SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Codeïnefosfaat Schmid Pharma 10 mg, tabletten
Codeïnefosfaat Schmid Pharma 15 mg, tabletten
Codeïnefosfaat Schmid Pharma 20 mg, tabletten
Codeïnefosfaat Schmid Pharma 30 mg, tabletten

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

{[Nationally completed name] 10 mg tablets}
Each tablet contains 10 mg codeine phosphate hemihydrate equivalent to 7.37 mg of codeine.

{[Nationally completed name] 15 mg tablets}
Each tablet contains 15 mg codeine phosphate hemihydrate equivalent to 11.05 mg of codeine.

{[Nationally completed name] 20 mg tablets}
Each tablet contains 20 mg codeine phosphate hemihydrate equivalent to 14.73 mg of codeine.

{[Nationally completed name] 30 mg tablets}
Each tablet contains 30 mg codeine phosphate hemihydrate equivalent to 22.10 mg of codeine.

Excipient(s) with known effect

{[Nationally completed name] 10 mg tablets}
Each tablet contains 29.45 mg lactose (as monohydrate).

{[Nationally completed name] 15 mg tablets}
Each tablet contains 44.18 mg lactose (as monohydrate).

{[Nationally completed name] 20 mg tablets}
Each tablet contains 58.90 mg lactose (as monohydrate).

{[Nationally completed name] 30 mg tablets}
Each tablet contains 88.35 mg lactose (as monohydrate).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

{[Nationally completed name] 10 mg tablets}
White or almost white, biconvex tablet of round shape (diameter 6 mm), debossed 'COD' over '10' on one side.

{[Nationally completed name] 15 mg tablets}
White or almost white, biconvex tablet of round shape (diameter 7 mm), debossed 'COD' over '15' on one side.

{[Nationally completed name] 20 mg tablets}
White or almost white, biconvex tablet of round shape (diameter 8 mm), debossed 'COD' over '20' on one side.

{[Nationally completed name] 30 mg tablets}
White or almost white, biconvex tablet of round shape (diameter 9 mm), debossed 'COD' over '30' on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Codeine is indicated for:
- treatment of acute moderate pain that cannot be relieved by other pain medication such as (only) paracetamol or ibuprofen in adults and children older than 12 years of age
- symptomatic relief of diarrhoea after an insufficient clinical response to loperamide in adults
- symptomatic relief of a non-productive cough in adults and children older than 12 years of age

4.2 Posology and method of administration

Posology

Analgesia
Codeine must be used as briefly as possible in the lowest effective dose. This dose may be taken up to 4 times daily, but with an interval of no less than 6 hours. The maximum daily dosage of codeine must not exceed 240 mg.

Duration of treatment must be limited to 3 days and if the pain is not effectively relieved, patients/caretakers should be advised to consult a physician.

The analgesic effect is not really potentiated by an increase of the dose until a higher level than recommended below.

Adults
Recommended dose for adults is 30-60 mg every 6 hours up to a maximum dose of 240 mg per day.

Paediatric population
Children from 12 to 18 years of age:
Recommended dose for children from 12 years of age and older is 30-60 mg every 6 hours up to a maximum dose of 240 mg per day. The dose must be based on body weight (0.5-1 mg/kg).

Children younger than 12 years of age:
Codeine should not be used for the treatment of acute moderate pain in children younger than 12 years of age due to the risk of opioid toxicity as a result of the variable and unpredictable conversion of codeine into morphine (see sections 4.3 and 4.4).

Diarrhoea
Adults
Recommended dose for adults is 15-60 mg three to four times daily.

Paediatric population
Children from 12 to 18 years of age:
For the diarrhoea indication, the safety and efficacy of codeine in paediatric patients aged 12 to 18 years have not been established. No recommendation on a posology can be made..

Children younger than 12 years of age:
Codeine should not be used for the treatment of diarrhoea in children younger than 12 years of age due to the risk of opioid toxicity as a result of the variable and unpredictable conversion of codeine into morphine (see sections 4.3 and 4.4).

Coughing
Adults
Recommended dose for adults is 15-30 mg three to four times daily.

Paediatric population
Children from 12 to 18 years of age:
Recommended dose is 15-30 mg three to four times daily.
Codeine is not recommended for symptomatic treatment of cough in children from 12 to 18 years of age with a reduced respiratory function (see section 4.4).

Children younger than 12 years of age:
Codeine is contra-indicated in children under 12 years of age for symptomatic treatment of coughing (see section 4.3).

Special populations
Renal impairment
Renal impairment results in a delayed elimination of codeine and the active metabolite morphine, which may lead to toxicity, even with a therapeutic dose.

Hepatic impairment
There are no known data available for the use of codeine in patients with mild to moderate hepatic impairment. Caution is needed in these patients to determine the correct therapeutic dose.

Method of administration
For oral use.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Reduced respiration
- Obstructive pulmonary disorders, e.g. emphysema
- Partially controlled or uncontrolled asthma
- Hepatic impairment
- Acute alcohol toxicity
- Codeine is also contra-indicated in conditions in which inhibition of the peristalsis must be avoided, when there is a risk of paralytic ileus, with development of abdominal distension, or in conditions with acute diarrhoea such as with acute ulcerative colitis or colitis in connection with antibiotics (e.g. pseudomembranous colitis) or diarrhoea caused by poisoning.
- Use must be avoided in patients with an increased intracranial pressure or head injury (also for the risk of respiratory depression and increased intracranial pressure, which may affect the pupil reaction and other reactions important to the neurological examination).
- Codeine must not be given to comatose patients.
- Symptomatic treatment of coughing in children under the age of 12 years due to an increased risk of developing serious and life-threatening adverse reactions.
- Children (0 - 18 years of age) who undergo tonsillectomy or adenoidectomy surgery for obstructive sleep apnoea syndrome due to an increased risk of developing serious and life-threatening adverse reactions (see section 4.4).
- Breast-feeding (see section 4.6)
- Patients who are ultra-rapid metabolisers of CYP2D6
- Concomitant use of MAO inhibitors. There is a possible risk of a stimulating or suppressing effect on the central nervous system (see section 4.5).

Codeine may be administered 2 weeks after the discontinuation of MAO inhibitors.

4.4 Special warnings and precautions for use

Codeine should be applied with caution for the following conditions:

- Convulsions, may be caused or potentiated
- Toxic psychosis
- Shock
- Hypotension and shock
- Cardiovascular disorders
  The vagolytic effect of codeine should be taken into account in patients with a history of supraventricular tachycardia.
- Asthma or a history of reduced respiratory function
- Inflammatory intestinal diseases
  Codeine reduces the peristalsis, increases the tension and segmentation in the intestines and can increase the pressure in the colon and should therefore be used with caution in case of diverticulitis, acute colitis, diarrhoea caused by pseudomembranous colitis or after intestinal surgery.
- Gastro-intestinal surgery
  Use with caution after recent gastro-intestinal surgeries; opioids can change the gastro-intestinal motility.
- Acute abdominal disorders
- The use of codeine can cause obstipation. Therefore the concomitant administration of a laxative is recommended unless the codeine phosphate is used for the treatment of diarrhoea.
- Hepatic impairment
  Avoid the use of codeine if the hepatic impairment is serious. Codeine can cause coma.
- Gall bladder disease or gall stones
  Opioids can cause biliary tract contraction. Avoid use with biliary tract disorders.
- Renal impairment
- Urinary tract surgery
  After recent surgery patients are more susceptible to urine retention directly caused by spasms of the urethral sphincter and by obstipation caused by codeine.
- Prostate hypertrophy
- Stricture of the urethra
- Pheochromocytoma
  Opioids can stimulate catecholamine release by inducing the release of endogenic histamine.
- Adrenocortical insufficiency, e.g. Addison's disease

- Myasthenia gravis
- Hypothyroidism and untreated myxoedema
- Drug abuse or drug dependency (including alcoholism)
- Pregnancy (see section 4.6)
- Older patients
  They may metabolise and eliminate opioids slower than younger patients (see section 4.2).
- Prolonged use
  Benefits and disadvantages should be regularly determined by the prescribing physician.

CYP2D6 metabolism
Codeine is metabolised into morphine, its active metabolite, by the liver enzyme CYP2D6. If a patient has a deficiency of this enzyme or if this enzyme is missing entirely, an adequate therapeutic effect will not be reached. Estimates show that up to 7% of the Caucasian population can have this deficiency. However, if the patient is an extensive or ultra-rapid metaboliser, there is an increased risk of developing symptoms of opioid toxicity, even with doses that are usually prescribed. These patients rapidly convert the codeine into morphine, which leads to higher than expected morphine levels in the serum.
General symptoms of opioid toxicity consist of confusion, somnolence, superficial respiration, pinpoint pupils, nausea, vomiting, constipation and lack of appetite. In severe cases it can include symptoms of circulatory and respiratory depression, which can be life-threatening and fatal in very rare cases.

Estimates of the prevalence of ultra-rapid metabolisers and the various populations are summarized below:

Population group	**Prevalence %**
African/Ethiopian	29%
African-American	3.4% to 6.5%
Asian	1.2% to 2%
White (Caucasian)	3.6% to 6.5%
Greek	6%
Hungarian	1.9%
Northern European	1% to 2%

Risk of concomitant use with sedatives, such as benzodiazepines or related medicinal products
Concomitant use of codeine and sedatives (such as benzodiazepines or related medicinal products) can cause sedation, respiratory depression, coma and death. Therefore concomitant prescribing of these sedatives should be limited to patients for whom no alternative treatment options are

possible. If a concomitant use of codeine and sedatives cannot be avoided, the lowest possible effective dose should be used and duration of treatment should be as brief as possible.

Patients should be carefully monitored for signs and symptoms of respiratory depression and sedation. It is strongly recommended to inform patients as well as their care takers about these symptoms (see section 4.5).

Paediatric population

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 a reduced respiratory function
Codeine is not recommended for use in children with a reduced respiratory function, neuromuscular disorders, severe cardiac or respiratory disorders, infections of the upper respiratory tract or lung infections, multiple traumas or major surgical procedures. These factors can potentiate symptoms of morphine toxicity.

Lactose
{[Nationally completed name]} contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucosegalactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Contra-indicated combinations (see section 4.3)

MAO inhibitors (and medicinal products with a MAO inhibiting effect, such as linezolid, moclobemide and selegiline), due to the possible risk of a stimulating or suppressing effect on the central nervous system. Avoid concomitant use of MAO inhibitors. Codeine may only be used two weeks after use of MAO inhibitors has been discontinued.

Combinations for which caution is needed

Respiratory related
- Alcohol - increased sedative and hypotensive effect, increased risk of respiratory depression
- Sedative antihistamines - increased sedative and hypotensive effect, increased risk of respiratory depression
- Hypnotic agents, anxiolytic agents and other narcotic analgesics - increased sedative effect, increased risk of respiratory depression

Gastro-intestinal related

- Anticholinergic agents (for example atropine) - risk of severe obstipation that can lead to paralytic ileus and/or urinary retention
- Metoclopramide and domperidone - antagonistic effect on gastro-intestinal activity
- Medicinal products to treat diarrhoea (for example loperamide,kaolin) - increased risk of severe obstipation

CNS (central nervous system) related

- Anaesthetic agents - increased sedative and hypotensive effect
- Tricyclic antidepressants - increased sedative effect
- Antipsychotic agents - increased sedative and hypotensive effect
- Sedatives such as benzodiazepines and related products:
  Concomitant use of opioids and sedatives, such as benzodiazepines or related products, increases the risk of sedation, respiratory depression, coma and death due to the additive inhibiting CNS effect. Dose and duration of concomitant treatment should be limited (see section 4.4).
- Opioid receptor antagonists (for example buprenorphine, naltrexone, naloxone) - can cause withdrawal symptoms
- Quinidine - reduced analgesic effect
- Antihypertensive agents - increased hypotensive effect
- Sodium oxybate - concomitant administration of codeine and sodium oxybate can cause increased suppression of the central nervous system and/or respiratory depression and/or hypotension

Pharmacokinetic interactions

- Ritonavir - may increase plasma level of opioid analgesic agents such as codeine
- Mexiletine - delayed absorption of mexiletine
- Cimetidine - inhibits the metabolism of opioid analgesic agents which may cause an increased plasma concentration of codeine

Interference with laboratory tests

- Opioids may interfere with the gastric emptying examination due to a delay in the gastric emptying and it may interfere with the liver-bile imaging with technetium ^{99m}Tc disofenine. Treatment with opioids can possibly cause constriction of the sphincter of Oddi and increase pressure in the biliary tract.

4.6 Fertility, pregnancy and lactation

Pregnancy
A moderate amount of data on pregnant women do not provide evidence for an increased risk of major malformations with exposure during pregnancy.
Opioids cross the placenta. Long-term use of opiates can cause physical dependency in the foetus and withdrawal symptoms in the neonate. Animal studies did not show any direct harmful effects with respect to reproductive toxicity. Codeine should only be used during pregnancy if strictly necessary.

Administration of codeine just before delivery can cause respiratory depression in the neonate and delayed gastric emptying and a risk of pneumonia in the mother during delivery. Administration of codeine should be avoided during the late stages of delivery and during delivery of a premature neonate.

Breast-feeding
Codeine is contra-indicated in women during breast-feeding (see section 4.3)
With normal therapeutic doses, codeine and the active metabolite can be present in very low doses in breast milk. It is unlikely to have an undesirable effect on the infant. However, if the patient is a rapid metaboliser of CYP2D6, higher levels of the active metabolite morphine may be present in breast milk which in rare cases may result in symptoms of opioid poisoning in the baby. This might be fatal.
If symptoms of opioid poisoning develop in the mother or the baby, all codeine containing products must be stopped and non-opioid pain medication should be prescribed. Prescription of naloxone should be considered to combat the effects in severe cases.

Fertility
In animal studies in rabbits, sperm quality and effect on male reproductive organs were observed upon chronic dosing (see Section 5.3). There is no data on the effect of codeine on human fertility.

4.7 Effects on ability to drive and use machines

Codeine can negatively affect mental and physical ability needed to perform potentially dangerous tasks such as driving or using machines. Undesirable effects such as confusion, somnolence, dizziness, hallucinations, blurred or double vision or convulsions can occur. The effect of alcohol is potentiated by codeine.
Patients should be advised not to drive, use machines or participate in activities in which they could harm themselves or others.

4.8 Undesirable effects

Adverse Drug Reactions (ADRs) which can occur during codeine therapy are tabulated below.

All ADRs are listed by system organ class and frequency; very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000) and not known (cannot be estimated from the available data).

System Organ Class	**ADR**
Immune system disorders	
Rare	anaphylactic reaction
Not known	symptoms that may be the result of histamine release, e.g. skin rash, urticaria, pruritus, dyspnoea, hyperhidrosis, erythema or excessive blushing, oedema
Psychiatric disorders	
Not known	mood changes (dysphoria, euphoric mood), depression, hallucination, restlessness, agitation, nightmares, confusion, disorientation, codeine tolerance or dependency, reduced libido
Nervous system disorders	
Not known	confusion, somnolence, malaise, vertigo, dizziness, seizure, headache, increased intracranial pressure, hypothermia
Eye disorders	
Not known	miosis, blurred vision or diplopia
Cardiac disorders	
Not known	bradycardia, palpitations, tachycardia.
Vascular disorders	
Not known	syncope, hypotension, orthostatic hypotension
Respiratory, thoracic and mediastinal disorders	
Not known	suppressed respiration (using higher doses)
Gastrointestinal disorders	
Rare	gastrointestinal hypermotility, megacolon (with chronic ulcerative colitis)
Not known	constipation (also with long-term use), abdominal pain, pancreatitis, nausea, vomiting, dry mouth
Hepatobiliary disorders	
Not known	biliary colic
Musculoskeletal and connective tissue disorders	
Not known	muscle rigidity
Renal and urinary disorders	
Not known	urethral spasm, anti-diuretic effect, urinary retention
Reproductive system and breast disorders	
Not known	erectile dysfunction
Nutrition and metabolism disorders	
Not known	reduced appetite.

General disorders and administration site conditions	
Not known	asthenia, fatigue

Withdrawal symptoms

Abrupt discontinuation may result in withdrawal symptoms such as tremor, sleeplessness, restlessness, irritability, anxiety, depression, anorexia, nausea, vomiting, diarrhoea, sweating, tearing, severe rhinitis, yawning, piloerection, pupil dilation, weakness, fever, muscle cramp, dehydration, increased heart rate, increased respiration and elevated blood pressure. Note that tolerance reduces rapidly after discontinuation of codeine, so a previously tolerated dose may be fatal.
It is known that regular and long-term use of codeine causes addiction and tolerance. Restlessness and irritability can occur after discontinuation. Long-term use of any pain medication for headache may worsen the headache.

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 national reporting system listed in Appendix V.

4.9 Overdose

Effects of an overdose are potentiated by the concomitant use of alcohol or psychotropic products. The lethal dose in adults is estimated at 0.5-1.0 grams of codeine (equivalent to 7-14 mg/kg of bodyweight).

Symptoms
Suppression of the central nervous system, including respiratory depression, can occur but is probably not severe, unless codeine is taken together with other sedative products (including alcohol) or if the overdose is very high.
Triad coma, pinpoint pupils and respiratory depression indicate an opioid overdose with dilation of the pupils if hypoxia develops.
Nausea and vomiting are often other frequently occurring symptoms of an opioid overdose. Other overdose symptoms are: hypothermia, confusion, convulsions, severe dizziness, severe somnolence, hypotension and tachycardia (possible but not likely), tension or restlessness, excitement, hallucinations, bradycardia, circulatory failure, slow or difficult breathing, severe weakness, convulsions especially in babies and children. Rhabdomyolysis, progressive with kidney failure, has been reported after an opioid overdose.

Management
Management of overdose consists of general and supportive measures including a clear airway and monitoring of vital functions until a stable situation is obtained. Consider activated charcoal: more

than 350 mg within one hour after codeine intake for an adult and more than 5 mg/kg bodyweight after intake of codeine for a child. For an acute overdose with respiratory depression or coma, the specific opiate antagonist naloxone is indicated using the recommended dose regimen. Repeated administration may be needed in a severely poisoned patient, as naloxone is a competitive antagonist with a short half-life. Patients should be carefully monitored during the first four hours after codeine intake or for eight hours if an extended release form of codeine was administered.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Opium alkaloids and derivatives, ATC code: R05D A04

Mechanism of action
Codeine is a centrally active weak pain medication. Codeine acts via the opioid μ- receptors, although it has a low affinity for these receptors; the pain relieving effect is a result of the conversion of codeine into morphine. Codeine has a proven effectiveness for acute nociceptive pain especially in combination with other pain medications like paracetamol. It is also used for treatment of coughing and diarrhoea.

Its known that cough is much more than a reflex, and that a center in the brain plays a major role in controlling cough causes cough suppression by direct central action in the medulla.Codeine is believed to exert a relatively specific central inhibitory action on the "cough centre" in the medulla, without causing respiratory depression.

Codeine increases the pressure of the anal sphincter. In addition, codeine decreases gastro-intestinal transit. The contact time of luminal fluid with mucosal cells increases, resulting in an increase in the net intestinal absorption. Codeine does not increase the rate of absorption by the mucosal cells. The increased intestinal absorption results in a lower stool volume and defaecation frequency.

5.2 Pharmacokinetic properties

Absorption
Codeine and its salts are rapidly absorbed from the gastrointestinal tract. Codeine displays approximately 30–40% bioavailability after oral administration and is metabolized in the liver. Following oral administration, the maximal plasma concentration is attained within 1–2 h with a plasma half-life of 2.5–3.5 h and analgesia maintained for approximately 4–6 h. Similar absorption of oral and rectal dosage forms of codeine also suggests passive permeability as the main absorptive

mechanism. Neither dose linearity nor food effect studies for codeine phosphate are available in the literature.

Distribution
Codeine passes through the placenta and passes into breast milk.

In a pharmacokinetic study volunteers who didn´t use any co-medication took an oral dose of 30 mg codeine phosphate. The half-life of codeine was 1.47±0.32 h, that of codeine-6- glucuronide 2.75±0.79 h, and that of morphine-3-glucuronide 1.71±0.51 h. The systemic clearance of codeine was 2280±840 ml/min, the renal clearance of codeine was 93.8±29.8 ml/rnin, and that of codeine-6-glucuronide was 122±39.2 ml/min. The plasma AUC of codeine-6-glucuronide was approximately 10 times higher than that of codeine.

Protein binding of codeine and codeine-6-glucuronide in vivo was 56.1±2.5% and 34.0±3.6%, respectively.

Biotransformation
Codeine is metabolised by CYP3A4 into norcodeine, which is further inactivated by glucuronidation. Approximately 10% of the absorbed codeine is demethylated by CYP2D6 by which morphine is formed. Morphine is converted, among others, into the active metabolites codeine-6-glucuronide 81.0±9.3%, norcodeine 2.16±1.44%, morphine 0.56±0.39%, morphine-3-glucuronide 2.10±1.24%, morphine-6-glucuronide 0.80±0.63%, and normorphine 2.44±2.42%. Some people are unable to O-dealkylate codeine into morphine and lack therefore the cytochrome CYP2D6 isoenzyme.

Elimination
Codeine is metabolised in the liver and excreted with the urine, approximately 37% as glucuronide and 10% as unchanged codeine. Plasma half-life is 3-4 hours. It may increase up to 6 hours in case of liver diseases or after intake of an overdose.

Special patient groups, CYP2D6 polymorphism
Approximately 7% of the Caucasian population has a non-functioning CYP2D6 enzyme as a result of genetic variation. In these patients the pain relieving effect of codeine may be less because morphine is not formed. In addition, 1-5% of the Caucasian population has an increased activity of the CYP2D6 enzyme. These patients may have elevated plasma levels of morphine (see sections 4.4 and 4.6). Adverse effects of morphine may occur especially in patients with renal insufficiency, because the active metabolite morphine-6-glucuronide is excreted less. Increased CYP2D6 enzyme activity can occur more often in African and Mediterranean population groups.

5.3 Preclinical safety data

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

In rabbits chronic codeine exposure caused sperm DNA fragmentation and poor sperm quality primarily via oxidative stress rather than activation of caspase 3-dependent apoptosis [0.3 times maximum human daily dosage]. Oral administration of codeine resulted in testicular atrophy and alterations in testicular histomorphology, elevated testicular enzymes, and suppression of circulatory and intratesticular testosterone [0.3 times maximum human daily dosage].
The relevance of these findings for humans is unknown.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cellulose, microcrystalline
Lactose monohydrate
Potato starch
Silica, colloidal anhydrous
Talc
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

PVC//Alu blister:
2 years

HDPE container:
2 years
After first opening: 9 months

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PVC//Alu blister:
30 tablets

HDPE container:
250 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

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

7. HOUDER VAN DE VERGUNNING VOOR HET IN DE HANDEL BRENGEN

Schmid Pharma BV
Blokweg 8
4671 RA Zevenbergen
Nederland

8. NUMMER(S) VAN DE VERGUNNING VOOR HET IN DE HANDEL BRENGEN

Codeïnefosfaat Schmid Pharma 10 mg, tabletten - RVG 127427
Codeïnefosfaat Schmid Pharma 15 mg, tabletten - RVG 127428
Codeïnefosfaat Schmid Pharma 20 mg, tabletten - RVG 127429
Codeïnefosfaat Schmid Pharma 30 mg, tabletten - RVG 127430

9. DATUM VAN EERSTE VERLENING VAN DE VERGUNNING/VERLENGING VAN DE VERGUNNING

Datum van eerste verlening van de vergunning: 3 oktober 2022

10. DATUM VAN HERZIENING VAN DE TEKST

Laatste gedeeltelijke wijziging betreft de rubrieken 1 en 7: 19 april 2025