and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

Suitable justification has been provided for not submitting a Risk Management Plan for these products.

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC), PATIENT INFORMATION LEAFLETS (PILs) AND LABELS
The SmPCs, PILs and labels are acceptable.

CLINICAL EXPERT REPORT
The clinical expert report has been written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

CONCLUSION
The grant of Marketing Authorisations is recommended.
OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY
The important quality characteristics of Para-Supps Paracetamol 125 mg, 250 mg and 500 mg Suppositories are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit-risk balance.

NON-CLINICAL
No new non-clinical data were submitted and none were required for this type of application. A non-clinical overview has been provided by an appropriately qualified person and consists of a review of the published literature.

EFFICACY
No new data were submitted and none were required for applications of this type.

The efficacy of the active is well described and no new studies have been conducted. The applicant has summarised the current state of knowledge in their literature review.

SAFETY
The safety profile of paracetamol is well-known. The literature review identified no new or unexpected safety issues or concerns.

PRODUCT LITERATURE
The approved SmPCs are satisfactory. The PILs and labelling are satisfactory, and consistent with the approved SmPCs.

BENEFIT-RISK ASSESSMENT
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. Paracetamol is a well-known active substance. Extensive clinical experience with paracetamol is considered to have demonstrated the therapeutic value of the product. The benefit-risk is, therefore, considered to be positive.
PARA-SUPPS PARACETAMOL 125 MG, 250 MG AND 500 MG SUPPOSITORIES

PL 19255/0001-0003

STEPS TAKEN FOR ASSESSMENT

1. The MHRA received the marketing authorisation applications on 16 October 2002.
2. Following standard checks and communication with the applicant the MHRA considered the applications valid on 23 June 2006.
5. The applications were determined and granted on 27 February 2013.
SUMMARY OF PRODUCT CHARACTERISTICS

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPC) and Patient Information Leaflets (PIL) 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 Summaries of Product Characteristics (SmPC) and Patient Information Leaflets (PIL) for products granted Marketing Authorisations at a national level are available on the MHRA website.
CARTON:

Para-Supps Paracetamol 125 mg, 250 mg and 500 mg Suppositories

For the treatment of mild to moderate pain and fever in children.

For children 1-5 years: 125-250mg (1-2 suppositories).

The dosage should be based on age and weight:
- 1 year (10kg): 125mg (1 suppository)
- 5 years (20kg): 250mg (2 suppositories)

Up to 4 times a day.

Do not take more than 4 doses in any 24-hour period.

Leave at least 4 hours between doses. Only use whole suppositories.

Do not use more medicine than the label tells you to.

If you or your child does not get better, talk to your doctor.

Talk to a doctor at once if your child takes too much of this medicine, even if they seem well.

Please read the enclosed patient information leaflet carefully before use.

Do not give anything else containing paracetamol while giving this medicine. Keep out of sight and reach of children.
SUPPOSITORY FOIL STRIP:
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