

Co-Codamol 8mg/500mg Tablets
Co-codamol 30mg/500mg Tablets
(paracetamol, codeine phosphate)

PL 29831/0488-9

UKPAR

TABLE OF CONTENTS

Lay Summary	Page 2
Scientific discussion	Page 3
Steps taken for assessment	Page 12
Steps taken after authorisation	Page 14
Summary of Product Characteristics	Page 15
Product Information Leaflet	Page 31
Labelling	Page 41

Co-Codamol 8mg/500mg and 30mg/500mg Tablets

(paracetamol, codeine phosphate)

PL 29831/0488-9

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Wockhardt UK Limited Marketing Authorisations (licences) for the medicinal products Co-Codamol 8mg/500mg Tablets and Co-Codamol 30mg/500mg Tablets (PL 29831/0488-9) on 6th October 2011 and 5th October 2011, respectively. Co-Codamol 8mg/500mg Tablets is a P licensed medicine, available only from pharmacies, under the supervision of a pharmacist. Co-Codamol 30mg/500mg Tablets is a prescription-only medicine (POM).

The active ingredients, paracetamol and codeine phosphate, belong to a group of medicines called analgesics, which act as painkillers. Paracetamol is also an antipyretic which means that it helps to reduce fever and lower your temperature.

Co-Codamol 8mg/500mg Tablets are used for the short term treatment of acute moderate pain when other painkillers have not worked. They can be used for the symptomatic relief of pain including headache, migraine, toothache, period pains and rheumatic pains, including muscle pains and backache.

Co-Codamol 30mg/500mg Tablets are used for the relief of severe pain such as muscular and rheumatic pain, headache, migraine, neuralgia, toothache and period pains.

Co-Codamol 8mg/500mg and 30mg/500mg Tablets are not suitable for use in children under 12 years of age.

These Marketing Authorisations for Co-Codamol 8mg/500mg and 30mg/500mg Tablets are considered to be identical to the previously granted licences for Co-Codamol 8mg/500mg and 30mg/500mg Tablets (PL 29831/0045 and 0047), authorised to Wockhardt UK Limited on 9th June 2008 and 7th April 2008, respectively.

No new or unexpected safety concerns arose from these simple applications. It was judged that the benefits of Co-Codamol 8mg/500mg and 30mg/500mg Tablets outweigh the risk; hence Marketing Authorisations have been granted.

Co-Codamol 8mg/500mg and 30mg/500mg Tablets

(paracetamol, codeine phosphate)

PL 29831/0488-9

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

Introduction	Page 4
Pharmaceutical assessment	Page 6
Non-clinical assessment	Page 9
Clinical assessment	Page 10
Overall conclusion and benefit-risk assessment	Page 11

INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted Wockhardt UK Limited Marketing Authorisations (MAs) for the medicinal products Co-Codamol 8mg/500mg Tablets and Co-Codamol 30mg/500mg Tablets (PL 29831/0488-9) on 6th October 2011 and 5th October 2011, respectively. Co-Codamol 8mg/500mg Tablets is a P licensed medicine. Co-Codamol 30mg/500mg Tablets is a prescription-only medicine (POM).

These are simple, abridged, 'informed consent' applications, submitted according to Article 10c of EC Directive 2001/83 (as amended). The applications cross-reference the Marketing Authorisations for Co-Codamol 8mg/500mg and 30mg/500mg Tablets (PL 29831/0045 and 0047), authorised to Wockhardt UK Limited on 9th June 2008 and 7th April 2008, respectively. The cross-referenced products were originally authorised, respectively, to The Wallis Laboratory Limited (PL 00211/0007) in November 1987 and to CP Pharmaceuticals Limited (PL 04543/0388) in July 1998. These two MAs underwent Change of Ownership (CoA) procedures to the current Wockhardt UK Limited licences.

Co-Codamol 8mg/500mg Tablets are indicated in adults and children aged 12 years and over for the short term treatment of acute moderate pain which is not relieved by paracetamol, ibuprofen or aspirin alone. The tablets can be used for the symptomatic relief of pain including headache, migraine, toothache, period pains and rheumatic pains, including muscle pains and backache.

Co-Codamol 30mg/500mg Tablets are indicated in adults and children aged 12 years and over for the relief of severe pain.

Paracetamol has analgesic and antipyretic actions. Codeine phosphate is an opioid analgesic. It has similar uses to morphine but is much less potent as an analgesic.

The MHRA considers that the pharmacovigilance system described by the Marketing Authorisation Holder (MAH) fulfils the requirements and provides adequate evidence that the MAH has the services of a Qualified Person (QP) 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.

The MAH has provided adequate justification for not submitting a Risk Management Plan (RMP). As the applications are for products that are identical to already authorised reference products, for which safety concerns requiring additional risk minimisation have not been identified, a risk minimisation system is not considered necessary. The reference products have been in use for many years and the safety profiles of the actives are well-established.

The MAH has provided adequate justification for not submitting an Environmental Risk Assessment (ERA). It is not considered that these medicinal products represent any risk to the environment. There is no reason to conclude that marketing of these products will change the overall use pattern of the existing market. The availability of these medicinal products, which are identical to the cited reference products, will not

lead to any increase in environmental exposure concentrations of the active ingredients.

No new data were submitted nor was it necessary for these simple applications, as the data are identical to those of the previously granted cross-reference products. As the cross-reference products were granted prior to the introduction of current legislation, no Public Assessment Report (PAR) was generated for them.

PHARMACEUTICAL ASSESSMENT

LICENCE NUMBERS:	PL 29831/0488-9
PROPRIETARY NAME:	Co-Codamol 8mg/500mg and 30mg/500mg Tablets
ACTIVE INGREDIENTS:	Paracetamol, codeine phosphate
COMPANY NAME:	Wockhardt UK Limited
E.C. ARTICLE:	Article 10c of Directive 2001/83/EC (as amended)
LEGAL STATUS:	Co-Codamol 8mg/500mg Tablets - P Co-Codamol 30mg/500mg Tablets - POM

1. INTRODUCTION

These are simple abridged applications, submitted under Article 10c of Directive 2001/83/EC (as amended) for Co-Codamol 8mg/500mg and 30mg/500mg Tablets. The proposed MAH is Wockhardt UK Limited.

The reference products are Co-Codamol 8mg/500mg and 30mg/500mg Tablets (PL 29831/0045 and 0047), authorised to Wockhardt UK Limited on 9th June 2008 and 7th April 2008, respectively. The proposed and reference products are considered identical.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)

The approved names of the products are Co-Codamol 8mg/500mg Tablets and Co-Codamol 30mg/500mg Tablets. The products have been named in line with current requirements and the product names are acceptable.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

Each Co-Codamol 8mg/500mg tablet contains 8 mg of codeine phosphate and 500 mg of paracetamol. Each Co-Codamol 30mg/500mg tablet contains 30 mg of codeine phosphate and 500 mg of paracetamol.

Co-Codamol 8mg/500mg Tablets are licensed for marketing in polyvinylchloride (PVC)-aluminium foil blister strips, which are packaged with the Patient Information Leaflet (PIL) into cardboard outer cartons in pack sizes of 8, 10, 12, 16, 20, 24, 28, 30 or 32 tablets; and in polypropylene-polyethylene containers of 25 tablets.

Co-Codamol 30mg/500mg Tablets are licensed for marketing in polyvinylchloride (PVC)-aluminium foil blister strips or in polypropylene-polyethylene containers, which are packaged with the Patient Information Leaflet (PIL) into cardboard outer cartons in pack sizes of 28, 30, 56, 60, 84, 90 or 100 tablets.

The MAH has stated that not all pack sizes may be marketed. The container closure systems and pack sizes are identical to those for the respective reference products.

The approved shelf-life (3 years) and storage conditions ('Do not store above 25°C. Blisters: Store in the original package. Bottles: Keep the bottle tightly closed') are identical to the details registered for the respective reference products.

2.3 Legal status

P - Co-Codamol 8mg/500mg Tablets is a P licensed medicine available only from pharmacies, under the supervision of a pharmacist.

POM - Co-Codamol 30mg/500mg Tablets are subject to a medical prescription.

2.4 Marketing Authorisation Holder / Contact Persons/Company

The proposed Marketing Authorisation Holder is 'Wockhardt UK Ltd, Ash Road North, Wrexham, LL13 9UF, UK'.

The Qualified Person (QP) responsible for pharmacovigilance was stated and their CV included.

2.5 Manufacturers

The proposed manufacturing sites are consistent with those registered for the cross-reference products and evidence of GMP compliance has been provided.

2.6 Qualitative and quantitative composition

The proposed compositions are consistent with the details registered for the cross-reference products.

2.7 Manufacturing process

The proposed manufacturing process is consistent with the details registered for the cross-reference products and the maximum batch sizes are stated.

2.8 Finished product / shelf-life specification

The proposed finished product specifications are consistent with the details registered for the cross-reference products.

2.9 Drug substance specification

The proposed drug substance specifications are consistent with the details registered for the cross-reference products.

2.10 TSE Compliance

There are no materials of human or animal origin contained in or used in the manufacturing process for the proposed products. None of the excipients are sourced from genetically modified organisms.

3. EXPERT REPORT

A satisfactory quality overall summary has been prepared by an appropriately qualified expert. The CV of the expert was provided.

4. PRODUCT NAME & APPEARANCE

See 2.1 for details of the proposed product names. Co-Codamol 8mg/500mg Tablets are white, bevelled-edge tablets with a broken breakline on one side and <AB> on the other side. Co-Codamol 30mg/500mg Tablets are white, circular tablets, marked CCD 30 on one side and CP on the reverse. The appearance of the products is identical to that of the cross-reference products.

5. SUMMARY OF PRODUCT CHARACTERISTICS

The approved SmPCs are consistent with the details registered for the cross-reference products.

6. PATIENT INFORMATION LEAFLET (PIL) / LABELLING

The approved PILs are satisfactory and in line with the approved SmPCs. They have been prepared according to the Quality Review of Documents (QRD) template.

For Co-Codamol 8mg/500mg Tablets, a satisfactory mock-up of the PIL has been provided. PIL user-testing has been accepted based on a bridging report provided by the applicant making reference to the successful user-testing of the PIL for Co-Codamol 30mg/500mg Tablets (Sandoz Ltd.). The text, content and layout of the proposed PIL are considered sufficiently similar to that of the approved PIL for the reference product. The bridging is accepted.

For Co-Codamol 30mg/500mg Tablets, the MAH has submitted a text version PIL only and has committed to submitting a mock-up version and supporting PIL user-testing report to the MHRA for approval before packs are marketed.

Mock-ups of the labelling have been provided and are satisfactory. The approved artwork is comparable to the artwork registered for the cross-reference products and complies with statutory requirements.

The MAH has stated that not all licensed pack sizes may be marketed. They have committed to submitting mock-ups for currently unmarketed pack sizes to the MHRA for approval before those packs are commercially marketed.

7. CONCLUSIONS

The grounds for these applications are considered adequate. Marketing Authorisations were therefore granted.

NON-CLINICAL ASSESSMENT

These are simple, abridged, 'informed consent' applications made under Article 10c of EC Directive 2001/83 (as amended).

No new non-clinical data have been supplied with these applications and none are required for applications of this type. A non-clinical overview has been written by a suitably qualified person and is satisfactory. The CV of the non-clinical expert has been supplied.

The Marketing Authorisation Holder has provided adequate justification for not submitting an Environmental Risk Assessment (ERA).

CLINICAL ASSESSMENT

These are simple, abridged, 'informed consent' applications made under Article 10c of EC Directive 2001/83 (as amended), cross-referring to the Marketing Authorisations for Co-Codamol 8mg/500mg and 30mg/500mg Tablets (PL 29831/0045 and 0047, Wockhardt UK Limited).

No new clinical data have been supplied with the applications, and none are required for applications of this type. A clinical overview has been written by a suitably qualified person and is satisfactory. The CV of the clinical expert has been supplied.

OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY

The data for these applications are consistent with those previously assessed for the cross-reference products and as such have been judged to be satisfactory.

NON-CLINICAL

No new non-clinical data were submitted and none are required for applications of this type.

EFFICACY

These applications are considered identical to the previously granted licences for Co-Codamol 8mg/500mg and 30mg/500mg Tablets (PL 29831/0045 and 0047, Wockhardt UK Limited).

No new or unexpected safety concerns arise from these applications.

PRODUCT LITERATURE

The approved SmPCs, PILs and labelling are satisfactory and consistent with the details registered for the cross-reference products.

For Co-Codamol 8mg/500mg Tablets, a satisfactory mock-up of the PIL has been provided. PIL user-testing has been accepted based on a bridging report provided by the applicant making reference to the successful user-testing of the PIL for Co-Codamol 30mg/500mg Tablets (Sandoz Ltd.).

For Co-Codamol 30mg/500mg Tablets, the MAH has submitted a text version PIL only and has committed to submitting a mock-up version and supporting PIL user-testing report to the MHRA for approval before packs are marketed.

Mock-ups of the labelling have been provided and are satisfactory. The approved labelling artwork complies with statutory requirements. In line with current legislation, the name of the product in Braille appears on the outer packaging.

The MAH has stated that not all licensed pack sizes may be marketed. They have committed to submitting mock-ups for currently unmarketed pack sizes to the MHRA for approval before those packs are commercially marketed.

BENEFIT-RISK ASSESSMENT

The quality of the products is acceptable and no new non-clinical or clinical safety concerns have been identified. The applicant's products are identical to the cross-reference products. The benefit: risk ratio is considered to be positive.

Co-Codamol 8mg/500mg Tablets

(paracetamol, codeine phosphate)

PL 29831/0488

STEPS TAKEN FOR ASSESSMENT

- 1 The MHRA received the marketing authorisation application on 22nd March 2011.
- 2 Following standard checks and communication with the applicant the MHRA considered the application valid on 6th April 2011.
- 3 Following assessment of the application the MHRA requested further information relating to the quality dossier on 1st July 2011, 4th August 2011 and 7th September 2011.
- 4 The applicant responded to the MHRA's requests, providing further information for the quality sections on 19th July 2011, 24th August 2011 and 7th September 2011.
- 5 The application was determined on 6th October 2011.

Co-Codamol 30mg/500mg Tablets

(paracetamol, codeine phosphate)

PL 29831/0489

STEPS TAKEN FOR ASSESMENT

- 1 The MHRA received the marketing authorisation application on 27th January 2011.
- 2 Following standard checks and communication with the applicant the MHRA considered the application valid on 15th February 2011.
- 3 Following assessment of the application the MHRA requested further information relating to the quality dossier on 19th April 2011 and 25th July 2011.
- 4 The applicant responded to the MHRA's requests, providing further information for the quality sections on 11th July 2011 and 31st August 2011.
- 5 The application was determined on 5th October 2011.

Co-Codamol 8mg/500mg and 30mg/500mg Tablets

(paracetamol, codeine phosphate)

PL 29831/0488-9

STEPS TAKEN AFTER AUTHORISATION

Not applicable

SUMMARY OF PRODUCT CHARACTERISTICS

The UK Summary of Product Characteristics (SmPC) for Co-Codamol 8mg/500mg Tablets (PL 29831/0488) is as follows:

1 NAME OF THE MEDICINAL PRODUCT

Co-Codamol 8mg/500mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Paracetamol 500mg Codeine phosphate 8mg

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

White tablets, broken breakline on one face. Debossed <AB> on other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the short term treatment of acute moderate pain which is not relieved by paracetamol, ibuprofen or aspirin alone.

For the symptomatic relief of pain including headache, migraine, toothache, period pains, rheumatic pains, including muscle pains and backache.

4.2 Posology and method of administration

For oral use.

Adults and children over 12 years: one or two tablets to be swallowed with water. The dose should not be repeated more frequently than every four to six hours and not more than four times in any 24 hour period. Maximum dose is 8 tablets (4.0gm of paracetamol and 64mg of codeine in divided doses) per 24 hours

Elderly: The dosage should be reduced.

Hepatic impairment: The dosage should be reduced. Use in liver disease is contraindicated (see 4.3 Contraindications). Renal impairment

The dosage should be reduced in moderate to severe renal impairment (see also 4.8 Undesirable Effects). For concomitant illnesses/conditions where dose reduction may be appropriate, see 4.4 Special Warnings and Precautions for Use.

Do not take for more than 3 days continuously without medical review.

4.3 Contraindications

i. Paracetamol: Hypersensitivity to paracetamol or to any of the excipients.

ii. Codeine: Acute respiratory depression. Hypersensitivity to codeine or to any of the excipients. Hypersensitivity to other opioid analgesics. Liver disease. Acute alcoholism. Use should be avoided in patients with raised intracranial pressure or head injury (in addition to the risk of respiratory depression and increased intracranial pressure, may affect pupillary and other responses vital for neurological assessment).

Codeine is also contraindicated in conditions where inhibition of peristalsis is to be avoided, where there is a risk of paralytic ileus, where abdominal distension develops, or in acute diarrhoeal conditions such as acute ulcerative colitis or antibiotic associated colitis. Not to be used in children of 12 years and under.

4.4 Special warnings and precautions for use

i. Paracetamol: Care is advised in the administration of paracetamol to patients with renal or hepatic impairment. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease. Paracetamol should be given with care to patients with alcoholic dependence. Paracetamol is well tolerated by the majority of people with asthma. However, a small percentage of aspirin sensitive asthmatics are also sensitive to paracetamol. The likelihood of a reaction to paracetamol increases with a patient's level of sensitivity to aspirin (see also 4.8 Undesirable Effects). Do not exceed the recommended dose. Patients should be advised not to take other paracetamol-containing products concurrently.

Label:

- Immediate medical advice should be sought in the event of an overdose, even if you feel well.
- Do not take with any other paracetamol-containing products. Leaflet: Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage.

ii. Codeine: Use with caution in asthma, and decreased respiratory reserve. Avoid use during an acute attack (see 4.3 Contraindications). It should only be used with caution or in reduced dose in debilitated patients, hypotension, hypothyroidism, urethral stricture, adrenocortical insufficiency, prostatic hypertrophy, shock, convulsive disorders, renal impairment or hepatic impairment (see 4.2 posology).

It should be used with caution in those with a history of drug abuse. Discontinuation should be carried out gradually in patients who may have developed physical dependence, to avoid precipitating withdrawal symptoms.

Codeine is partially metabolised by CYP2D6. If a patient has a deficiency or is completely lacking this enzyme they will not obtain adequate analgesic effects. Estimates indicate that up to 7% of the caucasian population may have this deficiency. However, if the patient is an ultra-rapid metaboliser there is an increased risk of developing side effects of opioid toxicity even at low doses. General symptoms of opioid toxicity include nausea, vomiting, constipation, lack of appetite and somnolence. In severe cases this may include symptoms of circulatory and respiratory depression. Estimates indicate that up to 1 to 2% of the caucasian population may be ultra-rapid metabolisers.

Co-codamol 8mg/500mg Tablets contain parahydroxybenzoates (E218, E214 and E216), which may cause allergic reactions (possibly delayed).

The label will state (to be displayed prominently on outer pack – not boxed in bold):

Front of Pack:

- **Can cause addiction**
- **For three days use only**

Back of Pack:

For the short term treatment of acute moderate pain when other pain killers have not worked. For the symptomatic relief of pain including headache, migraine, toothache, period pains, rheumatic pains, including muscle pains and backache.

- **If you need to take this medicine continuously for more than three days you should see your doctor or pharmacist.**
- **This medicine contains codeine which can cause addiction if you take it continuously for more than three days. If you take this medicine for headaches for more than three days it can make them worse.**

The leaflet will state:

Headlines section (to be prominently displayed):

- This medicine can only be used for the short term treatment of acute moderate pain when other pain killers have not worked.
- You should only take this product for a maximum of three days at a time. If you need to take it for longer than three days you should see your doctor or pharmacist for advice
- **This medicine contains codeine which can cause addiction if you take it continuously for more than three days. This can give you withdrawal symptoms from the medicine when you stop taking it**
- If you take this medicine for headaches for more than three days it can make them worse.

Section 1: What the medicine is for

For the short term treatment of acute moderate pain when other pain killers have not worked. For the symptomatic relief of pain including headache, migraine, toothache, period pains, rheumatic pains, including muscle pains and backache.

Section 2: Before taking:

This medicine contains codeine which can cause addiction if you take it continuously for more than three days. This can give you withdrawal symptoms from the medicine when you stop taking it

If you take a painkiller for headaches for more than three days it can make them worse.

- Refer to section 4 (possible side effects) for the signs and symptoms of an allergic reaction.

Pregnancy and breast-feeding

Usually it is safe to take Co-codamol Tablets while breast-feeding as the levels of the active ingredients of this medicine in breast milk are too low to cause your baby any problems.

However, some women who are at increased risk of developing side effects at any dose may have higher levels in their breast milk. If any of the following side effects develop in you or your baby, stop taking this medicine and seek immediate medical advice; feeling sick, vomiting, constipation, decreased or lack of appetite, feeling tired or sleeping for longer than normal, and shallow or slow breathing.

Section 3: Dosage

If you stop taking Co-codamol

Do not take for more than 3 days. If you need to use this medicine for more than three days you must speak to your doctor or pharmacist

This medicine contains codeine which can cause addiction if you take it continuously for more than three days. When you stop taking it you may get withdrawal symptoms. You should talk to your doctor or pharmacist if you think you are suffering from withdrawal symptoms.

Section 4: Side effects

- **Some people may have side-effects when taking this medicine. If you have any unwanted side-effects you should seek advice from your doctor, pharmacist or other healthcare professional. Also you can help to make sure that medicines remain safe as possible by reporting any unwanted side-effects via the internet at www.yellowcard.gov.uk; alternatively you can call Freephone 0808 100 3352 (available between 10am-2pm Monday – Friday) or fill in a paper form available from your local pharmacy.**

How do I know if I am addicted?

If you take this medicine according to the instructions on the pack it is unlikely that you will become addicted to the medicine. However, if the following apply to you it is important that you talk to your doctor:

- You need to take the medicine for longer periods of time
 - You need to take more than the recommended dose
- When you stop taking the medicine you feel very unwell but you feel better if you start taking the medicine again.

4.5 Interaction with other medicinal products and other forms of interaction

i. Paracetamol: Alcohol: Paracetamol should be given with care to patients with alcohol dependence (see Section 4.4).

Analgesics: Diflunisal increases blood concentrations of paracetamol.

Anion-exchange resins: Absorption reduced by colestyramine; administration should be separated by at least 1 hour.

Antibacterials: Isoniazid may increase the risk of hepatotoxicity with therapeutic doses of paracetamol.

Anticoagulants: The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

Antiepileptics: Carbamazepine, phenobarbital, phenytoin and primidone can reduce the effects of paracetamol and increase the risk of hepatotoxicity.

Motility stimulants: The speed of absorption of paracetamol may be increased by metoclopramide or domperidone.

Oral Contraceptives: Paracetamol is cleared from the body more quickly in women taking oral contraceptives and the analgesic effects may be reduced. Uricosurics: Probenecid can reduce the loss of paracetamol from the body.

ii. Codeine:

Alcohol: the effects of alcohol may be enhanced.

Anti-arrhythmics: codeine delays the absorption of mexiletine. The analgesic activity of codeine is likely to be significantly impaired by quinidine in extensive metabolisers of codeine.

Antidepressants: Severe CNS excitation or depression (including hypertension or hypotension) has been reported with the concurrent use of monoamine oxidase inhibitors (MAOIs) and pethidine. It is therefore possible that a similar interaction may occur with other opioid analgesics. The depressant effects of opioid analgesics may be enhanced by tricyclic antidepressants.

Antipsychotics: enhanced sedative and hypotensive effect.

Anxiolytics and hypnotics: enhanced sedative effect.

Domperidone and metoclopramide: codeine antagonises the effect of metoclopramide and domperidone on gastrointestinal activity.

Antidiarrhoeal and antiperistaltic agents: Concurrent use of codeine with agents such as loperamide and kaolin may increase the risk of severe constipation.

Ulcer-healing drugs: cimetidine inhibits the metabolism of opioid analgesics resulting in increased plasma concentrations. Interference with laboratory tests- Opioid analgesics interfere with a number of laboratory tests including plasma amylase, lipase, bilirubin, alkaline phosphatase, lactate dehydrogenase, alanine aminotransferase and aspartate aminotransferase. Opioids may also interfere with gastric emptying studies as they delay gastric emptying and with hepatobiliary imaging using technetium Tc 99m disofenin as opioid treatment may cause constriction of the sphincter of Oddi and increase biliary tract pressure.

4.6 Pregnancy and lactation

Pregnancy

i. Paracetamol: Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol use in the recommended dosage, but patients should follow the advice of their doctor regarding its use.

ii. Codeine: As with all medications caution should be exercised during pregnancy, especially in the first trimester. A possible association with respiratory and cardiac malformations has been reported. Regular use of codeine during pregnancy may cause physical dependence in the foetus leading to withdrawal symptoms in the neonate. Administration of codeine during labour may depress respiration in the neonate. Opioid analgesics may cause gastric stasis during labour, increasing the risk of inhalation pneumonia in the mother.

At normal therapeutic doses, codeine and its active metabolites may be present in breast milk at very low doses and is unlikely to adversely affect the breast fed infant.

However, if the patient is an ultra-rapid metaboliser of CYP2D6, higher levels of the active metabolites may be present in breast milk and on very rare occasions may result in symptoms of opioid toxicity in the infant.

If symptoms of opioid toxicity develop in either the mother or the infant, then all codeine containing medicines should be stopped and alternative non-opioid analgesics prescribed. In severe cases consideration should be given to prescribing naloxone to reverse these effects.

Breastfeeding

Paracetamol: Paracetamol is excreted in breast milk, but not in a clinically significant amount. Available published data do not contraindicate breast-feeding.

4.7 Effects on ability to drive and use machines

i. Paracetamol: Paracetamol has no or negligible influence on the ability to drive and use machines.

ii. Codeine: Codeine produces sedation and may cause blurred or double vision. If affected patients should be advised not to drive or operate machines.

4.8 Undesirable effects

i. Paracetamol:

Adverse effects of paracetamol are rare.

Blood and lymphatic system disorders: There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis, but these were not necessarily causally related to paracetamol.

Immune system disorders: Hypersensitivity including skin rash may occur. A small percentage of aspirin-sensitive asthmatics are also sensitive to paracetamol. In such cases, the deterioration in respiratory function induced by paracetamol is milder and shorter than with aspirin (see also 4.4 Special Warnings and Precautions for Use)

Renal and urinary disorders: Nephropathy has been associated with chronic high dose use.

ii. Codeine:

The most common side effects include constipation, drowsiness, nausea and vomiting (particularly in the initial stages). Other less frequent and rare side-effects include the following:

Skin and subcutaneous disorders: rashes, urticaria and pruritus, sweating, flushing and facial oedema.

Gastrointestinal disorders: dry mouth, biliary spasm.

General disorders and administrative site conditions: Malaise, tiredness.

Eye disorders: blurred or double vision or other changes in vision.

Metabolism and nutrition disorders: Anorexia.

Musculoskeletal and connective tissue disorders: Uncontrolled muscle movements. Muscle rigidity.

Nervous system disorders: confusion (with large doses), dizziness, headache (prolonged use of a painkiller for headaches can make them worse), vertigo, convulsions.

Psychiatric disorders: Hallucinations and nightmares, mood changes (including depression and more rarely euphoria).

Cardiac disorders: hypotension (with large doses), tachycardia, bradycardia and palpitations.

Respiratory, thoracic and mediastinal disorders: respiratory depression and dyspnoea.

Renal and urinary disorders: difficulty with micturition, increased frequency and/or decreased amount of micturition, dysuria, ureteric spasm.

Reproductive system and breast disorders: erectile dysfunction.

Regular prolonged use of codeine is known to lead to addiction and tolerance. Symptoms of restlessness and irritability may result when treatment is then stopped.

4.9 Overdose

i. Paracetamol: Liver damage is possible in adults who have taken 10g or more of paracetamol. Ingestion of 5g or more of paracetamol may lead to liver damage if the patient has risk factors (see below).

Risk Factors

If the patient

a. Is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.

Or

b. Regularly consumes ethanol in excess of recommended amounts.

Or

c. Is likely to be glutathione deplete e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms

Symptoms of paracetamol overdose in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion.

Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin

pain, haematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

Treatment

Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention. Symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines, see BNF overdose section. Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post ingestion. The effectiveness of the antidote declines sharply after this time. If required the patient should be given intravenous N-acetylcysteine in line with the established dosage schedule. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital. Management of patients who present with serious hepatic dysfunction beyond 24h from ingestion should be discussed with the NPIS or a liver unit.

ii. Codeine:

Symptoms

Central nervous system depression, including respiratory depression, may develop but is unlikely to be severe unless other sedative agents have been co-ingested, including alcohol, or the overdose is very large. The triad of coma, pinpoint pupils and respiratory depression is considered indicative of opioid overdosage with dilation of the pupils occurring as hypoxia develops. Nausea and vomiting are common. Other opioid overdose symptoms include hypothermia, confusion, convulsions, severe dizziness, severe drowsiness, hypotension and tachycardia (possible but unlikely), nervousness or restlessness, excitement, hallucinations, bradycardia, circulatory failure, slow or troubled breathing, severe weakness, convulsions, especially in infants and children. Rhabdomyolysis, progressing to renal failure, has been reported in overdosage with opioids. The effects in overdosage will be potentiated by simultaneous ingestion of alcohol and psychotropic drugs.

Treatment

This should include general symptomatic and supportive measures, including a clear airway and monitoring of vital signs until stable. Consider activated charcoal if an adult presents within one hour of ingestion of more than 350mg or a child more than 5mg/kg. In acute overdosage with respiratory depression or coma, the specific opioid antagonist naloxone is indicated using one of the recommended dose regimens—repeated doses may be required in a seriously poisoned patient as naloxone is a competitive antagonist with a short half life. Patients should be observed closely for at least four hours after ingestion, or eight hours if a sustained release preparation has been taken.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics, ATC Code: N02B E51

i. Paracetamol: Paracetamol has analgesic and antipyretic actions.

ii. Codeine: Codeine has similar uses to morphine but is much less potent as an analgesic.

5.2 Pharmacokinetic properties

i. Paracetamol: Paracetamol is readily absorbed from the gastro-intestinal tract with peak plasma concentrations occurring 30 minutes to two hours after ingestion. It is metabolised in the liver and excreted in the urine, mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half-life varies from about one hour to four hours. At usual therapeutic concentrations plasma protein binding is negligible.

ii. Codeine: Codeine is well absorbed from the gastrointestinal tract following oral administration. It is metabolised in the liver to morphine and norcodeine which are both excreted in the urine partly as conjugates with glucuronic acid. Most of the excretion products appear in the urine within 6 hours and up to 86% of the dose is excreted in 24 hours. About 70% of the dose is excreted as free codeine, 10% as free and conjugated morphine and a further 10% as free or conjugated norcodeine. Only traces are found in the faeces. The plasma half life is between approximately three and four hours.

5.3 Preclinical safety data

Paracetamol & codeine: There are no preclinical data of relevance to the prescriber, which are additional to those already included in the other sections of the SmPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Potato starch
Maize starch
Talc Povidone
Stearic acid
Magnesium stearate
Nipasept *

* Nipasept consists of methyl-p-hydroxybenzoate (E218), ethyl-p-hydroxy benzoate (E214) and propyl-p-hydroxybenzoate (E216).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.
Blisters: Store in the original package.
Bottles: Keep the bottle tightly closed.

6.5 Nature and contents of container

Blister packs: 8, 10, 12, 16, 20, 24, 28, 30, 32 as Pharmacy packs. Blister strips consist of a 35gsm paper/9µ soft tempered aluminium foil lid and 250µ PVC film base in cartons.

Polypropylene/polyethylene containers: 25 as Pharmacy packs

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Wockhardt UK Ltd
Ash Road North
Wrexham
LL13 9UF
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 29831/0488

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

06/10/2011

10 DATE OF REVISION OF THE TEXT

06/10/2011

The UK Summary of Product Characteristics (SmPC) for Co-Codamol 30mg/500mg Tablets (PL 29831/0489) is as follows:

1 NAME OF THE MEDICINAL PRODUCT

Co-codamol 30mg/500mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Codeine Phosphate	30mg
Paracetamol	500mg

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of severe pain.

4.2 Posology and method of administration

For oral use.

Adults

One or two tablets every four to six hours with a maximum dose of eight tablets in any 24 hour period.

Elderly

The dosage should be reduced.

Hepatic impairment

The dosage should be reduced.

Children (under 12 years)

Not recommended.

Dosage should be adjusted accordingly to the severity of the pain and the response of the patient. However, it should be kept in mind that tolerance to codeine can develop with continued use and that the incidence of untoward effects is dose related. Doses of codeine higher than 60 mg fail to give commensurate relief of pain but merely prolong analgesia and are associated with an appreciable increased incidence of undesirable side effects.

4.3 Contraindications

Known hypersensitivity to paracetamol or codeine, or other opioid analgesics, or to any of the excipients.

Acute respiratory depression.

Obstructive airways disease.

Acute alcoholism.

Severe hepatic dysfunction

Head injury or raised intracranial pressure (in addition to the risk of respiratory depression and increased intracranial pressure, may affect papillary and other responses vital for neurological assessment).

Comatose patients.

Where there is a risk of paralytic ileus.

In acute diarrhoeal conditions such as acute ulcerative colitis or antibiotic associated colitis (e.g. pseudomembranous colitis) or diarrhoea caused by poisoning.

4.4 Special warnings and precautions for use

Co-codamol 30mg/500mg Tablets may cause drowsiness. Co-codamol 30mg/500mg Tablets should be given in reduced doses or with caution to elderly patients or debilitated patients or patients with hypothyroidism, asthma, decreased respiratory reserve, adrenocortical insufficiency, prostatic hypertrophy, hypotension, shock, inflammatory or obstructive bowel disorders, urethral stricture, convulsive disorders, myasthenia gravis. It should be avoided or the dose reduced in patients with hepatic or renal impairment. Use with caution in those with a history of drug abuse. Discontinuation should be carried out gradually in patients who may have developed physical dependence, to avoid precipitating withdrawal symptoms.

Avoid use during an acute asthma attack.

Codeine is partially metabolised by CYP2D6. If a patient has a deficiency or is completely lacking this enzyme they will not obtain adequate analgesic effects. Estimates indicate that up to 7% of the caucasian population may have this deficiency. However, if the patient is an ultra-rapid metaboliser there is an increased risk of developing side effects of opioid toxicity even at low doses. General symptoms of opioid toxicity include nausea, vomiting, constipation, lack of appetite and somnolence. In severe cases this may include symptoms of circulatory and respiratory depression. Estimates indicate that up to 1 to 2% of the caucasian population may be ultra-rapid metabolisers.

Opioid analgesics should be avoided in patients with biliary tract disorders or used in conjunction with an antispasmodic.

Administration of pethidine and possibly other opioid analgesics to patients taking a monoamine oxidase inhibitor (MAOI) has been associated with very severe and sometimes fatal reactions. If the use of codeine is considered essential then great care should be taken in patients taking MAOIs or within 14 days of stopping MAOIs (see section 4.5).

Co-codamol 30mg/500mg Tablets enhance the effects of alcohol. Their concurrent use should be avoided.

The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease.

Patients should be advised that immediate medical advice should be sought in the event of an overdose, because of the risk of delayed, serious liver damage. They should be advised not to take other paracetamol-containing products concurrently and to keep the product out of the reach of children.

The risk-benefit of continued use should be assessed regularly by the prescriber.

The leaflet will state in a prominent position in the 'before taking' section:

- Do not take for longer than directed by your prescriber
- Taking codeine regularly for a long time can lead to addiction, which might cause you to feel restless and irritable when you stop the tablets.
- Taking a painkiller for headaches too often or for too long can make them worse.

The leaflet will state in the 'Pregnancy and breast-feeding' subsection of section 2 'Before taking your medicine':

Usually it is safe to take Co-codamol Tablets while breast-feeding as the levels of the active ingredients of this medicine in breast milk are too low to cause your baby any problems.

However, some women who are at increased risk of developing side effects at any dose may have higher levels in their breast milk. If any of the following side effects develop in you or

your baby, stop taking this medicine and seek immediate medical advice; feeling sick, vomiting, constipation, decreased or lack of appetite, feeling tired or sleeping for longer than normal, and shallow or slow breathing.

The label will state (To be displayed prominently on outer pack –not boxed):

- Do not take for longer than directed by your prescriber as taking codeine regularly for a long time can lead to addiction.

4.5 Interaction with other medicinal products and other forms of interaction

In high doses or with regular treatment, paracetamol may potentiate the effects of warfarin. The absorption of paracetamol is reduced by cholestyramine and accelerated by domperidone and metoclopramide.

Anaesthetics: concomitant administration of codeine and anaesthetics may cause increased CNS depression and/or respiratory depression and/or hypotension.

Antihistamines: concomitant administration of codeine and antihistamines with sedative properties may cause increased CNS depression and/or respiratory depression and/or hypotension.

Codeine antagonises the effect of metoclopramide and cisapride on gastrointestinal activity. It delays the absorption of flecainide and mexiletine and potentiates the effect of hypnotics and anxiolytics. The analgesic activity of codeine is likely to be significantly impaired by quinidine which impairs codeine metabolism.

Antidepressants: The depressant effects of opioid analgesics may be enhanced by tricyclic antidepressants. MAOIs taken with pethidine have been associated with severe CNS excitation or depression (including hypertension or hypotension). Although this has not been documented with codeine, it is possible that a similar interaction may occur and therefore the use of codeine should be avoided while the patient is taking MAOIs and for 2 weeks after MAOI discontinuation.

Antipsychotics: enhanced sedative and hypotensive effect.

Alcohol: the hypotensive, sedative and respiratory depressive effects of alcohol may be enhanced.

Concurrent use of codeine with antidiarrhoeal and antiperistaltic agents such as loperamide and kaolin may increase the risk of severe constipation.

Sodium oxybate: concomitant administration of codeine and sodium oxybate may cause increased CNS depression and/or respiratory depression and/or hypotension.

Concomitant use of antimuscarinics may lead to paralytic ileus or urinary retention.

Ulcer-healing drugs: Cimetidine may inhibit the metabolism of dihydrocodeine resulting in increased plasma concentrations.

Interference with laboratory tests: Opioids may interfere with gastric emptying studies as they delay gastric emptying and with hepatobiliary imaging using technetium Tc 99m disofenin as opioid treatment may cause constriction of the sphincter of Oddi and increase biliary tract pressure.

4.6 Fertility, Pregnancy and Lactation

Pregnancy

As with all medication, caution should be exercised during pregnancy, especially in the first trimester. A possible association with respiratory and cardiac malformations has been reported following first trimester exposure to codeine. Regular use during pregnancy may cause physical dependence in the foetus leading to withdrawal symptoms in the neonate.

Administration of codeine during labour may depress respiration in the neonate. Opioid analgesics may cause gastric stasis during labour, increasing the risk of inhalation pneumonia in the mother.

There is epidemiological evidence of safety in human pregnancy when paracetamol is used in normal stated dosages.

Breastfeeding

Paracetamol is excreted in breast milk but not in clinically significant quantities.

At normal therapeutic doses, codeine and its active metabolites may be present in breast milk at very low doses and is unlikely to adversely affect the breast fed infant.

However, if the patient is an ultra-rapid metaboliser of CYP2D6, higher levels of the active metabolites may be present in breast milk and on very rare occasions may result in symptoms of opioid toxicity in the infant.

If symptoms of opioid toxicity develop in either the mother or the infant, then all codeine containing medicines should be stopped and alternative non-opioid analgesics prescribed. In severe cases consideration should be given to prescribing naloxone to reverse these effects.

4.7 Effects on ability to drive and use machines

Codeine produces sedation and may also cause changes in vision, including blurred or double vision. If affected, patients should not drive or operate machinery. The effects of alcohol are enhanced by opioid analgesics.

4.8 Undesirable effects

Regular prolonged use of codeine is known to lead to addiction and tolerance. Symptoms of restlessness and irritability may result when treatment is then stopped.

Prolonged use of a painkiller for headaches can make them worse.

Tolerance and some of the most common side effects – drowsiness, nausea, and vomiting, and confusion – generally develops with long term use.

Immune system disorders: maculopapular rash has been seen as part of a hypersensitivity syndrome associated with oral codeine phosphate; fever, splenomegaly and lymphadenopathy also occurred.

Endocrine disorders: hyperglycaemia.

Metabolism and nutrition disorders: anorexia.

Psychiatric disorders: mental depression, hallucinations and nightmares, restlessness, confusion, mood changes, euphoria, dysphoria.

Nervous system disorders: convulsions (especially in infants and children), dizziness, drowsiness, headache. Raised intracranial pressure may occur in some patients.

Eye disorders: miosis, blurred or double vision, other visual disturbances.

Ear and labyrinth disorders: vertigo

Cardiac disorders: orthostatic hypotension, palpitations, tachycardia and bradycardia.

Vascular disorders: postural hypotension, facial flushing. Large doses produce hypotension.

Respiratory, thoracic and mediastinal disorders: Dyspnoea, larger doses produce respiratory depression.

Gastrointestinal disorders: nausea, vomiting, constipation, dry mouth, stomach cramps, pancreatitis.

Hepatobiliary disorders: Biliary spasm (may be associated with altered liver enzyme values).

Skin and subcutaneous tissue disorders: allergic reactions such as urticaria, pruritis, skin rashes, sweating and facial oedema.

Musculoskeletal and connective tissue disorders: Uncontrolled muscle movements. Muscle rigidity may occur after high doses.

Renal and urinary disorders: difficulty with micturation, urinary retention, ureteric spasm, dysuria. An antidiuretic effect may also occur with codeine.

Reproductive system and breast disorders: sexual dysfunction, erectile dysfunction, decreased potency. Decreased libido.

General disorders and administration site conditions : malaise, tiredness, hypothermia.

The paracetamol component of Co-codamol 30mg/500mg Tablets is relatively free of side-effects but skin rashes and other allergic reactions may occur. Renal damage may occur rarely with long term use. Haematological side-effects including thrombocytopenia, neutropenia, pancytopenia and leucopenia have occurred in isolated cases.

4.9 Overdose

Symptoms

Symptoms of paracetamol overdose in the first 24 hours are pallor, nausea, vomiting, anorexia, and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported. Liver damage is possible in adults who have taken 10 g or more of paracetamol. It is considered that excess quantities of a toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested),become irreversibly bound to liver tissue.

Treatment

Immediate treatment is essential in the management of paracetamol overdose. Despite of lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention and any patient who has ingested around 7.5 g or more of paracetamol in the proceeding 4 hours should undergo gastric lavage. Administration of oral methionine or intravenous N-acetylcysteine which may have a beneficial effect up to at least 48 hours after the overdose, may be required. General supportive measures must be available.

An overdose with codeine is characterised by respiratory depression, extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin and sometimes bradycardia and hypotension. In severe overdose with codeine, apnoea, circulatory collapse, cardiac arrest and death may occur. Primary attention should be given to the re-establishment of adequate respiratory function through the provision of a patent airway and the institution of controlled ventilation. Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated. Opioid antagonists, such as naloxone may be administered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics, ATC Code: N02B E51

Paracetamol has analgesic and antipyretic properties.

Codeine phosphate is an opioid analgesic.

5.2 Pharmacokinetic properties

Both paracetamol and codeine phosphate are readily absorbed from the gastro-intestinal tract giving peak plasma levels within one hour of administration.

Paracetamol is metabolised in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half life varies from about one to four hours. At usual therapeutic concentrations plasma-protein binding is negligible.

Codeine is metabolised in the liver to morphine and norcodeine which are both excreted in the urine partly as conjugates with glucuronic acid. Most of the excretion products appear in the urine within six hours and up to 80% of the dose is excreted in 24 hours. About 70% of the dose is excreted as free codeine, 10% as free and conjugated morphine and a further 10% as free or conjugated norcodeine. Only traces are found in the faeces. The plasma half life is approximately three to four hours.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to those included in other sections.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Pregelatinised Maize Starch
Magnesium Stearate
Povidone K30

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 25°C.
Blisters: Store in the original package.
Bottles: Keep the bottle tightly closed.

6.5 Nature and contents of container

28, 30, 56, 60, 84, 90 and 100 tablets in polypropylene/polyethylene containers or blister strips consisting of a 35gsm paper/9µ soft tempered aluminium foil lid and 250µ PVC film base in cartons.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Wockhardt UK Ltd
Ash Road North
Wrexham
LL13 9UF
U.K.

8 MARKETING AUTHORISATION NUMBER(S)

PL 29831/0489

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

05/10/2011

10 DATE OF REVISION OF THE TEXT

05/10/2011

PATIENT INFORMATION LEAFLET

Co-Codamol 8mg/500mg Tablets - PL 29831/0488

**Package leaflet: Information for the user
Co-codamol 8mg/500mg Tablets
Codeine phosphate and paracetamol**



Read all of this leaflet carefully because it contains important information for you.

- **This medicine is available without prescription. However, you still need to use co-codamol 8mg/500mg tablets carefully to get the best results from it.**
- Keep this leaflet. You may need to read it again.
- Ask your doctor or pharmacist if you need more information or advice.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.
- This medicine can only be used for the short term treatment of acute moderate pain when other painkillers have not worked.
- You should only take this product for a maximum of three days at a time. If you need to take it for longer than three days you should see your doctor or pharmacist for advice
- This medicine contains codeine which can cause addiction if you take it continuously for more than three days. This can give you withdrawal symptoms from the medicine when you stop taking it
- If you take this medicine for headaches for more than three days it can make them worse.

In this leaflet:

1. What Co-codamol is and what it is used for
2. Before you take Co-codamol
3. How to take Co-codamol
4. Possible side effects
5. How to store Co-codamol
6. Further information

Talk to your doctor or pharmacist before taking Co-codamol if:

- You are pregnant or breast-feeding (see 'Pregnancy and breast-feeding' below).
- You have asthma, bronchitis or emphysema. If your asthma is controlled you can take co-codamol tablets, but use with care, especially if your asthma is known to be made worse by aspirin or other painkillers. You should not take codeine if you are having an acute asthma attack.
- You have serious problems with your liver or kidneys.
- You have an under active thyroid (hypothyroidism) or adrenal glands.
- You have an enlarged prostate (men) or have difficulty passing water.
- Your alcohol consumption is excessive.
- You suffer from low blood pressure, are in a state of severe shock or very run down.
- You suffer from convulsions or have a seizure disorder (fits).
- You have had a drug addiction.

If you go into hospital for surgery or tests, tell your doctor you are taking co-codamol tablets, as they may interact with some anaesthetics and influence the results of certain tests and diagnostic procedures.

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines you have bought yourself without a prescription.

In particular you should tell your doctor if you are taking any of the following:

- Paracetamol or paracetamol-containing products.
- Barbiturates (to help you sleep or treat epilepsy).
- Anticonvulsants such as carbamazepine, phenobarbital, phenytoin and primidone (drugs used to treat epilepsy).
- Antidepressants (tricyclics or MAOIs).
- Antipsychotics such as chlorpromazine and haloperidol (used to treat mental illnesses including schizophrenia).
- Anxiolytics (to help with anxiety).
- Hypnotics e.g. diazepam and nitrazepam (to help you sleep).
- Sedatives (to help you relax).
- Colestyramine (used to lower cholesterol).
- Cisapride, metoclopramide or domperidone (used to help stop nausea and vomiting).
- Anticoagulants (medicines used to thin the blood, such as warfarin).
- Cimetidine (for stomach ulcers).
- Quinidine, mexiletine (used to regularise heart rhythm).

1. WHAT CO-CODAMOL IS AND WHAT IT IS USED FOR

The name of your medicine is Co-codamol 8mg/500mg Tablets. The active ingredients in Co-codamol are paracetamol and codeine phosphate. They belong to a group of medicines called analgesics, which act as painkillers.

These tablets are used for the short term treatment of acute moderate pain when other painkillers have not worked. For the symptomatic relief of pain including headache, migraine, toothache, period pains, rheumatic pains, including muscle pains and backache.

2. BEFORE YOU TAKE CO-CODAMOL

This medicine contains codeine which can cause addiction if you take it continuously for more than three days. This can give you withdrawal symptoms from the medicine when you stop taking it.

If you take a painkiller for headaches for more than three days it can make them worse.

Do not take Co-codamol if:

- You are allergic (hypersensitive) to paracetamol, codeine or any of the other ingredients in Co-codamol Tablets. Co-codamol Tablets contain parahydroxybenzoates (E218, E214 and E216), which may cause allergic reactions (possibly delayed). Refer to section 4 (possible side effects) for the signs and symptoms of an allergic reaction.
- You drink excessive amounts of alcohol.
- You have severe problems with breathing.
- You have recently had a head injury or have increased pressure within your head (raised intracranial pressure).
- You have been told you have liver disease.
- You are under 12 years of age.
- You are at risk from intestinal paralysis or have a swollen abdomen.
- You are suffering from severe diarrhoea.
- You are taking any other paracetamol or paracetamol-containing products.

Take special care with Co-codamol

Before taking this medicine, you need to know the following:

This product contains paracetamol.

- Do **not** take with any other paracetamol containing products.
- If your symptoms last for more than 3 days talk to your doctor.

- Isoniazid (used to treat tuberculosis).
- Diflunisal (a pain killer).
- Oral contraceptives.
- Probenecid (used to treat gout).
- Antidiarrhoeals such as loperamide or kaolin.

Taking Co-codamol with food and drink

Do not drink alcohol while you are taking Co-codamol. Alcohol may increase the sedative effects of Co-codamol and make you very sleepy. It can also increase the risk of some side effects.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding you should talk to your doctor or pharmacist before taking any medicine.

Usually it is safe to take Co-codamol Tablets while breast-feeding as the levels of the active ingredients of this medicine in breast milk are too low to cause your baby any problems. However, some women who are at increased risk of developing side effects at any dose may have higher levels in their breast milk. If any of the following side effects develop in you or your baby, stop taking this medicine and seek immediate medical advice; feeling sick, vomiting, constipation, decreased or lack of appetite, feeling tired or sleeping for longer than normal, and shallow or slow breathing.

Driving and using machines

Codeine may cause drowsiness and/or blurred or double vision in some people. Do not drive or use any tools or machines if you are affected in this way and do not drink alcohol, as this will make these effects worse. Other medicines may also increase these effects.

3. HOW TO TAKE CO-CODAMOL

Always take Co-codamol tablets exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. The usual dose is described below.

These tablets are for oral administration. They should be swallowed with a glass of water.

Dosage instructions

Adults and children over 12 years: Take one to two tablets every four hours. Do **not** take more than eight tablets in 24 hours.

Elderly: Your doctor may have reduced the dose for you. If this is the case follow your doctor's instructions.

You may need a reduced dose if your kidney or liver is not working as well as it should be. You may also be given a reduced dose if you suffer from any of the conditions listed above in the section headed 'Talk to your doctor or pharmacist before taking Co-codamol if'.

Children under 12 years: Not recommended.
Do not take more tablets than your doctor has prescribed for you.

If you take more Co-codamol than you should

Always take the medicine as recommended by your doctor. Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage.

If you forget to take Co-codamol

Take your usual dose as soon as you remember, provided it is at least 4 hours since your last dose.
Never take a double dose to make up for a missed dose.

If you stop taking Co-codamol

Do not take for more than 3 days. If you need to use this medicine for more than three days you must speak to your doctor or pharmacist.

This medicine contains codeine which can cause addiction if you take it continuously for more than three days. When you stop taking it you may get withdrawal symptoms. You should talk to your doctor or pharmacist if you think you are suffering from withdrawal symptoms.

4. POSSIBLE SIDE EFFECTS

Some people may have side-effects when taking this medicine. If you have any unwanted side-effects you should seek advice from your doctor, pharmacist or other healthcare professional. Also you can help to make sure that medicines remain safe as possible by reporting any unwanted side-effects via the internet at www.yellowcard.gov.uk; alternatively you can call Freephone 0808 100 3352 (available between 10am-2pm Monday – Friday) or fill in a paper form available from your local pharmacy.

It is very unlikely that you will experience the following side effects. However, you should **stop** taking this medicine and talk

How do I know if I am addicted?

If you take this medicine according to the instructions on the pack it is unlikely that you will become addicted to the medicine. However, if the following apply to you it is important that you talk to your doctor:

- You need to take the medicine for longer periods of time
- You need to take more than the recommended dose
- When you stop taking the medicine you feel very unwell but you feel better if you start taking the medicine again.

Print free area for
Pharmacode
on front of leaflet

5. HOW TO STORE CO-CODAMOL

Keep out of the reach and sight of children.
Do not use Co-codamol tablets after the expiry date which is stated on the carton or blister.
The expiry date refers to the last day of that month.
Do not store above 25°C. Store in the original package or container in order to protect from light and moisture.
Never transfer medicines from one container to another.
Never take medicines from an unlabelled container.

This medicine is for you. Never offer your tablets to other people, even if their symptoms seem the same as yours, the tablets may not be suitable for their use.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines that are no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

The active ingredients in Co-codamol Tablets are paracetamol, 500mg and codeine phosphate, 8mg.
The other ingredients are maize and potato starch, povidone, stearic acid, talc, magnesium stearate and nipasept (nipasept contains methyl-p-hydroxy benzoate (E218), ethyl-p-hydroxy benzoate (E214) and propyl-p-hydroxy benzoate (E216)).

What Co-codamol looks like and contents of the pack
Co-codamol Tablets are white round tablets.

They are available in packs of 8, 10, 12, 16, 20, 24, 25, 28, 30 and 32 tablets.

to your doctor **immediately** if you notice any of the following symptoms:

- You bruise more easily, have bleeding gums or bleed for longer after cutting yourself or you feel tired or look pale.
- You seem to be getting more infections than usual or you develop ulcers in your mouth or throat.
- You have a severe abdominal pain (in the upper middle or upper left part of the belly) usually accompanied by sickness, diarrhoea or fever.
- You have an allergic reaction. The signs of an allergic reaction may include: a rash, wheals or itching, difficulty breathing or swallowing, swelling of your lips, face, throat or tongue.
- You have problems with vision.
- You have mood changes (including depression and more rarely euphoria).
- You suffer from confusion, dizziness or vertigo.
- You have a dry mouth or a general feeling of discomfort.
- You seem to be getting more headaches (which can be made worse by taking co-codamol tablets for too long).
- You have respiratory depression, sweating, flushing.
- You develop anorexia.
- You have a slower or faster heart beat, palpitations (irregular heartbeat) or low blood pressure (which may cause fainting).
- You develop blood problems (which may cause sore throat or fever).
- You suffer from convulsions, hallucinations, nightmares, uncontrolled muscle movements, muscle rigidity, pain or difficulties when passing urine, an increased or decreased frequency of passing urine, weak erection in men.

Other more common side effects that some people notice when taking Co-codamol are listed below:

- Constipation
- Nausea
- Drowsiness
- Vomiting

Patients with asthma that is made worse by aspirin or other painkillers may find that co-codamol tablets also cause wheezing. Taking high doses of paracetamol for a long time can cause kidney problems.

If any of the side effects become serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Wockhardt UK Limited, Ash Road North, Wrexham, LL13 9UF, UK.
(PL29831/0488)

Manufacturer

CP Pharmaceuticals Ltd, Ash Road North, Wrexham, LL13 9UF, UK.

This leaflet was last revised in January 2011



Co-Codamol 30mg/500mg Tablets - PL 29831/0489

The MAH has submitted a text version only and has committed to submitting a mock-up PIL to the MHRA for approval before packs are marketed.

Co-codamol 30mg/500mg Tablets Codeine phosphate and paracetamol

Read all of this leaflet carefully because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it onto others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Co-codamol Tablets are and what they are used for
2. Before you take Co-codamol Tablets
3. How to take Co-codamol Tablets
4. Possible side effects
5. How to store Co-codamol Tablets
6. Further information

1. WHAT CO-CODAMOL TABLETS ARE AND WHAT THEY ARE USED FOR

The name of your medicine is Co-codamol 30mgmg/500mg Tablets.

The active ingredients in Co-codamol are paracetamol and codeine phosphate. They belong to a group of medicines called analgesics, which act as painkillers. Paracetamol is also an antipyretic which means that it helps to reduce fever and lower your temperature.

These tablets are usually used for relief of severe pain such as muscular and rheumatic pain, headache, migraine, neuralgia, toothache and period pains.

2. BEFORE YOU TAKE CO-CODAMOL TABLETS

Do not take Co-codamol Tablets if:

- You are allergic (hypersensitive) to paracetamol, codeine, any other opioid analgesic or any of the other ingredients in Co-codamol Tablets.
- You drink excessive amounts of alcohol.
- You have severe asthma, bronchitis, breathing problems or if you are having an asthma attack.
- You have recently had a head injury or have increased pressure within your head (raised intracranial pressure).
- You are under 12 years of age.
- You are suffering from severe diarrhoea.
- You have been told you have liver disease.
- You are at risk of a blocked intestine.
- You are in a coma.

Take special care with Co-codamol Tablets

Before taking this medicine, you need to know the following:

This product contains paracetamol. Do **not** take with any other paracetamol containing products.

- If your symptoms last for more than 3 days talk to your doctor.
- **Do not take for longer than directed by your prescriber.**
- **Taking codeine regularly for a long time can lead to addiction, which might cause you to feel restless and irritable when you stop the tablets.**
- **Taking a painkiller for headaches too often or for too long can make them worse.**

Talk to your doctor or pharmacist before taking Co-codamol Tablets if:

- You are pregnant or breast-feeding (see 'Pregnancy and breastfeeding' below).
- You are taking or have taken within the last two weeks, monoamine oxidase inhibitors (MAOIs) such as moclobemide or phenelzine used in the treatment of depression.
- You have asthma, bronchitis or emphysema. You should not take codeine if you are having an acute asthma attack.
- You have serious problems with your liver or kidneys.
- You are elderly, as you may need a lower dose.
- You are being treated with depressants (medicines used to treat anxiety).
- You have an enlarged prostate.
- You have an inflamed bowel or obstructive bowel disorder.
- You have an under active thyroid.
- You suffer from biliary tract disorders such as gallstones.
- You are very run down.
- You suffer from convulsions (fits).
- You are a poor metaboliser of codeine.
- You have had a drug addiction.
- You have Addison's disease.
- You have a poorly functioning adrenal gland.
- You have difficulty passing water.
- You have low blood pressure or shock.
- You have weak muscles (myasthenia gravis).

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines you have bought yourself without a prescription. In particular you should tell your doctor if you are taking any of the following:

- Antidepressants such as phenelzine, dosulepin (Tricyclic and MAOIs), chlorpromazine (phenothiazines).
- Anxiolytics (to help with anxiety).
- Antipsychotics (to help mood disorders).
- Hypnotics such as diazepam, nitrazepam and temazepam (to help you sleep).
- Cholestyramine (used to lower cholesterol).
- Cisapride, metoclopramide or domperidone (used to help stop nausea and vomiting).
- Anaesthetics, particularly general anaesthetics (used in surgery to numb pain).
- Antihistamines such as benadryl (used to treat allergies e.g. hayfever).
- Sodium oxybate (used to treat narcolepsy).
- Anticoagulants (medicines used to thin the blood, such as warfarin).
- Antidiarrhoeal agents such as loperamide or kaolin.

- Muscle relaxants such as atropine.
- Cimetidine (used to treat stomach ulcers and indigestion).
- Anti-arrhythmic agents such as flecainide, quinidine and mexiletine.

Taking Co-codamol Tablets with food and drink

Do not drink alcohol while you are taking Co-codamol Tablets. Alcohol may increase the sedative effects of co-codamol and make you very sleepy. It can also increase the risk of some side effects.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding you should talk to your doctor or pharmacist before taking any medicine.

Usually it is safe to take Co-codamol Tablets while breastfeeding as the levels of the active ingredients of this medicine in breast milk are too low to cause your baby any problems. However, some women who are at increased risk of developing side effects at any dose may have higher levels in their breast milk. If any of the following side effects develop in you or your baby, stop taking this medicine and seek immediate medical advice; feeling sick, vomiting, constipation, decreased or lack of appetite, feeling tired or sleeping for longer than normal, and shallow or slow breathing.

Driving and using machines

Codeine may cause drowsiness or changes in vision, including blurred or double vision in some people. Do not drive or use any tools or machines if you are affected in this way and do not drink alcohol, as this will make these effects worse. Other medicines may also increase these effects.

3. HOW TO TAKE CO-CODAMOL TABLETS

Always take Co-codamol Tablets exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. The usual dose is described below.

These tablets are for oral administration. They should be swallowed with a glass of water.

Dosage instructions

Adults and children over 12 years: Take one to two tablets every four hours. Do **not** take more than eight tablets in 24 hours.

Elderly: Your doctor may have reduced the dose for you. If this is the case follow your doctor's instructions.

Children under 12 years: Not recommended.

Do not take more tablets than your doctor has prescribed for you.

The dose should be reduced in patients with liver problems.

If you take more Co-codamol Tablets than you should

Always take the medicine as recommended by your doctor. Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage.

If you forget to take Co-codamol Tablets

Take your usual dose as soon as you remember, provided it is at least 4 hours since your last dose. Never take a double dose to make up for a missed dose.

If you stop taking Co-codamol Tablets

Do not stop taking these tablets immediately, it could make you feel restless or irritable. Talk to your doctor about reducing your dose gradually.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, co-codamol can cause side effects, although not everybody gets them. Tell your doctor if you think your medicine is making you feel unwell.

It is very unlikely that you will experience the following side effects.

However, you should **stop** taking this medicine and talk to your doctor **immediately** if you notice any of the following symptoms:

- You have an allergic reaction. The signs of an allergic reaction may include: a rash, wheals or itching, difficulty breathing or swallowing, swelling of your lips, face, throat or tongue.

Other side effects that some people notice when taking Co-codamol Tablets are listed below:

- Constipation
- Nausea (feeling sick)
- Vertigo (a feeling of dizziness or 'spinning')
- Dizziness
- Drowsiness
- Confusion
- Vomiting (being sick)
- Pain or difficulty in passing urine
- Dry mouth
- Sweating
- Facial flushing
- Slower or faster heart rate
- Palpitations (feeling your heartbeat)
- Feeling faint on standing up
- Low body temperature
- Difficulty breathing
- Stomach cramps
- Increased or decreased frequency of passing urine
- Restlessness
- Mood changes including depression, sadness and euphoria
- Hallucinations (seeing or hearing things that are not there)
- Pinpoint pupils
- Blurred vision

- Double vision or other changes in vision
- Pressure on the brain
- Kidney damage
- Blood disorders (such as thrombocytopenia (reduction in blood platelets, which increases risk of bleeding or bruising), neutropenia and leucopenia (reduction in white blood cells, which may make infection more likely) and pancytopenia (severe reduction in blood cells which can cause weakness, bruising or make infections more likely)
- Low sex drive
- Hyperglycaemia (abnormally high levels of glucose in the blood)
- Pancreatitis (inflammation of the pancreas)
- Feeling tired
- Feeling unwell
- Hypothermia
- Biliary spasms (causing a pain in the right side of your abdomen, particularly after eating a meal)
- Fever
- Enlarged spleen or swollen/enlarged lymph nodes
- Anorexia
- Uncontrolled muscle movements
- Muscle rigidity
- Weak erection in men

If any of the side effects become serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

If you have to take these tablets for a long time it is possible that you could become dependent on them and have withdrawal symptoms when you stop. This can also happen to babies born to mothers who have been given co-codamol during pregnancy.

Prolonged use of a painkiller for headaches can make them worse. Regular prolonged use of codeine is known to lead to addiction and tolerance.

5. HOW TO STORE CO-CODAMOL TABLETS

Keep out of the reach and sight of children.

Do not use Co-codamol Tablets after the expiry date which is stated on the carton or inner container or if the tablets show signs of 'going off' such as discoloration.

The expiry date refers to the last day of that month.

Do not store above 25°C. Store in the original container.

Remember this medicine is for **you** only. **Never** give it to anyone else. It may harm them, even if their symptoms are the same as yours.

Unless your doctor tells you to, do not keep tablets that you no longer need. Give them back to your pharmacist.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines that are no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Co-codamol Tablets contain

The active ingredients in Co-codamol Tablets are paracetamol, 500mg and codeine phosphate, 30mg.

The other ingredients are pregelatinised maize starch, magnesium stearate and povidone K30.

What Co-codamol Tablets looks like and contents of the pack

Co-codamol Tablets are white, circular tablets marked CCD 30 on one face and CP on the reverse.

They are available in packs of 28, 30, 56, 60, 84, 90 and 100 tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Wockhardt UK Limited, Ash Road North, Wrexham, LL13 9UF, UK.

Manufacturer

CP Pharmaceuticals Ltd, Ash Road North, Wrexham, LL13 9UF, UK.

Other formats:

To listen to or request a copy of this leaflet in Braille, large print or audio please call, free of charge: 0800 198 5000 (UK Only). Please be ready to give the following information:

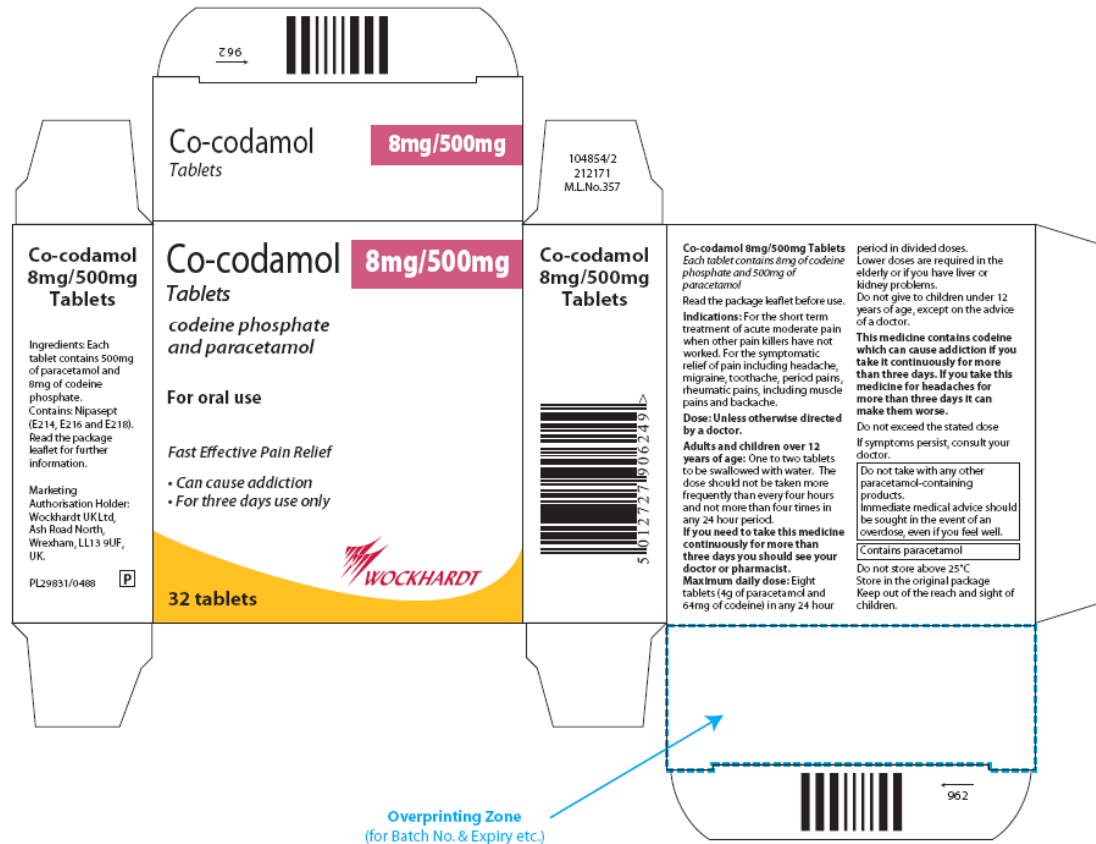
Product name	Reference number
Co-codamol 30mg/500mg Tablets	29831/0489

This leaflet was last revised in July 2011

LABELLING

Co-Codamol 8mg/500mg Tablets - PL 29831/0488

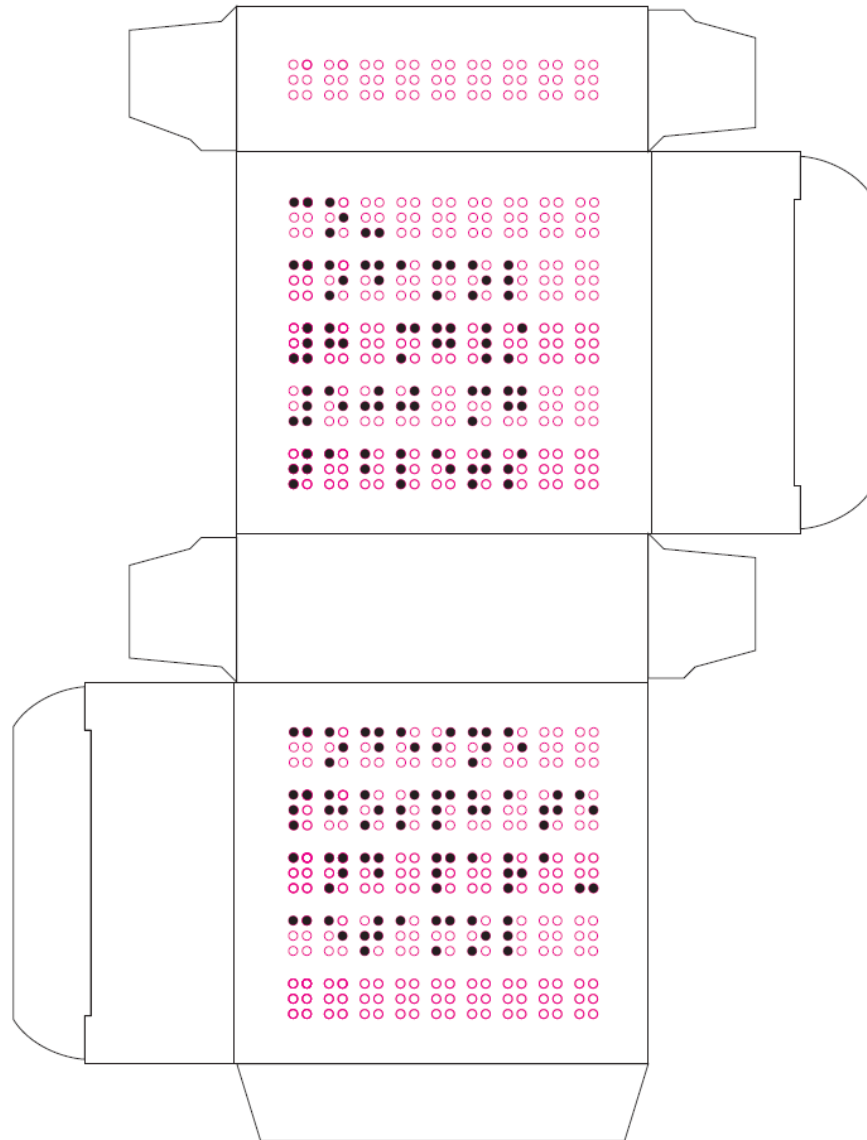
Carton for blisters



Carton showing Braille

Braille Reads:

co-
codamol
#8 mg/
#500 mg
tablets



Braille Reads:

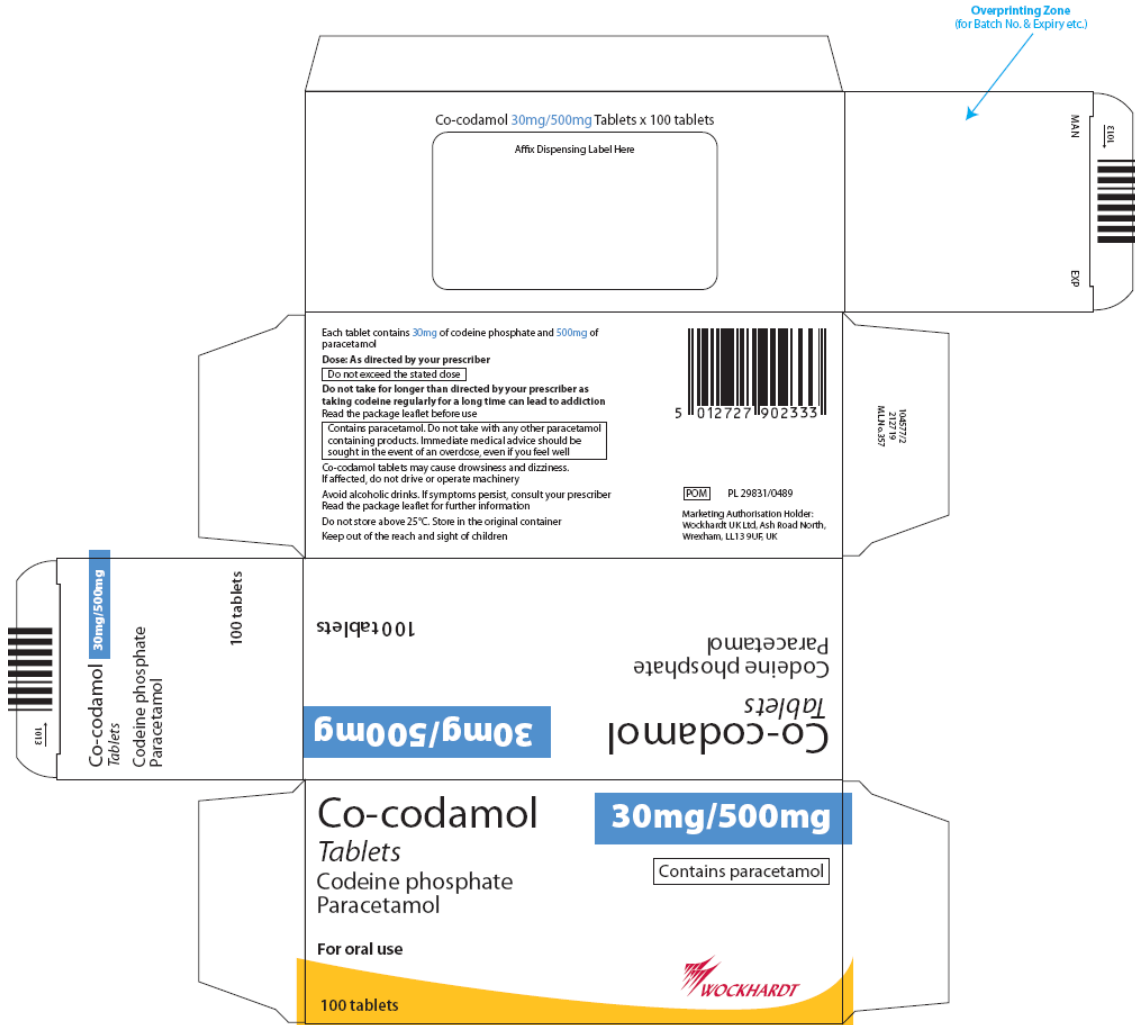
codeine
phosphate
and para-
cetamol

Blister foil

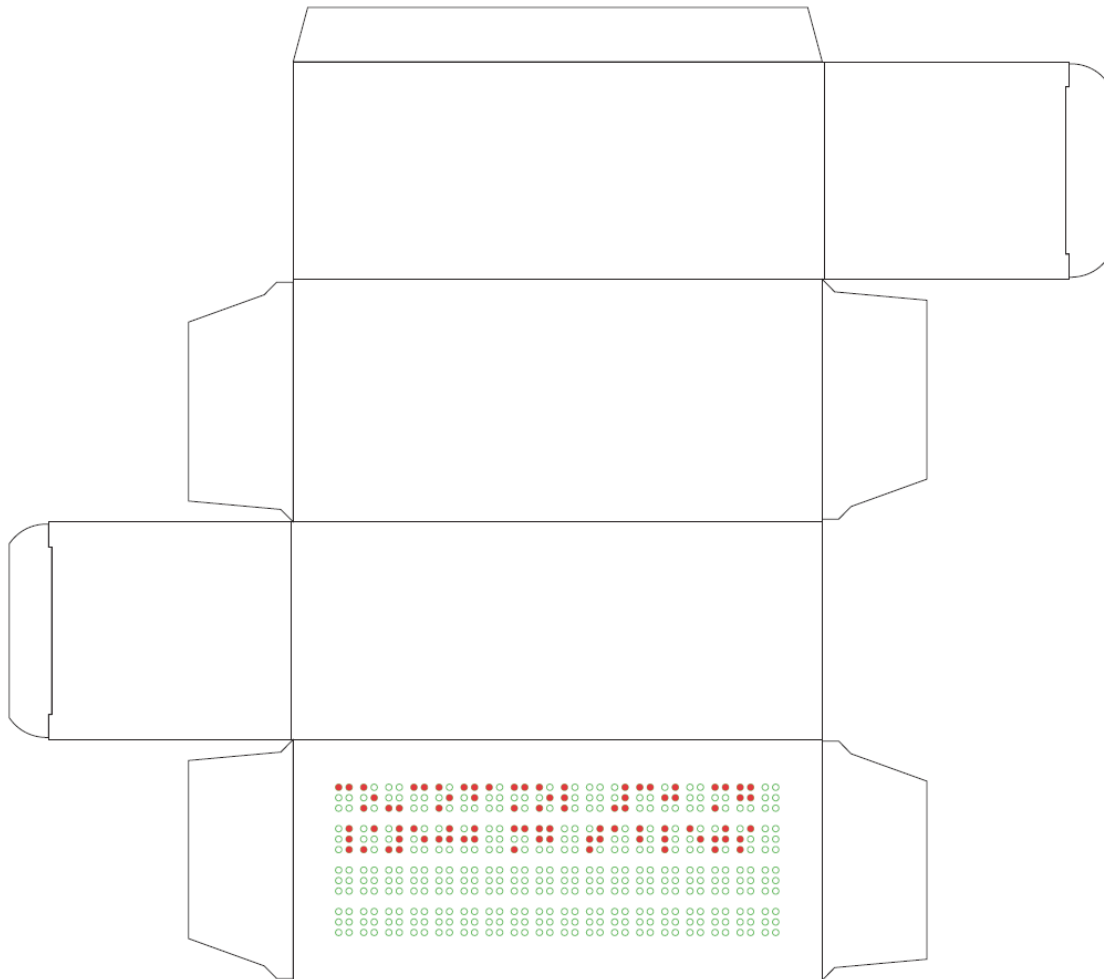


Co-Codamol 30mg/500mg Tablets - PL 29831/0489

Carton for blisters



Carton showing Braille



Braille Reads :

co-codamol #30 mg
/#500 mg tablets

Blister foil

