SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Co-codamol 8 mg/500 mg Tablets
Paracetamol & Codeine 500 mg/8 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Paracetamol Ph Eur. 500mg and Codeine phosphate Ph Eur. 8mg

Excipients with known effect:
Methyl p-hydroxybenzoate_E218: 73.2%, Ethyl p-hydroxybenzoate_E214: 16.1% and Propyl p-hydroxybenzoate_E216: 10.7%.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Clean, white capsule shaped tablets embossed ‘ac 500/08’ on either side of a broken-line on one side. The other side is plain.

4.1 Therapeutic indications

Co-codamol/Paracetamol & Codeine 500 mg/8 mg Tablets is indicated in patients older than 12 years of age for the treatment of acute moderate pain which is not considered to be relieved by other analgesics such as paracetamol or ibuprofen (alone).

For, headache, migraine, toothache, period pains, rheumatic pains, including muscle pains and backache.

4.2 Posology and method of administration

Posology

Adults: Two tablets not more frequently than every four to six hours, when necessary, up to a maximum of 8 tablets in 24 hours.

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

The dose should not be repeated more frequently than every four hours for adults. Not more than 4 doses should be administered in any 24-hour period.

Paediatric Population:

Children aged 16 - 18 years: Take one to two tablets every six hours, when necessary, up to a maximum of 8 tablets in 24 hours.

Children aged 12 - 15 years: Take one tablet every six hours, when necessary, up to a maximum of 4 tablets in 24 hours.

The dose should not be repeated more frequently than every six hours for children over 12 years. Not more than 4 doses should be administered in any 24-hour period.

Duration of treatment

The duration of treatment should be limited to 3 days or as short as possible and if no effective pain relief is achieved the patients/carers should be advised to seek the views of a healthcare professional.

Children under 12 years

Not recommended for children under 12 years of age because of the risk of opioid toxicity due to the variable and unpredictable metabolism of codeine to morphine (see section 4.3 and 4.4).

Method of administration

Oral administration only

Treatment goals and discontinuation

Before initiating treatment with Co-codamol 8 mg/500 mg tablets, treatment duration and treatment goals should be agreed together with the patient, in accordance with pain management guidelines.

4.3 Contraindications

- In all paediatric patients (0-18 years of age) who undergo tonsillectomy and /or adenoidectomy for obstructive sleep apnoea syndrome due to an increased risk of developing serious and life-threatening adverse reactions (see section 4.4).

- In women during breast feeding (see section 4.6).

- In patients for whom it is known they are CYP2D6 ultra-rapid metabolisers.

a) Paracetamol:
Known hypersensitivity to Paracetamol or any of the constituents.

b) Codeine

- Known hypersensitivity to Codeine or other opioid analgesics.
- Moderate to severe renal failure.
- Moderate to severe liver disease.
- Respiratory depression and obstructive airways disease.
- Bronchial asthma attack or heart failure secondary to chronic lung disease.

- Raised intracranial pressure, head injuries and acute alcoholism.
- Diarrhoea associated with pseudomembranous colitis. Diarrhoea caused by
  poisoning until toxic material has been eliminated from

gastrointestinal tract.

- Not to be used in infants.

4.4 Special warnings and precautions for use

Care should be observed in administering the product to any patient, whose condition may be exacerbated by opioids, including the elderly, who may be sensitive to their central and gastro-intestinal effects, those on concurrent CNS depressant drugs, those with prostatic hypertrophy, hypothyroidism and those with inflammatory or obstructive bowel disorders, Addison's disease or myasthenia gravis. Care should also be observed if prolonged therapy is contemplated.

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment and sepsis or in patients with malnutrition and other sources of glutathione deficiency (e.g., chronic alcoholism) who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If HAGMA due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.

Opioids can cause sleep-related breathing disorders including central sleep apnoea (CSA) and sleep-related hypoxemia. Opioid use increases the risk of CSA in a dose-dependent fashion. In patients who present with CSA, consider decreasing the total opioid dosage.

<u>CYP2D6 metabolism</u>

Codeine is metabolised by the liver enzyme CYP2D6 into morphine, its active metabolite. If a patient has a deficiency or is completely lacking this enzyme an adequate analgesic effect will not be obtained. Estimates indicate that up to 7% of the caucasian population may have this deficiency. However, if the patient is an extensive or ultra-rapid metaboliser there is an increased risk of developing side effects of opioid toxicity even at commonly prescribed doses. These patients convert codeine into morphine rapidly resulting in higher-than-expected serum morphine levels.

General symptoms of opioid toxicity include confusion, somnolence, shallow breathing, small pupils, nausea, vomiting, constipation and lack of appetite. In severe cases this may include symptoms of circulatory and respiratory depression, which may be life-threatening and very rarely fatal. Estimates of prevalence of ultra-rapid metabolisers in different populations are summarized below:

Population	**Prevalence %**
African/Ethiopian	29%
African/American	3.4% to 6.5%
Asian	1.2% to 2%
Caucasian	3.6% to 6.5%
Greek	6.0%
Hungarian	1.9%

Northern European	1%-2%

Post-operative use in children

There have been reports in the published literature that codeine given post-operatively in children after tonsillectomy and /or adenoidectomy for obstructive sleep apnoea, led to rare, but life-threatening adverse events including death (see also section 4.3). All children received doses of codeine that were within the appropriate dose range; however, there was evidence that these children were either ultra-rapid or extensive metabolisers in their ability to metabolise codeine to morphine.

Children with compromised respiratory function

Codeine is not recommended for use in children in whom respiratory function might be compromised including neuromuscular disorders, severe cardiac or respiratory conditions, upper respiratory or lung infections, multiple trauma or extensive surgical procedures. These factors may worsen symptoms of morphine toxicity.

Tolerance and opioid use disorder (abuse and dependence)

Tolerance, physical and psychological dependence, and opioid use disorder (OUD) may develop upon repeated administration of opioids such as Co-codamol 8 mg/500 mg tablets. Repeated use of Co-codamol 8 mg/500 mg tablets can lead to OUD. A higher dose and longer duration of opioid treatment can increase the risk of developing OUD. Abuse or intentional misuse of Co-codamol 8 mg/500 mg tablets may result in overdose and/or death. The risk of developing OUD is increased in patients with a personal or a family history (parents or siblings) of substance use disorders (including alcohol use disorder), in current tobacco users or in patients with a personal history of other mental health disorders (e.g. major depression, anxiety and personality disorders).

The patient should be made aware of the risks and signs of OUD as set out in the package leaflet. If these signs occur, patients should contact their physician.

For patients who experience signs and symptoms of OUD, and/or exhibit drug seeking behaviours, review of concomitant opioids and psycho-active drugs (like benzodiazepines) and consultation with an addiction specialist may be required.

Hepatobiliary disorders

Codeine may cause dysfunction and spasm of the sphincter of Oddi, thus increasing the risk of biliary tract symptoms and pancreatitis. Therefore, codeine/paracetamol has to be administered with caution in patients with pancreatitis and diseases of the biliary tract.

Hyperalgesia

As with other opioids, in case of insufficient pain control in response to an increased dose of codeine, the possibility of opioid-induced hyperalgesia should be considered. A dose reduction or treatment review may be indicated.

The leaflet will state in:

Headlines Section (to be prominently displayed)

- This medicine can only be used for the short-term relief of moderate pain that is not relieved by other painkillers such as paracetamol or ibuprofen alone.
- 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 relief of moderate pain that is not relieved by other painkillers such as paracetamol or ibuprofen alone. For 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.

Take special care and tell your doctor if you:

Section 3: Dosage

- Do not take for more than 3 days. If the pain does not improve after 3 days, you must speak to your doctor or pharmacist for advice.
- This medicine contains codeine and 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

Reporting of side effects.
Some people may have side-effects when taking this medicine. If you get any side-effects talk to your doctor, pharmacist or other healthcare professional. This includes any possible side effects not listed in this leaflet. You can also report side-effects directly via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App store. By reporting side effects, you can help provide more information on the safety of this medicine.

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 this 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

The label will state:

Front of pack (to be prominently displayed) –

- Can cause addiction
- For three days use only

Back of pack (to be prominently displayed) –

- For the short-term treatment of acute moderate pain when other painkillers have not worked. Do not take less than four hours after taking another painkiller. For headache, migraine, toothache, period pains, rheumatic pains, including muscle pains and backache.
- If you need to take this medicine for more than three days you must 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.

a) Paracetamol:
Care is advised in the administration of Paracetamol to patients with severe renal or hepatic impairment. The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease. Patients should be advised not to take more medicine than the label tells you to. If you do not get better, talk to your doctor. Talk to a doctor at once if you take too much of this medicine, even if you feel well, because of the risk of serious delayed liver damage. Patients should be advised not to take other paracetamol-containing products concurrently.

If symptoms persist, patients should consult a doctor.

Keep medicines out of the sight and reach of children.

b) Codeine:
Codeine should be given with caution or in reduced doses to patients with hypertension, hypothyroidism, adrenocortical insufficiency, impaired kidney or liver function, prostate hypertrophy, shock, obstructive bowel disorders, acute abdominal conditions, recent gastrointestinal surgery, gallstones, myasthenia gravis, a history of cardiac arrhythmias or convulsions and in patients with a history of drug abuse or emotional instability.

Codeine may induce faecal impaction, producing incontinence, spurious diarrhoea, abdominal pain and rarely colonic obstruction. Elderly patients may metabolise or eliminate opioid analgesics more slowly than younger adults.

4.5 Interaction with other medicinal products and other forms of interaction

a) Paracetamol:
Paracetamol may delay the elimination of chloramphenicol.

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.

Drugs which induce hepatic microsomal enzymes, such as alcohol and barbiturates, may increase the hepatotoxicity of paracetamol, particularly after overdosage.

Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis due to pyroglutamic acidosis, especially in patients with risks factors (see section 4.4).

b) Codeine:

The depressant effects of Codeine are enhanced by depressants of the central nervous system such as alcohol, anaesthetics, hypnotics, sedatives, tricyclic antidepressants and phenothiazines. The hypotensive actions of diuretics and anti-hypertensive agents may be potentiated when used concurrently with opioid analgesics. Concurrent use of hydroxyzine with Codeine may result in increased analgesia as well as increased CNS depressant and hypotensive effects.

Concurrent use of Codeine with antidiarroheal and anti-peristaltic agents such as loperamide and kaolin may increase the risk of severe constipation. Concomitant use of antimuscarine or medications with antimuscarinic action may result in an increased risk of severe constipation which may lead to paralytic ileus and/or urinary retention.

The respiratory depressant effect caused by neuromuscular blocking agents may be addictive to the central respiratory depressant effects of opioid analgesics. CNS depression or excitation may occur if Codeine is given to patients receiving monoamine oxidase inhibitors, or within two weeks of stopping treatment with them. Quinidine can inhibit the analgesic effect of Codeine.

Codeine may delay the absorption of mexiletine and thus reduce the antiarrythmic effect of the latter. Codeine may antagonise the gastrointestinal effects of metoclopramide, cisapride and domperidone. Cimetidine inhibits the metabolism of opioid analgesics resulting in increased plasma concentrations.

Naloxone antagonises the analgesics, CNS and respiratory depressant effects of opioid analgesics.

Naltrexone also blocks the therapeutic affect of opioids.

Interference with laboratory tests: Opioid analgesics interfere with a number of laboratory tests including plasma amylase, lipase, bilirubin, alkaline phosphatase, lactate: dehydrogenate, alanine aminotransferase and aspartate aminotranserase. 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.

Concomitant use of Co-codamol 8 mg/500 mg Tablets with gabapentinoids (gabapentin and pregabalin) may result in respiratory depression, hypotension, profound sedation, coma or death (see section 4.4).

4.6 Fertility, Pregnancy and lactation

a) Paracetamol

Paracetamol crosses the placenta. There is no known hazard in normal dosage, but like all non-essential medications, Paracetamol should be avoided, especially during the first trimester, unless considered essential by the Physician. Paracetamol is excreted in breast milk, but there is no evidence that this is clinically significant.

b) Codeine:

Codeine crosses the placenta. There is no adequate evidence of safety in human pregnancy and a possible association with respiratory and cardiac malformations has been reported. Regular use during pregnancy can cause physical dependence in the foetus leading to withdrawal symptoms in the neonate. Use during pregnancy should be avoided if possible.

Use of opioid analgesia during labour may cause respiratory depression in the neonate, especially the premature neonate. These agents should not be given during the delivery of a premature baby.

Codeine should not be used during breastfeeding (see section 4.3).
At normal therapeutic doses codeine and its active metabolite 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 metabolite, morphine, may be present in breast milk and on very rare occasions may result in symptoms of opioid toxicity in the infant, which may be fatal.

4.7 Effects on ability to drive and use machines

i) Paracetamol:
None

ii) Codeine:
May cause drowsiness; if affected patients should be advised not to drive or operate machinery.

4.8 Undesirable effects

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

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

a) Paracetamol:

Adverse events of paracetamol from historical clinical trial data are both infrequent and from small patient exposure. Accordingly, events reported from extensive post-marketing experience at therapeutic/labelled dose and considered attributable are tabulated below by system class. Due to limited clinical trial data, the frequency of these adverse events is not known (cannot be estimated from available data), but post-marketing experience indicates that adverse reactions to paracetamol are rare and serious reactions are very rare.

Post marketing data

Body System	**Undesirable effect**
Blood and lymphatic system disorders	Thrombocytopenia Agranulocytosis

Immune system disorders	Anaphylaxis Cutaneous hypersensitivity reactions including skin rashes and angioedema
Respiratory, thoracic and mediastinal disorders	Bronchospasm*
Hepatobiliary disorders	Hepatic dysfunction
Skin and subcutaneous tissue disorders	Very rare cases of serious skin reactions have been reported.

* There have been cases of bronchospasm with paracetamol, but these are more likely in asthmatics sensitive to aspirin or other NSAIDs.

b) Codeine:

Less frequent effects are nausea, vomiting, sweating, facial flushing, dry mouth, blurred or double vision, dizziness, orthostatic hypotension, malaise, tiredness, headache, anorexia, vertigo, bradycardia, palpitations, respiratory depression, dyspnoea, allergic reactions (itch, skin rash, facial oedema) and difficulties in micturition (dysuria, increased frequency, decrease in amount). Side effects which occur rarely include convulsions, hallucinations, nightmares, uncontrolled muscle movements, muscle rigidity, mental depression and stomach cramps.

Drug dependence

Repeated use of Co-codamol 8 mg/500 mg tablets can lead to drug dependence, even at therapeutic doses. The risk of drug dependence may vary depending on a patient's individual risk factors, dosage, and duration of opioid treatment (see section 4.4).

Metabolism and nutrition disorders

High anion gap metabolic acidosis with frequency “Not known” (cannot be estimated from the available data)

Description of selected adverse reactions
High anion gap metabolic acidosis

Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.

Sphincter of Oddi dysfunction

Frequency ‘Not known’

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App store.

4.9 Overdose

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:

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

• regularly consumes ethanol in excess of recommended amounts, or

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

Symptoms

Symptoms of paracetamol overdosage 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.

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. 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 serious hepatic dysfunction beyond 24 hours from ingestion should be discussed with the NPIS or a liver unit.

Codeine

The effects in overdosage 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

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.

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 four hours after ingestion, or eight hours if a sustained release preparation has been taken.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anilides, Paracetamol combinations
ATC Code: N02B E51

a) Paracetamol

Paracetamol is an effective analgesic and antipyretic agent but has only weak anti-inflammatory properties. Its mechanism of action is not fully understood. It has been suggested that it may act predominantly by inhibiting prostaglandin synthesis in the CNS and to a lesser extent through a peripheral action by blocking pain-impulse generation. The peripheral action may also be due to inhabitation of prostaglandin synthesis or to inhibition of the synthesis or actions of other substances that sensitive pain receptors to mechanical or chemical stimulation.
Paracetamol probably produces an antipyretic action by a central effect on the hypothalamic heat-regulating centre to produce peripheral vasodilatation resulting in increased blood flow through the skin, sweating and heat loss. The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus. The drug has no effect on the cardiovascular and respiratory systems and unlike salicylates, it does not cause gastric irritation or bleeding.

b) Codeine

Codeine is a centrally acting weak analgesic. Codeine exerts its effect

through μ opioid receptors, although codeine has low affinity for these receptors, and its analgesic effect is due to its conversion to morphine. Codeine, particularly in combination with other analgesics such as paracetamol, has been shown to be effective in acute nociceptive pain. Opioid analgesics bind with sterospecific receptors at many sites within the CNS to alter processes affecting both the perception of pain and the emotional response to it. It has been hypothesised that alterations in release of various neurotransmitters from afferent nerve sensitive to painful stimuli may be partially responsible for the analgesic effect. Codeine also has antitussive properties, probably via a direct suppressant action on the cough to relax at the level of the brainstem. Codeine also acts locally on intestinal smooth muscle and perhaps centrally to reduce intestinal motility.

5.2 Pharmacokinetic properties

i) *Paracetamol*:
Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion. It is metabolised in the liver (90-95%) 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 usual therapeutic concentrations but increases with increasing concentrations.

A minor hydroxylated metabolite (N-acetyl-p-benzoquinoneimine) (which is usually produced in very small amounts by mixed function oxidases in the liver which is usually detoxified by conjugation with liver glutathione) may accumulate following Paracetamol overdosage and cause liver damage. The time to peak concentrations of Paracetamol is 0.5 to 2 hours, the time to peak effect 1 to 3 hours and the duration of action 3 to 4 hours.

ii) *Codeine*:
Codeine is absorbed from the gastrointestinal tract and peak plasma concentrations occur after one hour. Codeine is metabolised by O- and N-demethylation in the liver to morphine, norcodeine and other metabolites. Codeine and its metabolites are excreted almost entirely by the kidney, mainly as conjugates with glucuronic acid. Codeine is not extensively bound to plasma proteins. The plasma half life has been reported to be between 3 and 4 hours.

5.3 Preclinical safety data

Paracetamol & Codeine:
There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Potato Starch Ph Eur.
Pre-gelatinised Maize Starch Ph Eur.
Talc Ph Eur.
Povidone Ph Eur.
Stearic Acid Ph. Eur.
Magnesium stearate Ph Eur.
Methyl-p-hydroxybenzoate (E218)
Ethyl-p-hydroxybenzoate (E214)
Propyl-p-hydroxybenzoate (E216)

6.2 Incompatibilities

(Major)

i) Paracetamol:
Paracetamol may interfere with a number of test results: blood glucose, urate, bilirubin, lactate, dehydrogenase and transaminase concentrations, urine 5-hydroxyindoleacetic acid determination, prothrombin time and pancreatic function using benitromide.

ii) *Codeine*:
Has been reported to be incompatible with phenobarbitone sodium forming a codeine-phenobarbitone complex and with potassium iodide, forming crystals of codeine periodide. Acetylation of codeine phosphate by aspirin has occurred in solid dosage forms containing the two drugs, even at low moisture levels.

6.3 Shelf life

3 years from date of manufacture (36 months)

6.4 Special precautions for storage

Store below 25°C in a dry place.
Protect from light.

6.5 Nature and contents of container

Blister pack: 12, 16, 24, 30 and 32's as Pharmacy packs

Materials;
Aluminium foil Hard tempered 20 micron, colour gravure heat sealed lacquer conforming to BS8404.

PVC Film: Standard vacuum forming film 250 micron glossy-glossy finish, opaque white.

Paper strip packs: 12, 16, 24, 30 and 32 as Pharmacy packs

Materials: PAPER
Bleached Craft: 44 gsm, 9 micron.
20gsm PVDC.

Plastic bottles: 25, 30 and 32 as Pharmacy packs

Materials: Body: Polypropylene
Cap: High Density Polyethylene (HDPE)

6.6 Special precautions for disposal

None

7 MARKETING AUTHORISATION HOLDER

Aspar Pharmaceuticals Limited

Albany House

Acrewood Way,

St Albans,

AL4 0JY,

United Kingdom

8 MARKETING AUTHORISATION NUMBER

PL 08977/0012

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

27/02/2026