

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Paracetamol and Codeine 500 mg/ 12.8 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

<u>Active ingredient</u>	<u>mg/tablet</u>
Paracetamol	500.0
Codeine phosphate hemihydrate	12.8

Excipient with known effect: sodium metabisulphite (E223)
For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet
White, pillow shaped tablet, with the letter 'M' debossed on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Paracetamol and Codeine 500mg/12.8mg Tablets are 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, ibuprofen or aspirin (alone).

This medicine is recommended for the relief of migraine, headache, dental pain, period pain, backache, arthritic & rheumatic pain, strains & sprains and sciatica.

4.2 Posology and method of administration

Adults

Two tablets up to 4 times a day. This dose should not be repeated more frequently

than every 4 hours, and not more than 4 doses (8 tablets) should be taken in any 24 hour period. Do not take for more than 3 days without consulting a doctor.

Paediatric population:

Children aged 16 years to 18 years

One to Two tablets up to 4 times a day. This dose should not be repeated more frequently than every 6 hours, and not more than 4 doses (8 tablets) should be taken in any 24 hour period. Do not take for more than 3 days without consulting a doctor.

Children aged 12 years to 15 years

One tablet up to 4 times a day. This dose should not be repeated more frequently than every 6 hours and not more than 4 doses (4 tablets) should be taken in any in 24 hours period. Do not take for more than 3 days without consulting a doctor.

Children aged less than 12 years

Codeine should not be used in children below the age of 12 years because of the risk of opioid toxicity due to the variable and unpredictable metabolism of codeine to morphine (see sections 4.3 and 4.4).

Elderly

In the elderly, the rate and extent of paracetamol absorption is normal, but plasma half-life is longer, and paracetamol clearance is lower than in young adults. Elderly patients may require a reduced dose or frequency of dosing.

For oral administration only.

Treatment goals and discontinuation

Before initiating treatment with Paracetamol and Codeine 500 mg/ 12.8 mg Tablets, treatment duration and treatment goals, should be agreed together with the patient, in accordance with pain management guidelines.

Duration of treatment

Do not take for more than 3 days continuously without medical review. The duration of treatment should be 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.

4.3 Contraindications

Hypersensitivity to paracetamol, codeine, opioid analgesics or any of the other constituents.

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 breastfeeding (see section 4.6).

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

Do not give to children under 12 years of age (see section 4.4)

In patients with respiratory depression, chronic constipation or raised intracranial pressure.

4.4 Special warnings and precautions for use

Care is advised in the administration of paracetamol to patients with renal or hepatic impairment. The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease.

Do not exceed the stated dose.

Patients should be advised to consult their doctor if their headaches become persistent.

Patients should be advised not to take other paracetamol or codeine-containing products concurrently.

If symptoms persist consult your doctor. Keep out of the reach and sight of children.

Patients with inflammatory or obstructive bowel disorders or acute abdominal conditions should consult a doctor before using this product.

Patients with a history of cholecystectomy should consult a doctor before using this product as it may cause acute pancreatitis in some patients.

Not recommended for use in children in whom respiratory function might be compromised as this may worsen the symptoms of morphine toxicity.

The label will state:

Talk to a doctor at once if you take too much of this medicine, even if you feel well.

Do not take more medicine than the label tells you to.

If you do not get better, talk to your doctor.

Keep all medicines out of the sight and reach of children.

Do not take anything else containing paracetamol while taking this medicine.

Front of pack

- Can cause addiction
- Contains opioid
- For three days use only

Back of pack

- This medicine is for the short term treatment of acute moderate pain when other painkillers have not worked. Wait at least four hours after taking any other painkiller before you take this medicine.
- List of indications as agreed in 4.1 of the SPC
- If you need to take this medicine continuously for more than 3 days you must speak to your doctor or pharmacist for advice
- This medicine contains codeine which can cause addiction if you take it continuously for more than 3 days. If you take this medicine for headaches for more than 3 days it can make them worse

The leaflet (or combined label/leaflet) will state:

Talk to a doctor at once if you take too much of this medicine, even if you feel well.

This is because too much paracetamol can cause delayed, serious liver damage.

'Headlines' section (to be prominently displayed)

- This medicine can only be used for.....(indications)
- This medicine is 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 3 days at a time. If you need to take it for longer than 3 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 3 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 3 days it can make them worse

'What this medicine is for' section

- Succinct description of the indications from 4.1 of the SPC

'Before you take this medicine' section

- This medicine contains codeine which can cause addiction if you take it continuously for more than 3 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 3 days it can make them worse

'How to take this medicine' section

- Do not take for more than 3 days. Paracetamol and Codeine 500 mg/ 12.8 mg Tablets should be used for 3 days only to relieve symptoms. If no effective pain relief is achieved while taking the medicine, you should seek the advice of a healthcare professional
- This medicine contains codeine and can cause addiction if you take it continuously for more than 3 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

'Possible side effects' section

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. 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?' section

If you take the 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 amount
- When you stop taking the medicine you feel very unwell but you feel better if you start taking the medicine again

Codeine

Sleep-related breathing disorders

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.

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.

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.

CYP2D6 metabolism

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 summarised below:

<u>Population</u>	<u>Prevalence %</u>
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% to 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 Paracetamol and Codeine 500 mg/ 12.8 mg Tablets. Repeated use of Paracetamol and Codeine 500 mg/ 12.8 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 Paracetamol and Codeine 500 mg/ 12.8 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.

Codeine should be used with caution in patients with:

- head injuries
- prostatic hypertrophy
- hypotension
- hypothyroidism
- Addison's disease
- myasthenia gravis

Caution should be used in patients with conditions which may be exacerbated by opioids, including the elderly, who may be sensitive to their respiratory depressant effects.

As with other opioids, codeine should be used with caution in patients taking benzodiazepines or other central nervous system (CNS) depressants, including alcohol, and in patients taking monoamine oxidase inhibitors (MAOIs) or within 14 days of stopping MAOIs (see section 4.5).

Paracetamol

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 or 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 the underlying cause of HAGMA in patients with multiple risk factors.

Glutathione deficiency can also increase the risk of hepatotoxicity with paracetamol use, even at therapeutic doses. Caution is advised for patients at risk of glutathione depletion (see section 4.9).

Hepatotoxicity at therapeutic dose

Cases of paracetamol induced hepatotoxicity, including fatal cases, have been reported in patients taking paracetamol at doses within the therapeutic range. These cases were reported in patients with one or more risk factors for hepatotoxicity including low body weight (adults <50 kg), renal and hepatic impairment, chronic

alcoholism, concomitant intake of hepatotoxic drugs and in acute and chronic malnutrition (low reserves of hepatic glutathione). Paracetamol should be administered with caution to patients with these risk factors. Caution is also advised in patients on concomitant treatment with drugs that induce hepatic enzymes and in conditions which may predispose to glutathione deficiency (see section 4.9).

Dosage adjustment of paracetamol should be considered where there are risk factors for glutathione deficiency or hepatotoxicity and for those of low weight (for adults weighing less than 50kg).

Information about some of the ingredients in this medicine

This medicine contains sodium metabisulphite (E223) which may rarely cause severe hypersensitivity reactions and bronchospasm.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Paracetamol

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine.

The anticoagulation 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.

Alcohol and drugs which induce hepatic microsomal enzymes e.g. antiepileptic drugs, may increase the hepatotoxicity of paracetamol, particularly after overdose.

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 risk factors (see section 4.4).

Codeine

Codeine may antagonise the effects of metoclopramide and domperidone on gastrointestinal motility.

The effect of CNS depressants (including alcohol general anaesthetics and centrally acting muscle relaxants, hypnotics, sedatives including benzodiazepines, tricyclic antidepressants antipsychotics (including phenothiazines) may be potentiated by codeine and may cause additive CNS and respiratory depression and hypotensive effects.

The concomitant use of Paracetamol and Codeine 500 mg/ 12.8 mg Tablets with gabapentinoids (gabapentin and pregabalin) may result in respiratory depression, hypotension, profound sedation, coma or death.

Opioid analgesics should be given with care to patients receiving monoamine oxidase inhibitors. 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.

4.6 Fertility, pregnancy and lactation

Pregnancy

Use during pregnancy should be avoided, unless advised by a physician. This includes maternal use during labour because of the potential for respiratory depression in the neonate.

The safety of paracetamol-codeine during pregnancy has not been established relative to the possible adverse effects of fetal development.

Codeine

There is inadequate evidence of the safety of codeine in human pregnancy. A possible association with respiratory and cardiac malformation has been reported following first trimester exposure to codeine. Regular use during pregnancy may cause physical dependence in the fetus 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.

Paracetamol.

A large amount of data on pregnant women indicate neither malformative nor fetoneonatal toxicity.

Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, paracetamol can be used during pregnancy however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency.

Breast-feeding

Codeine

Codeine must not be used during breastfeeding (see section 4.3).

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 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.

Paracetamol

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

Fertility

There is no information relating to the effects of codeine/paracetamol on fertility.

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. This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in

regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:

- The medicine is likely to affect your ability to drive
- Do not drive until you know how the medicine affects you
- It is an offence to drive while under the influence of this medicine
- However, you would not be committing an offence (called a 'statutory defence') if:
 - The medicine has been prescribed to treat a medical or dental problem and
 - You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and
 - It was not affecting your ability to drive safely

4.8 Undesirable effects

Adverse events 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. The following convention has been utilised for the classification of undesirable effects:

Very common ($\geq 1/10$), common ($\geq 1/100$ to, $< 1/10$), uncommon ($\geq 1/1,000$, to $< 1/100$), rare ($\geq 1/10,000$ to, $< 1/1000$), very rare ($< 1/10,000$), not known (cannot be estimated from the available data).

Paracetamol

Body System	Undesirable effect	Frequency
Blood and lymphatic system disorders	Thrombocytopenia Agranulocytosis	Not known
Immune system disorders	Anaphylaxis Cutaneous hypersensitivity reactions including skin rashes and angioedema.	Not known
Skin and subcutaneous tissue disorders	Serious skin reactions	Very rare
Respiratory, thoracic and mediastinal disorders	Bronchospasm*	Not known
Hepatobiliary disorders	Hepatic dysfunction	Not known
Metabolism and nutrition disorders	High anion gap metabolic acidosis**	Not known

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

** 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.

Codeine

Adverse reactions identified during post-marketing use are listed below by MedDRA system organ class.

Body System	Undesirable effect	Frequency
Psychiatric disorders	Drug dependency* can occur after prolonged use of codeine at higher doses	Not known
Gastrointestinal disorder	Constipation, nausea, vomiting, dyspepsia, dry mouth, pancreatitis, acute pancreatitis in patients with a history of cholecystectomy	Not known
Hepatobiliary disorders	Sphincter of Oddi dysfunction	Not known
Nervous system disorder	Dizziness, worsening of headache with prolonged use, drowsiness	Not known
Skin and subcutaneous tissue disorder	Pruritus, sweating	Not known

* Repeated use of Paracetamol and Codeine 500 mg/ 12.8 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).

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 professional 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

Overuse of this product, defined as consumption of quantities in excess of the recommended dose, or consumption for a prolonged period of time may lead to physical or psychological dependency. Symptoms of restlessness and irritability may result when treatment is stopped.

Paracetamol

Liver damage is possible in patients who have taken more than recommended doses of paracetamol.

Ingestion of paracetamol at therapeutic doses may lead to liver damage if the patient has risk factors:-

Risk Factors:

If the patient

- Is on long-term treatment with drugs that induce liver enzymes.

Or

- Regularly consumes ethanol in excess of recommended amounts.

Or

- Is likely to be glutathione deplete e.g. diet (malnutrition, fasting, dietary restrictions, eating disorders and starvation), catabolic states (sepsis), cachexia and chronic illness (cystic fibrosis, liver disease, HIV, and muscular dystrophy).

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.

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) but results should not delay initiation of treatment beyond 8 hours after ingestion, as 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.

Codeine

The effects of codeine in 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 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: N02B E51.

Paracetamol is both a centrally and peripherally acting analgesic with antipyretic activity.

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

5.2 Pharmacokinetic properties

Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion. Paracetamol is metabolised in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates, with about 10% as glutathione conjugates. Less than 5% is excreted as unchanged paracetamol. The plasma half-life is around 2 hours. Plasma protein binding is negligible at usual therapeutic concentrations, although this is dose dependent.

Codeine phosphate is absorbed from the gastrointestinal tract and peak plasma concentrations occur after about one hour. Codeine is metabolised by O- and 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 is variable between 2 and 3.5 hours.

5.3 Preclinical safety data

Non-clinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential.

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Pregelatinised maize starch
Maize starch
Microcrystalline cellulose
Purified water
Dried maize starch
Magnesium stearate
Sodium metabisulphite

6.2 Incompatibilities

None stated.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in the original package.

6.5 Nature and contents of container

A child-resistant push through pack of white opaque 250 micron PVC/40gsm PVdC blisters heat sealed to 35gsm Glassine paper/9 micron soft temper aluminium foil.

Pack sizes: 6/8/10/12/16/18/20/24/25/30/32

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

The Boots Company PLC
1 Thane Road West
Nottingham NG2 3AA
England

8 MARKETING AUTHORISATION NUMBER(S)

PL 00014/0865

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

22/09/2025

10 DATE OF REVISION OF THE TEXT

27/03/2026