Paracetamol 1000 mg Effervescent Tablets

PL 31388/0005

UKPAR

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LAY SUMMARY
Paracetamol 1000 mg Effervescent Tablets
(Paracetamol)

This is a summary of the Public Assessment Report (PAR) for Paracetamol 1000 mg Effervescent Tablets (PL 31388/0005). It explains how Paracetamol 1000 mg Effervescent Tablets were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use Paracetamol 1000 mg Effervescent Tablets.

For practical information about using Paracetamol 1000 mg Effervescent Tablets, patients should read the package leaflet or contact their doctor or pharmacist.

What are Paracetamol 1000 mg Effervescent Tablets and what are they used for?
The application for Paracetamol 1000 mg Effervescent Tablets was a hybrid application. This means that Paracetamol 1000 mg Effervescent Tablets are similar to a ‘reference medicine’, with a different strength, already authorised in UK called Panadol Soluble 500 mg Tablets (PL 00071/0072R; SmithKline Beecham (SWG) Limited).

Paracetamol 1000 mg Effervescent Tablets are recommended for use in treatment of mild to moderate pain and/or fever.

How are Paracetamol 1000 mg Effervescent Tablets used?
Paracetamol 1000 mg Effervescent Tablets are taken by mouth. This medicine can only be obtained on prescription from the doctor. A single tablet should be added to a full glass of water and it should be allowed to completely dissolve before the solution is swallowed.

Paracetamol 1000 mg Effervescent Tablets are for use, only in adults and adolescents aged 16 years and above. Details of the correct dose to be given are included in the package leaflet.

How do Paracetamol 1000 mg Effervescent Tablets work?
Paracetamol is an effective analgesic (relieves pain) and antipyretic agent (reduces the body temperature in fever). Paracetamol lowers body temperature in patients with fever by acting on the area of the brain that is responsible for controlling temperature and it also widens the blood vessels as a result blood flow increases.

How have Paracetamol 1000 mg Effervescent Tablets been studied?
No additional studies were needed as Paracetamol 1000 mg Effervescent Tablets is a hybrid medicine that is taken as a solution and it contains the same active substance as the reference medicine, Panadol Soluble 500 mg Effervescent Tablets (PL 00071/0072R; SmithKline Beecham (SWG) Limited).

What are the benefits and risks of Paracetamol 1000 mg Effervescent Tablets?
As Paracetamol 1000 mg Effervescent Tablets were approved with reference to Panadol Soluble 500 mg Tablets, their benefits and risks are taken as being the same as the reference medicine.

**Why are Paracetamol 1000 mg Effervescent Tablets approved?**
No new or unexpected safety concerns arose from this application. It was, therefore, considered that the benefits of taking Paracetamol 1000 mg Effervescent Tablets outweigh the risks; and the grant of a Marketing Authorisation was recommended.

**What measures are being taken to ensure the safe and effective use of Paracetamol 1000 mg Effervescent Tablets?**
A satisfactory pharmacovigilance system has been provided, which 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.

Safety information has also been included in the summary of product characteristics and the package leaflet for Paracetamol 1000 mg Effervescent Tablets, including the appropriate precautions to be followed by healthcare professionals and patients.

**Other information about Paracetamol 1000 mg Effervescent Tablets**
A Marketing Authorisation for Paracetamol 1000 mg Effervescent Tablets was granted on 23\textsuperscript{rd} December 2013.

The full PAR for Paracetamol 1000 mg Effervescent Tablets follows this summary.

For more information about treatment with Paracetamol 1000 mg Effervescent Tablets, read the package leaflet or contact your doctor or pharmacist.

This summary was last updated in February 2014.
Paracetamol 1000 mg Effervescent Tablets

PL 31388/0005

SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted a Marketing Authorisation (licence) for the medicinal product Paracetamol 1000 mg Effervescent Tablets (PL 31388/0005) to Alpex Pharma (UK) Limited on 23\textsuperscript{rd} December 2013.

This prescription only medicine (POM) is indicated for the treatment of mild to moderate pain and/or fever.

This is a national abridged application for Paracetamol 1000 mg Effervescent Tablets submitted under Article 10(3) of Directive 2001/83/EC, as amended, as a hybrid application. The applicant has cross-referred to Panadol Soluble 500 mg Tablets (PL 00071/0072R), granted to SmithKline Beecham (SWG) Limited on 12\textsuperscript{th} January 1982.

Satisfactory details of the pharmacovigilance system have been provided with this application.

A suitable justification for non-submission of the Risk Management Plan has been provided.
**PHARMACEUTICAL ASSESSMENT**

**DRUG SUBSTANCE**

Nomenclature

rINN: Paracetamol

Chemical Names: N-(4-Hydroxyphenyl)acetamide

Structure:

![Chemical structure of paracetamol](image)

Molecular Formula: C₈H₉NO₂

Molecular Weight: 151.2 g/mol

Appearance: white or almost white crystalline powder

Solubility: sparingly soluble in water, freely soluble in alcohol, 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.

**DRUG PRODUCT**

Other ingredients

Other ingredients consist of the pharmaceutical excipients anhydrous citric acid (E330), sodium bicarbonate (E500), sucralose (E955), sucrose monopalmitate (Sucroester 15) (E 473), sodium benzoate (E211), grapefruit flavor, and Kollidon 30 or Povidone K30 (E1201).

All excipients used comply with their respective European Pharmacopoeia monograph with the exception of sucralose which complies with the United States Pharmacopeia and grapefruit flavour which is controlled by an in-house specification. Satisfactory Certificates of Analysis have been provided for all excipients.
Pharmaceutical development
The objective of the development programme was to formulate robust, stable tablets containing paracetamol which could be considered to be similar to the reference product, Panadol Soluble 500 mg Effervescent Tablets (SmithKline Beecham (SWG) Limited).

Comparable dissolution and impurity profiles are provided for this product versus the originator product.

Manufacture
A satisfactory batch formula has been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated at pilot-scale and has shown satisfactory results. The applicant has committed to perform process validation studies on full-scale commercial batches.

Finished product specification
The finished product specification is satisfactory. Test methods have been described that have been adequately validated. Batch data have been provided which comply with the release specification. Certificates of Analysis have been provided for any working standards used.

Container Closure System
The tablets are packed in a nylon/aluminium/PVC/lacquer blisters. The tablets are packed in boxes containing 1, 2, 4, 5, 10, 12 or 20 blisters each containing 2 tablets ie pack sizes of 2, 4, 8, 10, 20, 24 or 40 tablets.

The packaging is opaque and child resistant.

Specifications and Certificates of Analysis for all packaging materials have been provided. These are satisfactory. All primary packaging complies with EU legislation regarding contact with food.

Stability
Finished product stability studies have been conducted in accordance with current guidelines and in the packaging proposed for marketing.

Based on the results, a shelf-life of 30 months with storage conditions “Store below 25°C” and “Store in the original package in order to protect from moisture and light” have been set. These are satisfactory.

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

A package leaflet has been submitted to the MHRA together 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 the package leaflet contains.

**Marketing Authorisation Application (MAA) Forms**

The MAA form is pharmaceutically satisfactory.

**Expert Report**

The quality overall summary is written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

**Conclusion**

There are no objections to the approval of this product from a pharmaceutical point of view.
**NON-CLINICAL ASSESSMENT**

The pharmacodynamic, pharmacokinetic and toxicological properties of paracetamol are well-known. Thus, the applicant has not provided additional studies and further studies are not required.

A non-clinical overview has been provided, written by an appropriately qualified person. This is satisfactory.

A suitable justification has been provided for non-submission of environmental risk assessment.

There are no objections to the approval of this product from a non-clinical point of view.
CLINICAL ASSESSMENT

CLINICAL PHARMACOLOGY

PHARMACOKINETICS

In accordance with the Note for Guidance on the investigation of bioavailability and bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1), a bioequivalence study is not required if the test product is a solution containing the same active substance as the reference product. As this product is a solution at the time of administration, no bioequivalence studies have been submitted and none are required.

No new data have been submitted and none are required for applications of this type.

EFFICACY

No new efficacy data have been submitted and none are required for this application.

SAFETY

No new safety data have been submitted and none are required for this application.

EXPERT REPORT

The clinical overview is written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

SUMMARY OF PRODUCT CHARACTERISTICS

This is satisfactory.

PATIENT INFORMATION LEAFLET

This is satisfactory.

LABELLING

This is satisfactory.

MAA FORM

This is satisfactory.

CONCLUSIONS

There are no objections to the approval of this product from a clinical point of view.
OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY
The important quality characteristics of Paracetamol 1000 mg Effervescent Tablets 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 are required for applications of this type.

CLINICAL
No new efficacy data were submitted and none are required for applications of this type. As the safety profile of paracetamol is well-known, no additional data were required. No new or unexpected safety concerns arose from this application.

PRODUCT LITERATURE
The SmPC and PIL are satisfactory and consistent with those of the reference product. Satisfactory labelling has also been submitted.

BENEFIT RISK ASSESSMENT
The quality of the product is acceptable and no new non-clinical or clinical concerns have been identified. Extensive clinical experience with paracetamol is considered to have demonstrated the therapeutic value of the compound. The benefit risk is, therefore, considered to be positive.
### STEPS TAKEN FOR ASSESSMENT

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<tr>
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<th>Description</th>
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<tr>
<td>1</td>
<td>The MHRA received the Marketing Authorisation application on 15&lt;sup&gt;th&lt;/sup&gt; June 2012</td>
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<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 18&lt;sup&gt;th&lt;/sup&gt; July 2012</td>
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<td>3</td>
<td>Following assessment of the application the MHRA requested further information on 16&lt;sup&gt;th&lt;/sup&gt; October 2012, 28&lt;sup&gt;th&lt;/sup&gt; June 2013 and 8&lt;sup&gt;th&lt;/sup&gt; November 2013</td>
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<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on 19&lt;sup&gt;th&lt;/sup&gt; April 2013, 30&lt;sup&gt;th&lt;/sup&gt; September 2013 and 19&lt;sup&gt;th&lt;/sup&gt; November 2013</td>
</tr>
<tr>
<td>5</td>
<td>The application was determined on 23&lt;sup&gt;rd&lt;/sup&gt; December 2013.</td>
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Module 2
Summary of Product Characteristics

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPCs) for products that are granted Marketing Authorisations at a national level are available on the MHRA website.
Module 3
Patient Information Leaflet

In accordance with Directive 2010/84/EU the Patient Information Leaflets (PILs) for products that are granted Marketing Authorisations at a national level are available on the MHRA website.
UKPAR Paracetamol 1000 mg Effervescent Tablets

PARACETAMOL 1000 mg Effervescent Tablets

Indications
Paracetamol 1000 mg Effervescent Tablets are indicated for the relief of mild to moderate pain and fever.

DOSAGE

Each effervescent tablet contains 1000 mg Paracetamol. Take one tablet (1000 mg) every 4 hours, up to a maximum of 4 tablets (4000 mg) in 24 hours.

Contraindications

Paracetamol 1000 mg Effervescent Tablets should not be used in the presence of hypersensitivity to Paracetamol.

Precautions

Paracetamol 1000 mg Effervescent Tablets should be used with caution in patients with liver or kidney disease.

Warning

Read the package leaflet before use. Do not exceed the recommended dose. If symptoms persist for more than 3 days, or if new symptoms appear, you should stop the treatment and consult a doctor.

Further information

For more information, please refer to the package leaflet.