Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

Public Assessment Report

Paracetamol 120mg/5ml Oral Suspension

UK Licence No: PL 20941/0001&0003

Edict Consulting Ltd

Lay Summary
Paracetamol 120mg/5ml Oral Suspension
(paracetamol)

This is a summary of the Public Assessment Report (PAR) for Paracetamol 120mg/5ml Oral Suspension (PL 20941/0001&0003). It explains how Paracetamol 120mg/5ml Oral Suspension 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 Paracetamol 120mg/5ml Oral Suspension.

For practical information about using Paracetamol 120mg/5ml Oral Suspension, patients should read the package leaflets or contact their doctor or pharmacist.

What is Paracetamol 120mg/5ml Oral Suspension and what is it used for?
Paracetamol 120mg/5ml Oral Suspension is a medicine with 'well-established use'. This means that the medicinal use of the active substance of Paracetamol 120mg/5ml Oral Suspension has been in well-established use in the European Union (EU) for at least ten years, with recognised efficacy and an acceptable level of safety.

This medicine is used to treat mild to moderate pain and other conditions, such as headache, toothache, earache, teething, sore throat, colds and influenza, aches and pains, and to bring down fever (high temperature), including fever caused by immunisation.

How does Paracetamol 120mg/5ml Oral Suspension work?
Paracetamol 120mg/5ml Oral Suspension contains the active ingredient paracetamol, which belongs to a group of medicines called analgesics that help to ease pain.

How is Paracetamol 120mg/5ml Oral Suspension used?
Paracetamol 120mg/5ml Oral Suspension is taken by mouth. The bottle must be shaken for at least 10 seconds before use. Patients must not exceed the dose stated in the label and should not take anything else containing paracetamol while taking this medicine.

For the relief of fever after vaccination at 2, 3 and 4 months
Patients must take one 2.5 ml spoonful (small end) not more often than every 4 hours. This dose may be given up to 4 times a day starting at the time of vaccination. This medicine should not be given more than 4 doses in any 24 hour period. A doctor or pharmacist must be consulted if a baby still needs this medicine two days after receiving the vaccine.

Age: 2 – 3 months	**Dose**
Pain and other causes of fever – if the baby weighs over 4kg and was born after 37 weeks (not premature)	One 2.5 mL spoonful (small end). If necessary, after 4-6 hours, give a second 2.5 mL dose
• Do not give to babies less than 2 months of age • Leave at least 4 hours between doses • Do not give more than 2 doses. This is to ensure that fever that may be due to a serious infection is quickly diagnosed. If the child is still feverish after two doses, talk to a doctor or pharmacist.	

Children aged 3 months – 6 years

Child's Age	How Much	How often (in 24 hours)
3 – 6 months	One 2.5 mL spoonful (small end)	4 times
6 – 24 months	One 5 mL spoonful (large end)	4 times
2 – 4 years	One 5 mL spoonful (large end) and one 2.5 mL spoonful (small end)	4 times
4 – 6 years	Two 5 mL spoonfuls (large end)	4 times
Do not give more than 4 doses in any 24 hour period Leave at least 4 hours between doses Do not give this medicine to a child for more than 3 days without speaking to a doctor or pharmacist		

Paracetamol 120mg/5ml Oral Suspension can be obtained without a prescription.

For further information on how Paracetamol 120mg/5ml Oral Suspension is used, please refer to the Summaries of Product Characteristics and the Patient Information Leaflets available on the MHRA website.

What benefits of Paracetamol 120mg/5ml Oral Suspension have been shown in studies?
As paracetamol is a well-known substance, and its use in the treatment of mild to moderate pain and other conditions such as headache, toothache, earache, teething, sore throat, colds and influenza, aches and pains and to bring down fever (high temperature) including fever caused by immunisation is well-established, the applicant presented data from the scientific literature. The literature provided confirmed the efficacy and safety of paracetamol for the proposed indications.

What are the possible side effects of Paracetamol 120mg/5ml Oral Suspension?
Like all medicines, this medicine can cause side effects, although not everybody gets them.

For information about side effects that may occur with taking Paracetamol 120mg/5ml Oral Suspension, please refer to the package leaflets or the Summaries of Product Characteristics available on the MHRA website.

Why is Paracetamol 120mg/5ml Oral Suspension approved?
The use of Paracetamol 120mg/5ml Oral Suspension for the approved indications is well-established. Literature data have been submitted to support these applications. No new or unexpected safety concerns arose from these applications. It was, therefore, considered that the benefits of Paracetamol 120mg/5ml Oral Suspension outweigh the risks and the grant of Marketing Authorisations was recommended.

What measures are being taken to ensure the safe and effective use of Paracetamol 120mg/5ml Oral Suspension?
A satisfactory pharmacovigilance system has been provided to monitor the safety of the product.

Other information about Paracetamol 120mg/5ml Oral Suspension
Marketing Authorisations for Paracetamol 120mg/5ml Oral Suspension (PL 20941/0001&0003) were granted in the UK on 03 March 2009.

The full PAR for Paracetamol 120mg/5ml Oral Suspension follows this summary.

For more information about treatment with Paracetamol 120mg/5ml Oral Suspension, read the Patient Information Leaflets (PIL), or contact your doctor or pharmacist.

This summary was last updated in December 2015.

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) granted Edict Consulting Ltd Marketing Authorisations for Paracetamol 120mg/5ml Oral Suspension (PL 20941/0001 and 0003) on 03 March 2009. The legal status for PL 20941/0001 is pharmacy (P) and for PL 20941/0003 is General Sales List (GSL). This medicine is indicated for the treatment of mild to moderate pain and as an antipyretic. It can be used in many conditions including headache, toothache, earache, teething, sore throat, colds and influenza, aches and pains and post-immunisation fever.

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

The product contains the active substance paracetamol, which has analgesic and antipyretic effects similar to those of aspirin and is useful in the treatment of mild to moderate pain. It has weak anti-inflammatory effects.

No new non-clinical or clinical studies were necessary for these applications, which is acceptable given that these are bibliographic applications for a product containing an active of well-established use. Bioequivalence studies are not necessary to support these applications.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product type at all sites responsible for the manufacturing and assembly of this product. Evidence of compliance with GMP has been provided for the named manufacturing and assembly sites.

A summary of the pharmacovigilance system has been provided with these applications and this is satisfactory.

II Quality aspects

II.1 Introduction

This product is an oral suspension and each 5 ml of the oral suspension contains 120 mg paracetamol, as an active ingredient. The excipients present are glycerol, polysorbate 80, xanthan gum, maltitol liquid, sodium saccharin, citric acid monohydrate, sodium methyl parahydroxybenzoate, sodium propyl parahydroxybenzoate, strawberry flavour (containing propylene glycol) and water purified.

All excipients with the exception of strawberry flavour comply with their relevant European Pharmacopoeia monographs. Strawberry flavour complies with an in-house specification.

None of the excipients used contain material of animal or human origin.

The product is packaged in type III glass bottles with child resistant tamper evident high density polypropylene caps with a polyethylene lining. A polypropylene double ended spoon is provided.

Specifications and Certificates of Analysis for the packaging types used have been provided. All primary product packaging complies with EU legislation regarding contact with food. The product is packaged in sizes of 100 ml and 200 ml for PL 20941/0001 and 100 ml for PL 20941/0003.

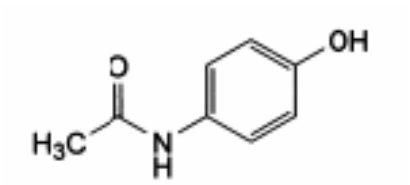
II.2 Drug Substance

Paracetamol

INN: Paracetamol

Chemical Name: Acetaminophen, N-Acetyl-p-aminophenol, Paracetamolum, 4'-hydroxyacetanilide, N-(4-hydroxyphenyl)acetanilide

Structure:



Molecular formula: $C_8H_9NO_2$

Molecular weight: 151.2 g/mol

Appearance: A white crystalline powder.

Solubility: Sparingly soluble in water, freely soluble in alcohol and very slightly soluble in methylene chloride. Solubility in water increases as the pH increases.

An appropriate specification based on the European Pharmacopoeia has been provided.

All aspects of the manufacture of the active substance, paracetamol, from its starting materials are controlled by a Certificate of Suitability.

Satisfactory specifications and Certificates of Analysis have been provided all aspects of the container-closure system. A declaration has been provided that the primary packaging complies with current regulations concerning contact with foodstuff.

An appropriate retest period has been proposed based on stability data submitted for the active substance paracetamol.

II.3 Medicinal Product

Pharmaceutical development

The applicant has provided a suitable product development section. Justifications for the use and amounts of each excipient have been provided and are valid.

Manufacture of the product

A description and flow-chart of the manufacturing method has been provided.

In-process controls are satisfactory based on process validation data and controls on the finished product. Process validation has been carried out on batches of finished product and the results appear satisfactory. The applicant has committed to perform process validation on future production-scale batches.

Product Specification

The finished product specification is satisfactory. The test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis for all working standards used have been provided and are satisfactory.

Stability of the product

Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 24 months for an unopened product and two months for an opened product has been set. This product has the storage conditions "Do not store above 25^{o}C" and 'Store the container in the outer carton. Discard after 2 months of first opening.' which are satisfactory.

II.4 Discussion on chemical, pharmaceutical and biological aspects

The grant of Marketing Authorisations is recommended.

III Non-clinical aspects

The pharmacodynamic, pharmacokinetic and toxicological properties of paracetamol are well-known. As paracetamol is a widely used, well-known active substance, the applicant has not provided additional studies and further studies are not required. The non-clinical overview based on a literature review is, thus, appropriate.

The non-clinical overview has been written by an appropriately qualified person. The non-clinical overview on the pharmacology, pharmacokinetics and toxicology is adequate.

Since Paracetamol 120mg/5ml Oral Suspension is intended for generic substitution, it will not lead to an increased exposure to the environment. An environmental risk assessment is, therefore, not deemed necessary.

IV Clinical aspects

IV.1 Introduction

No bioequivalence studies have been performed and none are required for these applications, as these are bibliographic applications and the active substance paracetamol, is a well-known, widely used substance.
The clinical expert report has been written by a suitably qualified person and is satisfactory.

IV.2 Pharmacokinetics
No new pharmacokinetics data are required for these applications and none have been submitted.

IV.3 Pharmacodynamics
No new pharmacodynamics data are required for these applications and none have been submitted.

IV.4 Clinical efficacy
No new clinical efficacy data are required for these applications and none have been submitted.

IV.5 Clinical safety
No new data have been provided and none are required for these applications.

IV.6 Pharmacovigilance System
A satisfactory pharmacovigilance system has been provided to monitor the safety of these products.

IV.7 Discussion on the clinical aspects
The grant of Marketing Authorisations is recommended for these applications.

V User consultation
The package leaflet has been evaluated via a user consultation study, in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PIL was English.

The package leaflet meets the criteria for readability, as set out in the *Guideline on the readability of the label and package leaflet of medicinal products for human use*.

VI Overall conclusion, benefit-risk assessment and recommendation
QUALITY
The important quality characteristics of Paracetamol 120mg/5ml Oral Suspension 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
Paracetamol is a well-known drug and has been used as an analgesic for many years.
No new or unexpected safety concerns arose from these applications.

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.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling

In accordance with Directive 2012/84/EU, the current approved UK versions of the SmPCs and PILs are available on the MHRA website.

The current approved UK labelling is available in Annex 1.

Table of content of the PAR update

Steps taken after the initial procedure with an influence on the Public Assessment Report (Type II variations, PSURs, commitments)

The following table lists non-safety updates to the Marketing Authorisations for the product that has been approved by the MHRA since the Marketing Authorisations were first granted. The table includes updates that are detailed in the annex to this PAR. This is not a complete list of the post-authorisation changes that have been made to these Marketing Authorisations.

Date submitted	Application type	Scope	Outcome
01/10/2015	**Type IB Variation**	To update section 4.2 of the SmPCs to include the new advice for Meningitis B vaccine as advised by the Commission on Human Medicines (CHM). Consequently, the PILs and label texts have been updated	**Approved**

Annex 1

Reference: **PL 20941/0001-0037 and PL 20941/0003-0044**

Product: **Paracetamol 120mg/5ml Oral Suspension**

Marketing Authorisation Holder: **Edict Consulting Ltd**

Active Ingredient: **paracetamol**

Reason:
To update section 4.2 of the SmPCs to include the new advice for Meningitis B vaccine as advised by the Commission on Human Medicines (CHM). Consequently, the PILs and label texts have been updated.

Supporting evidence
The applicant has submitted updated section of the SmPCs, PILs and labelling.

Evaluation
The amended section of the SmPCs, PILs and labelling are satisfactory.

Conclusion
The variations were approved on 06 November 2015 and the updated SmPC fragments, PILs and labelling have been incorporated into these Marketing Authorisations. The proposed changes are acceptable.

Following approval of the variations on 06 November 2015 the SmPCs and PILs were updated. In accordance with Directive 2010/84/EU, the current granted UK SmPCs and PIL are available on the MHRA website. The current approved UK labelling is presented below.

1. NAME OF THE MEDICINAL PRODUCT

Paracetamol 120mg/5ml Oral Suspension

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 5ml contains 120mg Paracetamol

3. LIST OF EXCIPIENTS

It also contains E965, E217, E219. See leaflet for full list of ingredients.

4. PHARMACEUTICAL FORM AND CONTENTS

Oral Suspension.
200ml./100ml.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For Oral use.
Shake the bottle for at least 10 seconds before use.
Use the enclosed double ended spoon to measure the dose.
The big spoon measures 5ml and the small spoon measures 2.5ml.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Do not give anything else containing Paracetamol while giving this medicine. Talk to a doctor at once if your child takes too much of this medicine, even if they seem well.

8. EXPIRY DATE

To be overprinted

9. SPECIAL STORAGE CONDITIONS

Do not store above 25ºC.

Store the container in the outer carton. Discard after 2 months of first opening.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

None

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

PL holder: Edict Consulting Limited, WD23 4SW (UK)

12. MARKETING AUTHORISATION NUMBER(S)

PL 20941/0001

13. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Product code:

200ml - XXXX/X

100ml – XXXX/X

Batch No.

2D Code

14. GENERAL CLASSIFICATION FOR SUPPLY

Legal status – P.

15. INSTRUCTIONS ON USE

Read the enclosed leaflet carefully before use.

For the relief of fever after vaccination at 2, 3 and 4 months: See leaflet in the box.

For pain and other causes of fever for babies aged between 2 – 3 months who weigh over 4kg and was born after 37 weeks (not premature): One 2.5ml spoonful (small end). If necessary, after 4-6 hours, give a second 2.5ml dose.

- Do not give to babies less than 2 months of age
- Leave at least 4 hours between doses
- Do not give more than 2 doses. This is to ensure that fever that may be due to a serious infection is quickly diagnosed. If your child is still feverish after two doses, talk to your doctor or pharmacist.

Children aged 3 months – 6 years:

Child's age	How much to give
3 – 6 months:	One 2.5ml spoonful (small end) four times a day.
6 – 24 months:	One 5ml spoonful (large end) four times a day.
2 – 4 years:	One 5ml spoonful (large end) and one 2.5ml spoonful (small end) four times a day.
4 – 6 years:	Two 5ml spoonfuls (large end) four times a day.
• Do not give more than 4 doses in any 24 hour period • Leave at least 4 hours between doses • Do not give this medicine to your child for more than 3 days without speaking to your doctor or pharmacist	

Do not give more medicine than the label tells you to. If your child does not get better, talk to your doctor.

16. INFORMATION IN BRAILLE

None.

1. NAME OF THE MEDICINAL PRODUCT

Paracetamol 120mg/5ml Oral Suspension

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each 5ml contains 120mg Paracetamol.

3. LIST OF EXCIPIENTS

It also contains maltitol liquid (E965), sodium methyl parahydroxybenzoate (E219), sodium propyl parahydroxybenzoate (E217). See enclosed leaflet for full list of ingredients.

4. PHARMACEUTICAL FORM AND CONTENTS

Oral Suspension
100ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For Oral use. Shake the bottle for at least 10 seconds each time before use. Use the enclosed double ended spoon to measure the dose. The big spoon measures 5ml and the small spoon measures 2.5ml.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Do not give anything else containing Paracetamol while giving this medicine.

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

Paracetamol is often included in cold and flu remedies, and in other medicines you can buy. (Such medicines have "contains paracetamol" printed on the pack). If you are unsure whether another medicine can be taken with this suspension speak to your doctor or pharmacist.

8. EXPIRY DATE

To be over printed.

9. SPECIAL STORAGE CONDITIONS

Do not store above 25ºC. Store the container in the outer carton. Discard after 2 months of first opening.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Not applicable.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Licence holder
Edict Consulting Ltd, 49 Ivinghoe Road
Bushey, Herts WD23 4SW

12. MARKETING AUTHORISATION NUMBER(S)

PL 20941/0003

13. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Product Code: XXXX/X

Batch No:
Barcode
2D pharmacode

14. GENERAL CLASSIFICATION FOR SUPPLY

Legal status – GSL.

15. INSTRUCTIONS ON USE

Paracetamol 120mg/5ml Oral Suspension is a specially formulated suspension for babies and children from 3 months. It can be used to relieve pain including headache, toothache, earache, teething, sore throat, colds & influenza, aches and pains and to bring down fever (high temperature) including fever caused by immunisation.

Read the enclosed leaflet carefully before use.

For the relief of fever after vaccination at 2, 3 and 4 months: See the leaflet in the box.

Age: 2 – 3 months	**Dose**
Pain and other causes of fever – if your baby weighs over 4kg and was born after 37 weeks (not premature)	**One 2.5 mL spoonful (small end). If necessary, after 4-6 hours, give a second 2.5 mL dose**

- **Do not give to babies less than 2 months of age**
- **Leave at least 4 hours between doses**
- **Do not give more than 2 doses. This is to ensure that fever that may be due to a serious infection is quickly diagnosed. If your child is still feverish after two doses, talk to your doctor or pharmacist.**

Children aged 3 months – 6 years:

Child's age	How much to give
3 – 6 months:	One 2.5ml spoonful (small end) four times a day.
6 – 24 months:	One 5ml spoonful (large end) four times a day.
2 – 4 years:	One 5ml spoonful (large end) and one 2.5ml spoonful (small end) four times a day.
4 – 6 years:	Two 5ml spoonfuls (large end) four times a day.

- Do not give more than 4 doses in any 24 hour period
- Leave at least 4 hours between doses
- Do not give this medicine to your child for more than 3 days without speaking to your doctor or pharmacist.

Do not give more medicine than the label tells you to. If your child does not get better, talk to your doctor.

16. INFORMATION IN BRAILLE

Paracetamol
#120 mg/ #5 ml
Oral Suspension