

Public Assessment Report

Co-Codamol 30/500 Effervescent Tablets

**Paracetamol 500mg
Codeine Phosphate Hemihydrate 30mg**

PL 15833/0025

Manx Pharma

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Lay Summary

The MHRA granted Manx Pharma a Marketing Authorisation (licence) for the medicinal product Co-Codamol 30/500 Effervescent Tablets (PI 15833/0025) on the 14th September 2007. The product is indicated in the relief of severe pain.

Co-Codamol 30/500 Effervescent Tablets contains the active ingredients paracetamol and codeine. Co-Codamol 30/500 Effervescent Tablets was considered the same as the original product Solpadol (Sanofi-Synthelabo Ltd, PL 11723/0072) based on the Quality profile, as the product is an oral solution a bioequivalence study was judged not to be necessary. It was judged that the benefits of taking Co-Codamol 30/500 Effervescent Tablets outweighed the risks, hence a Marketing Authorisation was granted.

Scientific Discussion

INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted marketing authorisations for the medicinal product Co-Codamol 30/500 Effervescent Tablets (Pl 15833/0025) on the 14th September 2007. Co-Codamol 30/500 Effervescent Tablets were shown to correspond to the current EU definition of a generic medicinal product because it complies with the criteria of having the same qualitative and quantitative composition in terms of active substance and the same dosage form to the reference product Solpadol (Sanofi-Synthelabo Ltd, PL 11723/0072).

Co-Codamol 30/500 Effervescent Tablets are indicated in the treatment of severe pain and are a prescription only medicine.

PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

1. Paracetamol

Nomenclature

INN: Paracetamol Ph Eur 500 mg

Chemical names: Paracetamol;

Acetaminophen

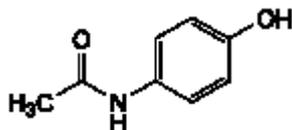
N-Acetyl-*p*-aminophenol

Paracetamololum

4'-hydroxyacetanilide

N-(4-hydroxyphenyl)acetanilide

Structure



A current certificate of suitability was provided for the source of the drug substance paracetamol. The certificate of suitability indicates that:

An appropriate specification has been provided.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Paracetamol is stored in appropriate packaging. The specifications and typical analytical test reports are provided and are satisfactory.

Batch analysis data are provided and comply with the proposed specification.

Satisfactory certificates of analysis have been provided for working standards used by the active substance manufacturer and finished product manufacturer during validation studies.

Appropriate stability data have been generated.

2 Codeine

Nomenclature

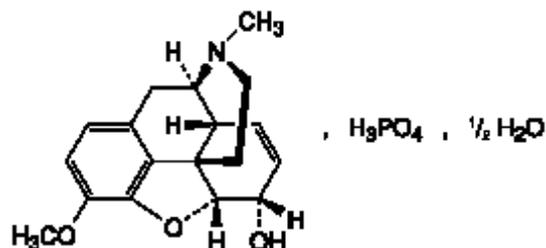
Chemical Names

Codeine Phosphate Hemihydrate;

Codeini Phosphas Hemihydricus

Methylmorphine phosphate hemihydrate

Structure



A current certificate of suitability was provided for the source of the drug substance codeine. The certificate of suitability indicates that:

An appropriate specification has been provided.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Codeine is stored in appropriate packaging. The specifications and typical analytical test reports are provided and are satisfactory.

Batch analysis data are provided and comply with the proposed specification.

Satisfactory certificates of analysis have been provided for working standards used by the active substance manufacturer and finished product manufacturer during validation studies.

Appropriate stability data have been generated.

DRUG PRODUCT

Composition of Drug Product

Paracetamol
 Codeine
 Sodium hydrogen carbonate
 Anhydrous sodium carbonate
 Anhydrous citric acid
 Sodium docusate
 Sorbitol (E420)
 Saccharin sodium
 Dimeticone
 Sodium benzoate
 Macrogol 6000
Natural grapefruit flavour
 Essential oil of grapefruit
 Concentrated lemon, orange, orange pulp and grapefruit juices
 Gentian infusion
 Cis-3-hexenol
 Ethyl 2-methylbutyrate
 Acacia gum
 Maltodextrin
 Butylated hydroxyanisole.

The pharmaceutical form was selected to enable good dissolution.

All excipients comply with the PhEur and certificates of analysis have been provided bar the Grapefruit flavour, satisfactory specifications were provided for this excipient which is compliance with EU directives. There are no excipients of animal or human origin, the magnesium stearate used is of plant origin. There were no novel excipients used and no overages.

Dissolution and impurity profiles

Dissolution of and impurity profiles for both strengths of drug product were found to be similar to those for the reference products.

Manufacture

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

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on batches of the drug product. The results are satisfactory.

Finished product specification

The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

Container Closure System

Primary packaging for the tablets is either Al/PE blister strips or round tubes of white PP closed with a PE stopper and containing a desiccant cartridge.

Stability

Satisfactory stability data was provided to support the shelf-life of two years under the following storage conditions

Protect from moisture

Protect from light

Store in the original packaging

Do not store above 25°C

ASSESSOR'S OVERALL CONCLUSIONS ON QUALITY AND ADVICE

A Marketing Authorisation was granted.

PRE-CLINICAL ASSESSMENT

No pre-clinical data were provided for this application and none were required.

MEDICAL ASSESSMENT

CLINICAL PHARMACOLOGY

Co-codamol is a compound analgesic preparation containing codeine phosphate and paracetamol.

Pharmacodynamics

Paracetamol has analgesic and antipyretic actions similar to those of aspirin with weak anti-inflammatory effects. Paracetamol is only a weak inhibitor of prostaglandin biosynthesis, although there is some evidence to suggest that it may be more effective against enzymes in the CNS than those in the periphery. This fact may partly account for its well documented ability to reduce fever and induce analgesia, effects that involve actions on the neural tissues.

Codeine is an analgesic with uses similar to those of morphine but has only mild sedative effects. The major effects of codeine are on the CNS and the bowel. However, its effects are remarkably diverse and include analgesia, drowsiness, changes in mood, respiratory depression and decreased gastrointestinal motility. The relief of pain is relatively selective, in that other sensory modalities (touch, vibration, vision, hearing etc.) are not obtunded.

Pharmacokinetics

Paracetamol is readily absorbed from the gastrointestinal tract with a peak plasma concentration occurring about 30 minutes to 2 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 1 to 4 hours. Plasma protein binding is negligible at the usual therapeutic concentrations but increases with increasing concentrations.

Codeine and its salts are absorbed from the gastro intestinal tract. Peak plasma codeine concentrations occur about an hour following ingestion. It is metabolised by O- & N-demethylation in the liver to morphine and norcodeine. Codeine and its metabolites are excreted almost entirely by the kidney, mainly as conjugates with glucuronic acid. The plasma half-life has been reported to be between 3 and 4 hours after oral administration.

Bioequivalence

The applicant submitted a detailed report justifying the absence of a bioequivalence study and this was found to be satisfactory.

EFFICACY

The applicant has submitted a report of an open multi-centre study which evaluated the acceptability of the present pharmaceutical preparation of paracetamol and codeine effervescent tablets in 30 adults (aged 24-82 years) in normal conditions of use. The subjects received 1 to 2 effervescent tablets of paracetamol (500mg) and codeine (30 mg), 1 to 3 times per day, for 3 to 5 days. The results concerning the

global acceptability of the tablets and the opinion of the taste of the solution are summarized tables 1 and 2 below:

Table 1: global acceptability of the tablets

Global acceptability	Frequency	Percent	95% CI
completely	13	43.3	[25.5-62.6]
rather yes	12	40.0	[22.7-59.4]
rather no	5	16.7	[5.7-34.7]

Table 2: Taste of the solution

Taste	Frequency	Percent	95% CI
good	7	23.3	[9.9-42.3]
quite good	14	46.7	[28.3-65.7]
not very good	7	23.3	[9.9-42.3]
bad	2	6.7	[0.8-22.1]

The global acceptability of the tablets was judged as good by more than 83% of the patients; the opinion of the taste of the solution was good for 71% of the subjects. Moreover, 70% of the patients were satisfied for the speed of the effervescent tablets dissolution.

The symptom evolution was judged as satisfactory for 20 subjects by investigators (66%) and for 21 subjects (77%) by the patients, without discrepancy between the investigators and the patients.

The applicant has also submitted copies of several publications with a summary review of the literature confirming the effectiveness of Co-codamol effervescent tablets.

SAFETY

In the study report mentioned above submitted with this application, ten patients (33%) experienced a total of 15 adverse events. All adverse events were well-known side effects qualified as probably (n=11) or possibly (n=4) related to the tested active ingredients: drowsiness: n=5, nausea: n=4, dry mouth: n=5, dizziness: n=1, constipation: n=1, abdominal pain: n=1. No serious adverse were reported.

The applicant has also provided several copies of publications with a safety review from the literature. No new safety issues have been detected

EXPERT REPORT

A satisfactory Clinical Expert Report has been submitted with appropriate brief CV.

SUMMARY OF PRODUCT CHARACTERISTICS

This is satisfactory.

PATIENT INFORMATION LEAFLET

This is satisfactory.

CONCLUSIONS

A Marketing Authorisation may be granted for this product.

Overall Conclusion and Risk/Benefit Analysis

Quality

The quality characteristics of Co-Codamol 30/500 Effervescent Tablets are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

Pre-Clinical

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

Efficacy

Efficacy has been demonstrated for this product. A satisfactory justification for the absence of a bioequivalence study was provided. No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory and consistent with that for

Risk/Benefit Analysis

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The risk benefit is, therefore, considered to be positive.

Steps Taken During Assessment

1	The MHRA received the application on 7 th October 2004.
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 20 th October 2004.
3	Following assessment of the application the MHRA requested further information from the applicant regarding the quality assessment on 6 th June 2005, 29 th March 2006, 22 nd May 2005 and on the medical assessment on 1 st July 2005.
4	The applicant provided further information in regard to the quality assessment on 9 th January 2006, 17 th May 2007 and 2 nd July 2007 and on the medical assessment on 9 th January 2006.
5	The application was determined on 14 th September 2007.

Steps Taken after Assessment

None

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Co-Codamol 30 mg/500 mg Effervescent Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each effervescent tablet contains:

Paracetamol 500.0mg

Codeine Phosphate Hemihydrate 30.0mg

Excipients: sorbitol (E420)

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Effervescent Tablet

White, bevelled, flat, round tablets with a scoreline on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of severe pain.

4.2 Posology and method of administration

Co-codamol 30 mg/500 mg Effervescent Tablets are given orally and should be dissolved in at least half a tumbler-full of water before taking.

Adults: One or two effervescent tablets every 4-6 hours, up to a maximum of 8 tablets in any 24 hour period.

Elderly: As for adults, however a reduced dose may be required. See warnings.

Children: Not recommended for children under 12 years of age.

4.3 Contraindications

Hypersensitivity to paracetamol or codeine which is rare, or hypersensitivity to any of the other constituents. Conditions where morphine and opioids are contraindicated e.g., acute asthma, respiratory depression, acute alcoholism, head injuries, raised intra-cranial pressure and following biliary tract surgery; monoamine oxidase inhibitor therapy, concurrent or within 14 days.

4.4 Special warnings and precautions for use

Each tablet contains 410mg sodium (17.83mEquivalents). This sodium content should be taken into account when prescribing for patients in whom sodium restriction is indicated.

Care should be observed in administering the product to any patient whose condition may be exacerbated by opioids, particularly the elderly, who may be sensitive to their central and gastro-intestinal effects, those on concurrent CNS

depressant drugs, those with prostatic hypertrophy and those with inflammatory or obstructive bowel disorders. Care should also be observed if prolonged therapy is contemplated.

Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazards of overdose are greater in those with alcoholic liver disease.

As this medicine contains sorbitol, patients with rare hereditary problems of fructose intolerance should not take this medicine.

Patients should be advised not to exceed the recommended dose and not take other paracetamol containing products concurrently.

4.5 Interaction with other medicinal products and other forms of interaction

Paracetamol may increase the elimination half-life of chloramphenicol. Oral contraceptives may increase its rate of clearance. The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by cholestyramine.

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.

The effects of CNS depressants (including alcohol) may be potentiated by codeine.

4.6 Pregnancy and lactation

There is inadequate evidence of the safety of codeine in human pregnancy, but there is epidemiological evidence for the safety of paracetamol. Both substances have been used for many years without apparent ill consequences and animal studies have not shown any hazard. Nonetheless careful consideration should be given before prescribing the products for pregnant patients. Opioid analgesics may depress neonatal respiration and cause withdrawal effects in neonates of dependent mothers.

Paracetamol is excreted in breast milk but not in a clinically significant amount.

4.7 Effects on ability to drive and use machines

Patients should be advised not to drive or operate machinery if affected by dizziness or sedation.

4.8 Undesirable effects

Codeine can produce typical opioid effects including constipation, nausea, vomiting, dizziness, light-headedness, confusion, drowsiness and urinary retention. The frequency and severity are determined by dosage, duration of treatment and individual sensitivity. Tolerance and dependence can occur, especially with prolonged high dosage of codeine.

Adverse effects of paracetamol are rare but hypersensitivity including skin rash may occur. There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis, but these were not necessarily causally related to paracetamol.

4.9 Overdose

Codeine:

The effects of Codeine overdose will be potentiated by simultaneous ingestion of alcohol and psychotropic drugs.

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 pupils may be pin-point in size; nausea and vomiting are common. Hypotension and tachycardia are possible but unlikely.

Management

Management 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 of codeine or a child more than 5mg/kg.

Give naloxone if coma or respiratory depression is present. Naloxone is a competitive antagonist and has a short half-life so large and repeated doses may be required in a seriously poisoned patient. Observe for at least 4 hours after ingestion, or 8 hours if a sustained release preparation has been taken.

Paracetamol:

Patients in whom oxidative liver enzymes have been induced, including alcoholics and those receiving barbiturates and patients who are chronically malnourished, may be particularly sensitive to the toxic effects of paracetamol in 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, coma 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 likely in adults who have taken 10g 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.

Management

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. Any patient who has ingested in excess of 150mg/kg or 12g within the previous hour should receive activated charcoal. Intravenous acetylcysteine is beneficial when given up to 24 hours after the ingestion of paracetamol, if more than 24 hours have elapsed since the overdose expert advice should be sought regarding appropriate management. Oral methionine may be given if acetylcysteine is not available as long as the overdose has been taken within the previous 10-12 hours and the patient is not vomiting. General supportive measures must be available.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Paracetamol is an analgesic which acts peripherally, probably by blocking impulse generation at the bradykinin sensitive chemo-receptors which evoke pain. Although it is a prostaglandin synthetase inhibitor, the synthetase system in the CNS rather than the prostaglandin synthetase inhibitor, the synthetase system in the CNS rather than the periphery appears to be more sensitive to it. This may explain paracetamol's lack of appreciable anti-inflammatory activity. Paracetamol exhibits antipyretic activity.

Codeine is a centrally acting analgesic which produces its effects by its action at opioid binding sites (m-receptors) within the CNS. It is a full agonist.

5.2 Pharmacokinetic properties

Following oral administration of two effervescent tablets (i.e., a dose of paracetamol 1000mg and codeine 60mg) the mean maximum plasma concentrations of paracetamol and codeine were 20.4mg/ml and 218.8ng/ml respectively. The mean times to maximum plasma concentrations were 0.34 hours of paracetamol and 0.42 hours for codeine phosphate.

The mean AUC for the 10 hours following administration was 50.0mg.ml⁻¹.h for paracetamol and 450.0 ng/ml⁻¹.h for codeine.

The bioavailabilities of paracetamol and codeine when given as the combination are similar to those when they are given separately.

5.3 Preclinical safety data

There are no preclinical data of relevance which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet

Sodium hydrogen carbonate

Anhydrous sodium carbonate

Anhydrous citric acid

Sodium docusate

Sorbitol (E420)

Saccharin sodium

Dimeticone

Sodium benzoate

Macrogol 6000

Natural grapefruit flavour

Essential oil of grapefruit

Concentrated lemon, orange, orange pulp and grapefruit juices

Gentian infusion

Cis-3-hexenol

Ethyl 2-methylbutyrate

Acacia gum

Maltodextrin

Butylated hydroxyanisole.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package in order to protect from moisture and light.

6.5 Nature and contents of container

Aluminium/polyethylene blister strips (30 micron aluminium strip with internal polyethylene coating) containing 4 or 10 tablets per strip in an outer cardboard carton. Pack sizes of 28, 30, 50, 56 and 100.

White polypropylene tubes sealed with a polyethylene stopper containing a desiccant cartridge in an outer cardboard carton. Tube sizes of 8, 10 and 16 tablets. Pack sizes of 10, 16, 32 and 96 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements. Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Manx Pharma
Taylor Group House
Wedgnoek Lane
Warwick
CV34 5YA
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 15833/0025

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

14/09/2007

10 DATE OF REVISION OF THE TEXT

14/09/2007

Leaflet and Labels

Co-codamol 30mg/500mg Effervescent Tablets

(Paracetamol and Codeine phosphate hemihydrate)

Information for the User

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- This medicine has been prescribed for you personally and you should not pass it on to 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 are Co-codamol 30mg/500mg Effervescent Tablets?
2. What are Co-codamol 30mg/500mg Effervescent Tablets used for?
3. Before you take Co-codamol 30mg/500mg Effervescent Tablets
4. How to take Co-codamol 30mg/500mg Effervescent Tablets
5. Possible side effects
6. Storing Co-codamol 30mg/500mg Effervescent Tablets

The name of this medicine is Co-codamol 30mg/500mg Effervescent Tablets.

1. What are Co-codamol 30mg/500mg Effervescent Tablets?

Each tablet contains 30mg of the active ingredient Codeine phosphate hemihydrate and 500 mg of the active ingredient Paracetamol. Other ingredients are included to aid the manufacture of the tablets and to make them soluble. These other ingredients are sodium hydrogen carbonate, anhydrous sodium carbonate, anhydrous citric acid, sodium docusate, sorbitol (E420), saccharin sodium, dimeticone, sodium benzoate, macrogol, natural grapefruit flavour which contains essential oil of grapefruit, concentrated lemon, orange, orange pulp and grapefruit juices, gellan infusion, cse-3-hexenol, ethyl 2-methylbutyrate, aocsa gum, maltodextrin and butylated hydroxyanisole.

The sodium content of each tablet is approximately 410 mg, which amounts to 3.28 g of sodium daily at a maximum dose of 8 effervescent tablets per day. To be taken into consideration by patients on sodium controlled diet.

Co-codamol 30mg/500mg Effervescent Tablets are white, bevelled, flat, round tablets with a score-line

on one side.

Co-codamol 30mg/500mg Effervescent Tablets are available in blister packs of 100.

The holder of the marketing authorisation for this medicine is Manx Pharma Limited, Taylor Group House, Wedgcock Lane, Wernick, CV34 5YA, United Kingdom. The effervescent tablets are made by CREAPHARM GANNAT SA, ZI Le Maboislet, 03800 Gannat, France.

2. What are Co-codamol 30mg/500mg Effervescent Tablets used for?

Co-codamol 30mg/500mg Effervescent Tablets are painkillers. They are recommended for the relief of severe pain.

3. Before you take Co-codamol 30mg/500mg Effervescent Tablets

Do not take Co-codamol 30mg/500mg Effervescent Tablets if you:

- are allergic to codeine, paracetamol or any other of the ingredients
- experience severe asthmatic attacks or severe breathing problems
- have recently had a head injury
- have had recent gall bladder surgery or a similar operation
- have raised pressure in the brain
- take monoamine oxidase inhibitors (used to treat depression) or you have taken them in the last 14 days
- are an alcoholic.

Co-codamol 30mg/500mg Effervescent Tablets should not be given to children under 12 years of age.

Take special care with Co-codamol 30mg/500mg Effervescent Tablets (check with your doctor) if you:

- are pregnant or breast feeding
- have severe kidney or liver problems
- have prostate problems (e.g. difficulty passing water)
- have a bowel disorder
- are elderly.

Pregnancy: Ask your doctor or pharmacist for advice before taking any medicine.

Breast feeding: Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines: Co-codamol 30mg/500mg Effervescent Tablets may

cause drowsiness or dizziness. If affected you should not drive or operate machinery.

Important information about some of the ingredients of Co-codamol 30mg/500mg Effervescent Tablets:

Each Co-codamol 30mg/500mg Effervescent Tablet contains 410mg of sodium which may be harmful to people on a low sodium diet.

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

Taking other medicines: Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, even those not prescribed.

Co-codamol 30mg/500mg Effervescent Tablets may change the effects of some medicines. Please check with your doctor or pharmacist if you are taking any of the following:

- chloramphenicol (an antibiotic)
 - drugs which make you sleepy, including alcohol
 - drugs used to thin the blood (e.g. warfarin)
- In addition the following medicines may alter the effectiveness of Co-codamol 30mg/500mg Effervescent Tablets. However, Co-codamol 30mg/500mg Effervescent Tablets should not affect their action:
- metoclopramide/domperidone (used to treat nausea and vomiting)
 - cholestyramine (used to treat high blood cholesterol (fat) levels)
 - oral contraceptives ('the pill')

4. How to take Co-codamol 30mg/500mg Effervescent Tablets

Always take Co-codamol 30mg/500mg Effervescent Tablets exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

The usual dose of Co-codamol 30mg/500mg Effervescent Tablets is 1 or 2 effervescent tablets not more often than every 4 to 6 hours. Do not take more than 8 effervescent tablets in any 24 hour period. If you are elderly, you may be prescribed a lower dose.

Dissolve the effervescent tablets in half a tumblerfull of water before taking.

Whilst taking Co-codamol 30mg/500mg Effervescent Tablets you should not take any other medicines which contain paracetamol. Do not exceed the recommended dose.

If you take more Co-codamol 30mg/500mg Tablets than you should: 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 or someone else has taken an overdose tell your doctor or go to the nearest hospital casualty department immediately.

If you forget to take Co-codamol 30mg/500mg Effervescent Tablets: Do not take a double dose to make up for forgotten individual doses.

5. Possible side effects

Like all medicines, Co-codamol 30mg/500mg Effervescent Tablets can have side effects.

If any of the following become troublesome you should tell your doctor: constipation, nausea (feeling sick), vomiting, dizziness, light-headedness, drowsiness, confusion and difficulty in passing water. If you suffer any unusual symptoms tell your doctor as soon as possible.

Rarely an allergic reaction can occur - this may involve a skin rash, swelling, itching or difficulty in breathing. If this occurs, tell your doctor immediately. There have been a few reports of low blood cell counts (platelets and white cells) associated with paracetamol-containing products but these were not necessarily due to paracetamol. Taking Co-codamol 30mg/500mg Effervescent Tablets for a long time may lead to tolerance and addiction. If you have taken regular daily doses of Co-codamol 30mg/500mg Effervescent Tablets over a long period of time, you should not increase the dosage or suddenly stop your treatment without discussing this with your doctor. If symptoms persist, consult your doctor.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

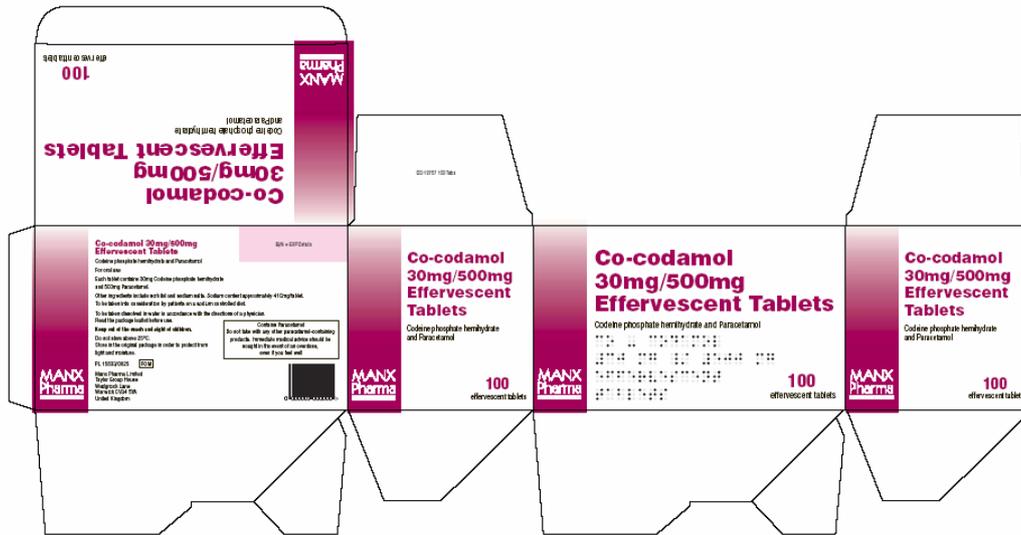
6. Storing Co-codamol 30mg/500mg Effervescent Tablets

Keep out of the reach and sight of children. Do not use after expiry date stated on the label. Store your medicine in the original package in order to protect from light and moisture. Do not store above 25°C.

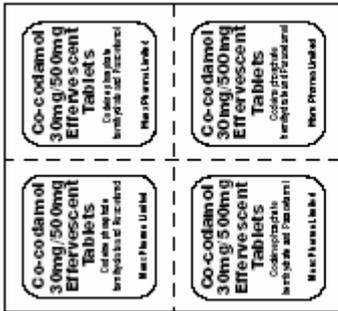
This leaflet was last approved in August 2007

**MANX
Pharma**

LEA 1706/PL



(RECTO side)



(VERSO side)

