1. NAME OF THE MEDICINAL PRODUCT

Dispersible co-codaprin tablets 8/400mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 8mg Codeine Phosphate and 400mg Aspirin.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

White circular, flat bevelled-edge uncoated tablets impressed “C” and the identifying letters “AV” on either side of a central division line on one face.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

1) For the relief of headaches, toothache, migraine, neuralgia, sore throat and period pains.

2) For the symptomatic relief of influenza, feverishness, rheumatic pains, sciatica, lumbago, fibrositis, muscular aches and pains.

4.2 Posology and method of administration

Prior to starting treatment with opioids, a discussion should be held with patients to put in place a strategy for ending treatment with codeine phosphate in order to minimise the risk of addiction and drug withdrawal syndrome (see section 4.4).

Posology
Adults over 18 years:

1 to 2 tablets. This dose may be taken, up to 4 times a day at intervals of not less than 4 hours.

Paediatic population aged 16 years to 18 years:
The recommended dose for children 16 years and older is 1 to 2 tablets every 6 hours when necessary up to a maximum of 8 tablets in 24 hours.
Do not give to children aged under 16 years, unless specifically indicated (e.g. for Kawasaki's disease).
Co-codaprin is not recommended for use in children in this age group with compromised respiratory function for the systematic treatment of cold (see section 4.4).

Paediatric population 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).
Co-codaprin is contraindicated in children below the age of 12 years for the symptomatic treatment of cold see section 4.3).

Elderly: The normal adult dose is still appropriate in the elderly.

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

Method of Administration
To be dispersed in water for oral use.

4.3 Contraindications

Co-codaprin should not be taken by patients with the following conditions:

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Other ingredients in the product, other opioids, other salicylates or non-steroidal anti-inflammatory drugs (a patient may have developed anaphylaxis, angioedema, asthma, rhinitis or urticaria induced by aspirin or other NSAIDs).
- Nasal polyps associated with asthma (high risk of severe sensitivity reactions).
- Active peptic ulceration or a past history of peptic ulceration or dyspepsia.
- Haemophilia or other haemorrhagic disorder (including thrombocytopenia) as there is an increased risk of bleeding.
- Concurrent anticoagulant therapy should be avoided.
- Diarrhoea caused by poisoning until the toxic material has been eliminated, or diarrhoea associated with pseudomembraneous colitis
- respiratory depression
- obstructive airways disease
- third trimester of pregnancy
- In children below the age of 12 years for the symptomatic treatment of cold due to an increased risk of developing serious and life-threatening adverse reactions.

- children under 16 years old, unless specifically indicated (e.g. Kawasaki's disease).
- 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

4.4 Special warnings and precautions for use

Drug dependence, tolerance and potential for abuse

For all patients, prolonged use of this product may lead to drug dependence (addiction), even at therapeutic doses. The risks are increased in individuals with current or past history of substance misuse disorder (including alcohol misuse) or mental health disorder (e.g., major depression).

Additional support and monitoring may be necessary when prescribing for patients at risk of opioid misuse.

A comprehensive patient history should be taken to document concomitant medications, including over-the-counter medicines and medicines obtained on-line, and past and present medical and psychiatric conditions.

Patients may find that treatment is less effective with chronic use and express a need to increase the dose to obtain the same level of pain control as initially experienced. Patients may also supplement their treatment with additional pain relievers. These could be signs that the patient is developing tolerance. The risks of developing tolerance should be explained to the patient.

Overuse or misuse may result in overdose and/or death. It is important that patients only use medicines that are prescribed for them at the dose they have been prescribed and do not give this medicine to anyone else.

Patients should be closely monitored for signs of misuse, abuse, or addiction.

The clinical need for analgesic treatment should be reviewed regularly.

Drug withdrawal syndrome

Prior to starting treatment with any opioids, a discussion should be held with patients to put in place a withdrawal strategy for ending treatment with codeine phosphate.

Drug withdrawal syndrome may occur upon abrupt cessation of therapy or dose reduction. When a patient no longer requires therapy, it is advisable to taper the dose gradually to minimise symptoms of withdrawal. Tapering from a high dose may take weeks to months.

The opioid drug withdrawal syndrome is characterised by some or all of the following: restlessness, lacrimation, rhinorrhoea, yawning, perspiration, chills, myalgia, mydriasis and palpitations. Other symptoms may also develop including irritability, agitation, anxiety, hyperkinesia, tremor, weakness, insomnia, anorexia, abdominal cramps, nausea, vomiting, diarrhoea, increased blood pressure, increased respiratory rate or heart rate.

If women take this drug during pregnancy, there is a risk that their newborn infants will experience neonatal withdrawal syndrome.

Hyperalgesia
Hyperalgesia may be diagnosed if the patient on long-term opioid therapy presents with increased pain. This might be qualitatively and anatomically distinct from pain related to disease progression or to breakthrough pain resulting from development of opioid tolerance. Pain associated with hyperalgesia tends to be more diffuse than the pre-existing pain and less defined in quality. Symptoms of hyperalgesia may resolve with a reduction of opioid dose.

There is a possible association between aspirin and Reye's syndrome when given to children. Reye's syndrome is a very rare disease, which affects the brain and liver, and can be fatal. For this reason aspirin should not be given to children aged under 16 years unless specifically indicated (e.g. for Kawasaki's disease).

Risk from concomitant use of sedative medicines such as benzodiazepines or related drugs: Concomitant use of Co-codaprin and sedative medicines such as benzodiazepines or related drugs may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing with these sedative medicines should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe Co-codaprin concomitantly with sedative medicines, the lowest effective dose should be used, and the duration of treatment should be as short as possible.
The patients should be followed closely for signs and symptoms of respiratory depression and sedation. In this respect, it is strongly recommended to inform patients and their caregivers to be aware of these symptoms (see section 4.5).

Co-codaprin should be used with caution in patients with:

- allergic disease
- anaemia (may be exacerbated by GI blood loss)
- asthma (increased risk of bronchospastic sensitivity reactions)
- cardiac failure (conditions which predispose to fluid retention)
- dehydration
- glucose-6-phosphate dehydrogenase deficiency (aspirin rarely causes haemolytic anaemia)
- gout (serum urate may be increased)
- hepatic function impairment (avoid if severe)
- renal function impairment

- surgery. Aspirin should be discontinued several days before scheduled surgery (including dental extractions)
- systemic lupus erythematosus and other connective tissue disorders (hepatic and renal function may be impaired in these conditions)
- thyrotoxicosis (may be exacerbated by large doses of salicylates)
- hypothyroidism (risk of depression and prolonged CNS depression is increased)
- inflammatory bowel disease - risk of toxic megacolon
- Opioids should not be administered during an asthma attack
- convulsions - may be induced or exacerbated
- drug abuse, dependence (including alcoholism), enhanced instability, suicidal ideation or attempts - predisposed to drug abuse
- head injuries or conditions where intracranial pressure is raised
- gall bladder disease or gall stones - opioids may cause biliary contraction
- gastro-intestinal surgery - use with caution after recent GI surgery as opioids may alter GI motility
- prostatic hypertrophy or recent urinary tract surgery
- adrenocortical insufficiency, eg Addison's Disease
- hypotension and shock
- myasthenia gravis
- phaeochromocytoma - opioids may stimulate catecholamine release by inducing the release of endogenous histamine

CYP2D6 metabolism[4]

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.

Medicine Overuse Headache:
Overuse of analgesics to treat headaches may result in the development or aggravation of headache symptoms. Headache caused by overuse of analgesics (MOH - medication-overuse headache) should not be treated by increasing the dose. In such cases the use of analgesics should be discontinued gradually in consultation with a doctor.

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 label will state (To be displayed prominently on the 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 Interactions with other medicinal products and other forms of interaction

The following drug interactions should be considered when prescribing co-codaprin:
- Sedative medicines such as benzodiazepines or related drugs: The concomitant use of opioids with sedative medicines such as benzodiazepines or related drugs increases the risk of sedation, respiratory depression, coma and death because of additive CNS depressant effect. The dose and duration of concomitant use should be limited (see section 4.4).
- Alcohol - may enhance gastro-intestinal side effect of aspirin.

- Analgesics - avoid concomitant administration of other salicylates or other NSAIDs (including topical formulations) as increased risk of side effects.
- Alkalizers of urine (*eg* carbonic anhydrase inhibitors, antacids, citrates) - increased excretion of aspirin.
- Anticoagulants or platelet aggregation inhibitors - increased risk of bleeding.
- Antiepileptic drugs (*eg* phenytoin, sodium valproate) - increased effect.
- Corticosteroids - increased risk of gastro-intestinal bleeding or ulceration.
- Dipyridamole - increase in peak concentration.
- Diuretics - frusemide and acetazolamide (risk of toxic effects), spironolactone (antagonized diuretic action).
- Hypoglycaemics - enhanced activity.
- Methotrexate - increased toxicity.
- Metoclopramide and domperidone - increased rate of absorption of aspirin.
- Mifepristone - avoid aspirin until 8-12 days after mifepristone.
- Ototoxic medicine (*eg* vancomycin) - potential for ototoxicity increased. Hearing loss may occur and may progress to deafness even after discontinuation of the medication. Effects may be reversible but are usually permanent.
- Uricosurics (*eg* probenecid, sulfinpyrazone) - effects of uricosurics reduced.
- Laboratory investigations - aspirin may interfere with some laboratory tests such as urine 5-hydroxyindoleacetic acid determinations and copper sulfate urine sugar tests.
- CNS depressants - enhanced sedative and/or hypotensive effect with alcohol, anaesthetics, hypnotics, anxiolytics, antipsychotics, hydroxyzine, tricyclic antidepressants
- Antibacterials, *eg* ciprofloxacin, - avoid premedication with opioids as reduced plasma ciprofloxacin concentration
- MAOIs - use only with extreme caution
- Cyclizine
- Mexiletine - delayed absorption
- Metoclopramide and domperidone - antagonise GI effects
- Cisapride - possible antagonism of GI effects
- Dopaminergics (*eg* selegiline) - possible risk of hyperpyrexia and CNS toxicity. This risk is greater with pethidine but with other opioids the risk is uncertain
- Ulcer healing drugs - cimetidine inhibits the metabolism of opioid analgesics.
- Anticholinergics (*eg* atropine) - risk of severe constipation which may lead to paralytic illness, and /or urinary retention
- Antidiarrhoeal drugs (*eg* loperamide, kaolin) - increased risk of severe constipation
- Antihypertensive drugs (*eg* guanethidine, diuretics) - enhanced hypotensive effect
- Opioid antagonists (*eg* buprenorphine, naltrexone, naloxone)
- Neuromuscular blocking agents - additive respiratory depressant effects
- SSRIs – additive gastrointestinal irritation. Increased risk of gastrointestinal haemorrhage

- Metamizole may reduce the effect of acetylsalicylic acid on platelet aggregation, when taken concomitantly. Therefore, this combination should be used with caution in patients taking low dose aspirin for cardioprotection.

  Experimental data suggest that ibuprofen may inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1).

4.6 Fertility, pregnancy and lactation

Pregnancy
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiology studies suggest an increased risk of miscarriage and of cardiac malformation after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5%.

Studies in animals have shown that salicylates can cause birth defects including fissure of the spine and skull, facial clefts and malformations of the CNS, viscera and skeleton, pre and post implantation loss and embryo-foetal lethality. During the first and second trimester aspirin should not be given unless necessary.

Studies in animals have shown codeine to cause delayed ossification in mice and increased resorption in rats. Risk benefit must be considered because opioid analgesics cross the placenta.

Regular or high dose use of salicylates late in pregnancy may result in:
- constriction or premature closing of the foetal ductus arteriosus
- increased risk of still birth or neonatal death
- decreased birth weight
- prolonged labour
- complicated deliveries and increased risk of maternal or foetal haemorrhage
- possibly persistent pulmonary hypertension of newborn
- kernicterus in jaundiced neonates
- renal dysfunction, which may progress to renal failure with oligo-hydramniosis

Administration is contraindicated in the last trimester of pregnancy and should be avoided during the late stages of labour and during the delivery of a premature infant.

Regular use during pregnancy may cause drug dependence in the foetus, leading to withdrawal symptoms in the neonate.

If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

Administration during labour may depress respiration in the neonate and an antidote for the child should be readily available.

Breast-feeding
Administration to nursing women is not recommended as codeine may be secreted in breast milk and may cause respiratory depression in the infant.

Aspirin and codeine are distributed into breast milk.
Co-codaprin is contraindicated in women 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 metabolites, 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.

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.

The risk of infant exposure to aspirin and codeine through breast milk should be weighed against the benefits for both mother and baby.

Fertility
Aspirin should not be given to women wishing to become pregnant, since it is thought that prostaglandin synthesis inhibitors can reduce fertility. The effect on fertility is reversible.

4.7 Effects on ability to drive and use machines

Opioid analgesics can impair mental function and can cause blurred vision and dizziness. Patients should make sure they are not affected before driving or operating machinery.

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 effects of aspirin treatment which have been reported include:

- Allergic reaction - aspirin may precipitate bronchospasm and induce asthma attacks or other hypersensitivity reactions in susceptible individuals. Allergic reactions can include rhinitis, urticaria, angioneurotic oedema.Effects on GI system - gastrointestinal bleeding or ulceration which can occasionally be major (may develop bloody or black tarry stools, severe stomach pain and vomiting blood), gastrointestinal irritation (mild stomach pain, heartburn and nausea) and hepatitis (particularly in patients with SLE or connective tissue disease)
- Effects on blood - anaemia, haemolytic anaemia, hypoprothrombinaemia, thrombocytopenia, aplastic anaemia, pancytopenia
- Effects on sensory system - tinnitus
- Salicylism - mild chronic salicylate intoxication may occur after repeated administration of large doses, symptoms include dizziness, tinnitus, deafness, sweating, nausea, vomiting, headache and mental confusion, and may be controlled by reducing the dose

Adverse effects of opioid treatment which have been reported include:

- Allergic reactions (may be caused by histamine release) - including rash, urticaria, difficulty breathing, increased sweating, redness or flushed face
- effects on CNS - confusion, drowsiness, vertigo, dizziness, changes in mood, hallucinations, CNS excitation (restlessness/excitement), convulsions, mental depression, headache, trouble sleeping, or nightmares, raised intracranial pressure, tolerance or dependence
- effects on GI system - constipation, GI irritation, biliary spasm, nausea, vomiting, loss of appetite, dry mouth, paralytic ileius or toxic megacolon
- effects on CVS - bradycardia, palpitations, hypotension
- effects on sensory system -blurred or double vision
- effects on GU system - ureteral spasm, antidiuretic effect
- other effects - trembling, unusual tiredness or weakness, malaise, miosis, hypothermia
- effects of withdrawal - abrupt withdrawal precipitates a withdrawal syndrome. Symptoms may include tremor, insomnia, nausea, vomiting, sweating and

increase in heart rate, respiratory rate and blood pressure. NOTE - tolerance diminishes rapidly after withdrawal so a previously tolerated dose may prove fatal

- Psychiatric disorders - Drug dependence (see section 4.4)
- General disorders and administration site conditions - Drug withdrawal syndrome
- Prolonged use of a painkiller for headaches can make them worse.

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; website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Salicylates:
Symptoms of overdose depend upon plasma salicylate concentration.
Concentration greater than 300mgl^{-1} - tinnitus and vertigo
Concentration approx 400mgl^{-1} - hyperventilation
Concentration above 600mgl^{-1} - metabolic acidosis
Concentration range 700-900mgl^{-1} - coma, fever, hypothrombinaemia, cardiovascular collapse, renal failure.
Treatment - Aspirin may remain in the stomach for many hours after ingestion and should be removed by gastric lavage.
Plasma salicylate, pH and electrolytes should be measured. Fluid losses replaced and forced alkaline diuresis (eg with sodium bicarbonate) should be considered when the plasma salicylate concentration is greater than 500mgl^{-1} (3.6 mmol l^{-1}) in adults or 300mgl^{-1} (2.2 mmol l^{-1}) in children. In very severe cases of poisoning haemodialysis may be needed.

Opioids:
Codeine phosphate:
Patients should be informed of the signs and symptoms of overdose and to ensure that family and friends are also aware of these signs and to seek immediate medical help if they occur.
Symptoms: cold clammy skin, confusion, convulsions, severe drowsiness, tiredness, low blood pressure, pinpoint pupils of eyes, slow heart beat and respiratory rate coma.
Treatment: Treat respiratory depression or other life-threatening adverse effects first. Empty the stomach via gastric lavage or induction of emesis. The opioid antagonist naloxone (0.4-2mg subcutaneous) can be given and repeated at 2-3 minute intervals to a maximum of 10mg. Naloxone may also be given by intramuscular injection or intravenous infusion. The patient

should be monitored as the duration of opioid analgesic may exceed that of the antagonist.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other analgesics and antipyretics
ATC code: N02BA51

Aspirin is an anti-inflammatory analgesic and antipyretic.
Codeine is a centrally acting weak analgesic and is used in the treatment of cough and diarrhoea. 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.

Experimental data suggest that ibuprofen may inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400 mg was taken within 8 h before or within 30 min after immediate release acetylsalicylic acid dosing (81 mg), a decreased effect of ASA on the formation of thromboxane or platelet aggregation occurred. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use.

5.2 Pharmacokinetic properties

Absorption of non-ionised aspirin occurs in the stomach. Hydrolysis to salicylic acid occurs rapidly in the intestine and in the circulation. Aspirin is bound to plasma proteins and is rapidly distributed to all body tissues. It appears in breast milk and crosses the placenta. The rate of excretion of aspirin depends upon urinary pH, increasing as pH rises and being greatest at pH 7.5 and above. It is excreted as salicylic acid and as glucuronide conjugates and as salicyluric and gentisic acids.

Codeine and its salts are readily absorbed from the gastrointestinal tract. Ingestion of codeine phosphate produces peak plasma concentrations in about one hour. Codeine and its metabolites are excreted almost entirely by the kidney, mainly as conjugates with glucuronic acid. The plasma half-life is reported to be 3-4 hours after administration by mouth.

5.3 Preclinical safety data

There are no pre-clinical data additional to that already included in other sections of the SmPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Calcium carbonate
Cetrimide
Maize starch
Saccharin sodium
Silica
Citic acid (E330)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25^{o}C
Keep the bottle tightly closed.
Keep the bottle in the outer carton in order to protect from light.

6.5 Nature and contents of container

PE tablet container with a child-resistant PP closure. A silica gel container is included in each pack. Compliant with ISO8317.

Pack sizes:
POM: 100

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Accord-UK Ltd
(Trading style: Accord)
Whiddon Valley
Barnstaple
Devon
EX32 8NS
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 00142/0077R.

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10th August 1981
Date of last Renewal: 01st April 2009

10 DATE OF REVISION OF THE TEXT

01/05/2020