Medicines & Healthcare products
Regulatory Agency

MHRA

# Public Assessment Report

# National Procedure

# Co-Codamol 15/500 mg Tablets

# (paracetamol, codeine phosphate hemihydrate)

# PRODUCT LICENCE NUMBER;
# PL 34424/0020

# Key Pharmaceuticals Limited.

# LAY SUMMARY

## Co-Codamol 15/500 mg Tablets
## (codeine phosphate hemihydrate, paracetamol)

This is a summary of the Public Assessment Report (PAR) for Co-Codamol 15/500 mg Tablets. It explains how this product 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 this product.

This product will be referred to as Co-Codamol Tablets in this lay summary for ease of reading.

For practical information about using Co-Codamol Tablets, patients should read the package leaflet or contact their doctor or pharmacist.

**What are Co-Codamol Tablets and what are they used for?**
This application is the same as Co-codamol 15mg/500mg Tablets (PL 21880/0161) which is already authorised.

The Company responsible for Co-codamol 15mg/500mg Tablets has agreed that its scientific data can be used as the basis for the grant of an identical licence for Co-Codamol Tablets.

Co-Codamol Tablets are one of a group of medicines called analgesics or painkillers and they are used to relieve moderate pain. Codeine can be used in children over 12 years of age for the short-term relief of moderate pain that is not relieved by other painkillers such as paracetamol or ibuprofen alone.

**How do Co-Codamol Tablets work?**
Co-Codamol Tablets contains two active ingredients; paracetamol and codeine phosphate hemihydrate. Codeine belongs to a group of medicines called opioid analgesics which act to relieve pain. It also contains paracetamol, another analgesic to relieve pain.

**How are Co-Codamol Tablets used?**
The pharmaceutical form of this medicine is a tablet and the route of administration is oral (by mouth).

The score line is only there to help break the tablet if the patient has difficulty swallowing it whole. This medicine should only be taken when necessary. The patient should not take more than the stated dose and they should not take this medicine for more than three days. If the pain does not improve after three days, the patient must talk to their doctor for advice.

***Dosage in adults and the elderly***
The recommended dose for adults and the elderly is two tablets taken every six hours. The patient should not take more than eight tablets in any 24-hour period.

***Dosage in children and adolescents***
The recommended dose for children aged 16 and over is two tablets taken every six hours. The patient should not take more than eight tablets in any 24-hour period. The recommended dose for children aged 12 to 15 years is one tablet taken every six hours, up to a maximum of four tablets in any 24-hour period.

Doctors sometimes prescribe different doses to these. The patient should read the pharmacist's label, which will explain how many tablets to take.

This medicine should not be taken by children under 12 years of age, due to the risk of severe breathing problems.

For further information on how Co-Codamol Tablets are used, refer to the package leaflet and Summary of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should always take the medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

**What benefits of Co-Codamol Tablets have been shown in studies?**
Co-Codamol Tablets are considered identical to the previously authorised product with the same benefits and risks. No new studies have been provided for Co-Codamol Tablets; however, reference is made to the studies for Co-codamol 15mg/500mg Tablets.

**What are the possible side effects of Co-Codamol Tablets?**
Co-Codamol Tablets are considered to be identical to the previously authorised product with the same benefits and risks.

For the full list of all side effects reported with this/these medicine/medicines, see Section 4 of the package leaflet or the Summary of Product Characteristics (SmPC/SmPCs) available on the MHRA website.

**Why were Co-Codamol Tablets approved?**
The MHRA decided that the benefits of Co-Codamol Tablets are greater than the risks and recommended that this medicine is approved for use.

**What measures are being taken to ensure the safe and effective use of Co-Codamol Tablets?**
A Risk Management Plan (RMP) has been developed to ensure that Co-Codamol Tablets are used as safely as possible. Based on this plan, safety information has been included in the SmPC and the package leaflet, 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 and reviewed continuously.

**Other information about Co-Codamol Tablets**
A Marketing Authorisation was granted in the UK on 29 January 2020.

The full PAR for Co-Codamol Tablets follows this summary.

This summary was last updated in February 2020.

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## I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Co-Codamol 15/500 mg Tablets (PL 34424/0020) could be approved.

The product is approved for the following indications:

- for the relief of moderate pain
- codeine is indicated in patients older than 12 years of age for the treatment of acute moderate pain which is not considered to be relieved by other analgesics such as paracetamol or ibuprofen (alone).

Co-Codamol 15/500 mg Tablets contain two active substances; paracetamol and codeine phosphate hemihydrate. Paracetamol has analgesic and antipyretic effects that do not differ significantly from that of aspirin. Its anti-inflammatory action is weak, and it has practically no anti-platelet effect. The mechanism of action is unclear although it is believed to exert its action by inhibition of prostaglandin synthesis.

Codeine is a centrally acting weak analgesic. Codeine exerts its effects through μ opioid receptors, although codeine has low affinity for these receptors, and its analgesic effect is due to its conversion to morphine. Codeine, particularly in combination with other analgesics such as paracetamol, has been shown to be effective in acute nociceptive pain.

This is a national abridged application submitted under Article 10c of Directive 2001/83/EC, as amended (an informed consent application). The application cross-refers to the reference product Co-codamol 15mg/500mg Tablets (PL 21880/0161), currently held by Medreich PLC.

No new non-clinical or clinical data have been supplied and none are required for this informed consent application.

Suitable justification has been provided for non-submission of an Environmental Risk Assessment (ERA). As the application is for an identical version of an already authorised product, no increase in environmental exposure is anticipated and no ERA is required.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this/these application and are satisfactory.

A Marketing Authorisation was granted on 29 January 2020.

## II. EXPERT REPORT

The applicant cross-refers to the data for Co-codamol 15mg/500mg Tablets (PL 21880/0161; Medreich PLC), to which this application is claimed to be identical. This is acceptable.

## III. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION SUMMARY OF PRODUCT CHARACTERITICS (SmPC)

The SmPC is in line with that for Co-codamol 15mg/500mg Tablets (PL 21880/0161), dated 08/2019.

**PATIENT INFORMATION LEAFLET**
A leaflet mock-up has been provided which has been aligned with that for Co-codamol 15mg/500mg Tablets (PL 21880/0161), dated for 04/2019. The user test report submitted for PL 34424/0020 has been provided.

**LABEL**
Label mock-up has been provided.

## IV. QUALITY ASPECTS

### IV.1 Drug Substance

**Drug substance specification**
The source of the active substances is in line with the cross-reference product. The proposed drug substance specification is consistent with the details registered for the cross-reference product.

### IV.2. Drug Product

**Name**
The product has been named in line with current requirements.

**Strength, pharmaceutical form, route of administration, container and pack sizes**
Co-codamol 15mg/500mg Tablets are available in Alu – PVC/PVdC blister pack in a pack size of 100 tablets.

The appearance of the product is identical to that of the cross-reference product.

The proposed shelf life of the product is 36 months with no special storage conditions.

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

**Legal status**
Prescription only medicine (POM).

**Manufacturers**
The proposed manufacturing site are consistent with the details registered for the cross-reference product and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

**Qualitative and quantitative compositions**
The composition of the proposed product is consistent with the details registered for the cross-reference product.

**Manufacturing process & control of critical steps**
The proposed manufacturing processes and process controls are consistent with the details registered for the reference product and the maximum batch size is stated.

**Finished product release/shelf life specifications**
The proposed finished product specification is in line with the details registered for the cross-

reference product.

**TSE Compliance**
No excipients of animal or human origin are used in the final product.

Confirmation has been given that the magnesium stearate used in the tablets is of vegetable origin.

This product does not contain or consist of genetically modified organisms (GMO).

## V. NON-CLINICAL ASPECTS
As this application is submitted under Article 10c of Directive 2001/83/EC, as amended, (as an informed consent application) no new non-clinical data have been supplied and none are required.

## VI. CLINICAL ASPECTS
As this application is submitted under Article 10c of Directive 2001/83/EC, as amended, (as an informed consent application) no new clinical data have been supplied and none are required.

## VII. RISK MANAGEMENT PLAN (RMP)
The applicant has submitted an RMP, in accordance with the requirements of Directive 2001/83/EC, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

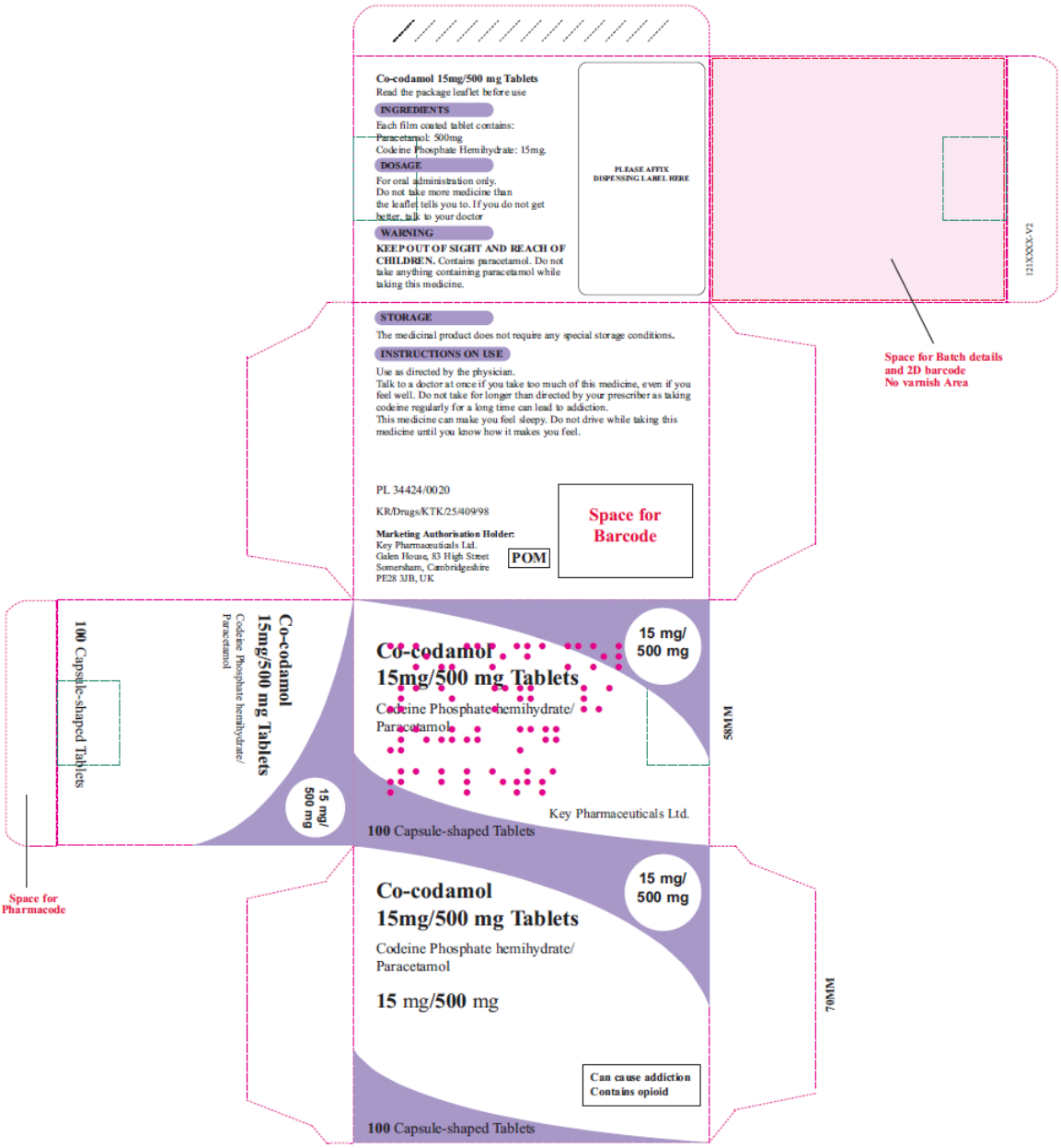
## VIII. USER CONSULTATION
A user consultation with target patient groups on the Patient Information Leaflet (PIL) has been performed on the basis of a bridging report making reference to Co-codamol 15mg/500mg Tablets (PL 21880/0161; Medreich PLC). The bridging report submitted by the applicant is acceptable.

## IX. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION
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. The benefit/risk balance is, therefore, considered to be the same as for the cross-reference product and positive.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the cross-reference product.

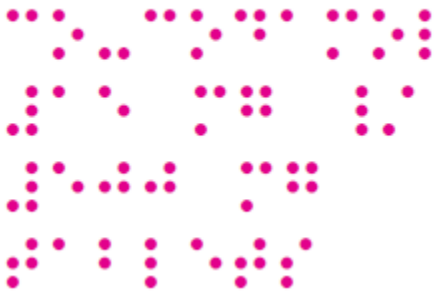
In accordance with Directive 2012/84/EU, the current approved UK versions of the SmPCs and PILs for these products are available on the MHRA website.

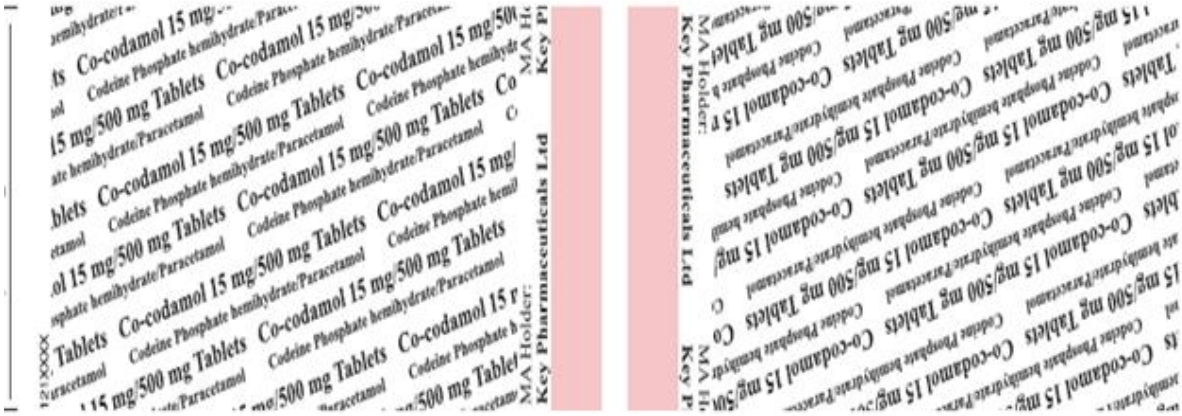
Representative copies of the labels at the time of UK licensing are provided below:




**Braille reads:**

**CO-CODAMOL #15 MG / #500 MG TABLETS**




Co-codamol 15 mg/500 mg Tablets
Codeine Phosphate hemihydrate/Paracetamol
Key Pharmaceuticals Ltd
MA Holder:

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Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

| **Application type** | **Scope** | **Product information affected** | **Date of grant** | **Outcome** | **Assessment report attached Y/N** |
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