1.3.2 PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S5

STILPANE 150 mg/8 mg/ 320 mg/ 32 mg Tablets

Meprobamate, Codeine phosphate, Paracetamol, Caffeine anhydrous

Sugar free

Read all of this leaflet carefully before you start taking STILPANE

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- STILPANE has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours

What is in this leaflet

1. What STILPANE is and what it is used for

STILPANE is indicated for short term use (no longer than 10 days) in mild to moderate pain and fever associated with anxiety or tension.

2. What you need to know before you take STILPANE

Do not take STILPANE:

- If you are hypersensitive (allergic) to meprobamate, codeine phosphate, paracetamol, caffeine anhydrous or to any of the other ingredients in STILPANE (see section 6).
- If you are hypersensitive to other opioid analgesics such as morphine, tramadol, oxycodone.
- If you are pregnant or breastfeeding (see Pregnancy and breastfeeding).
- If you have porphyria (a disorder relating to the pigment of blood), as symptoms may be aggerated.
- If you have severe liver, kidney or lung problems.
- If you have a history of convulsions (epilepsy), as STILPANE can induce convulsions.
- If you have any breathing problems or bronchitis, especially in the presence of cyanosis (condition where your skin or lips turn blue due to an insufficient level of oxygen in the blood) and excessive mucus and fluid secretion in the airways.
- If you have just had an operation on your bile tract.
- If you are an alcoholic.
- If you have had a recent head injury or if you have a condition in which the pressure in your skull is increased.
- If the patient is in a coma.
- During an asthma attack.
- If you have heart failure caused by chronic lung disease.
- If you are using monoamine oxidase inhibitors (usually used to treat depression) or within fourteen days of stopping such treatment (see Other medicines and STILPANE).
- If you are an ultra-rapid metaboliser of CYP2D6 (see Warnings and precautions).

- If you are a child under the age of 12 years.
- If you have any of the following conditions where inhibition of contractions of the digestive tract (peristalsis) should be avoided: where there is a risk of a condition where the movement of the bowel is impaired (paralytic ileus), where bloating and swelling in the belly area (abdominal distension) develops, or in acute diarrhoeal conditions such as acute ulcerative colitis or antibiotic associated colitis (e.g. pseudomembranous colitis) or diarrhoea caused by poisoning.
- If a paediatric patient and you are undergoing a procedure to remove your tonsils or adenoids for obstructive sleep apnoea syndrome.

Warnings and precautions

STILPANE contains paracetamol which may be fatal in overdose. In the event of overdosage or suspected overdose and notwithstanding the fact that the person may be asymptomatic, the nearest doctor, hospital or Poison Centre must be contacted immediately.

If more tablets than recommended are taken or if used for a longer period of time than recommended, STILPANE may lead to dependency and addiction (see How to take STILPANE).

Even if taken at normal doses, STILPANE can cause increased morphine (active metabolite of codeine) levels which may produce clinical signs of morphine intoxication.
The lowest effective dose should be used, and the duration of treatment should be as short as possible (see How to take STILPANE).

Take special care with STILPANE due to the paracetamol content:

- As taking higher doses of paracetamol than recommended may cause severe liver damage. STILPANE use for a period longer than recommended can cause irreversible kidney damage. STILPANE should not be used for periods longer than 10 days.
- If you are suffering from liver or kidney disease, as STILPANE should be taken under medical supervision. Consult your doctor if no relief is obtained from the recommended dosage.
- If you are taking other medicines that affect the liver, e.g. barbiturates (used to treat epilepsy).
- If you are also taking flucloxacillin (an antibiotic) as the combination with paracetamol, as contained in STILPANE, has been associated with a condition where acid accumulates in the body (high anion gap metabolic acidosis), especially in patients with risk factors (see Other medicines and STILPANE).
- If you have a compromised ability to remove chemicals from the body (glutathione depleted states), as the use of paracetamol, as contained in STILPANE, can increase your risk of developing a condition in which too much acid accumulates in the body (metabolic acidosis).
- As STILPANE can cause very serious skin reactions that are potentially life threatening (see Possible side effects), you should stop taking STILPANE if you develop any skin reactions and contact your doctor.

Take special care with STILPANE due to the codeine phosphate content:

- If you have any of the following conditions:
  - Under active thyroid gland (a condition where the thyroid gland does not produce enough hormones),
  - adrenocortical insufficiency (a condition where the adrenal glands do not produce enough steroid hormone),
  - asthma (see Do not take STILPANE),

- narrowing of the tube connected to the bladder (urethral stricture),
- impaired liver function (see Do not take STILPANE),
- enlarged prostate gland,
- low blood pressure,
- shock (a condition where there is not enough blood flow through the body),
- inflammatory or obstructive bowel disorders (a problem or blockage of your bowel) (see Do not take STILPANE),
- diseases or conditions that cause weakness of muscles around the eyes, mouth and throat (myasthenia gravis).

- If you are elderly and debilitated (very weak or sick), as STILPANE should be avoided (see How to take STILPANE). If administered to elderly and debilitated patients, the dose should be reduced.
- If you are pregnant or in labour. STILPANE administration during labour may cause breathing problems in the new-born infant. If women take STILPANE during pregnancy, there is a risk that their newborn infants will experience neonatal withdrawal syndrome (see Pregnancy and breastfeeding).
- Since codeine may cause a decrease in the function and activity of the brain. This effect may be increased by medicines that slow down brain activity such as alcohol, anaesthetics, calming and sleeping tablets, and phenothiazines. The prolonged use of high doses of codeine has produced addiction similar to morphine addiction. Codeine, as contained in STILPANE, should be used with caution in patients with a history of substance abuse or mental health disorders.
- If you are taking codeine for a long period of time, as you might notice that you need more to obtain pain control than when you initially started taking it. This could be a sign of tolerance. If tolerance or dependence to codeine has occurred, you should stop taking codeine gradually. This will help to avoid the occurrence of withdrawal

symptoms. If you were dependant on a high dose, tapering down can take weeks to months.

- If you feel that you are experiencing even more pain (hyperalgesia). Your doctor might need to reduce your dose.
- If you are an ultra-rapid metaboliser of CYP2D6, you should not take STILPANE (see Do not take STILPANE). Even small doses of codeine can lead to increased formation of the active metabolite morphine resulting in clinical signs of morphine intoxication (see If you take more STILPANE than you should).
- If you are a child and you might have compromised respiratory function, as worsened symptoms of morphine toxicity can occur (see Do not take STILPANE).
- If you are a paediatric patient and you have had your tonsils and/or adenoids removed due to obstructive sleep apnoea. Rare, but life-threating adverse events such as death can occur (see Do not take STILPANE).

Take special care with STILPANE due to the caffeine anhydrous content:

- If any of the following is applicable to you:
  - Peptic ulcer (sores in the stomach or intestine),
  - overactive thyroid gland (a condition where the thyroid gland produces more hormones than needed),
  - high blood pressure,
  - epilepsy (a brain disorder causing seizures) (see Do not take STILPANE),
  - abnormal heartbeat or other diseases involving the heart or blood vessels as these conditions may worsen,
  - alcoholics (chronic alcoholism) (see Do not take STILPANE),
  - heart problems (see Do not take STILPANE),
  - liver problems (see Do not take STILPANE),
  - acute fever,

- newborn babies and the elderly (see Do not take STILPANE and Pregnancy and Breastfeeding).

Take special care with STILPANE due to the meprobamate content:

- As STILPANE should be avoided in elderly and debilitated (very sick or weak) patients and in those with mental depression.
- If you have any of the following conditions:
  - Reduced liver or kidney function (see Do not take STILPANE),
  - reduced lung functions (see Do not take STILPANE).
- As there is a serious addiction risk with a typical withdrawal syndrome. STILPANE should not be used for the stress of daily living.
- If you are also taking other central nervous system depressants and other medicines metabolised by your liver (see Other medicines and STILPANE).
- If you have porphyria as symptoms may be exacerbated (see Do not take STILPANE).

Children and adolescents

STILPANE tablets are not recommended for use in children under the age of 12 (see Do not take STILPANE).

Other medicines and STILPANE

Always tell your healthcare provider if you are taking any other medicines (this includes complementary or traditional medicines).

Tell your doctor if you are taking any of the following medicines:

- Alcohol, as the depressant, sedative and blood pressure lowering effects of STILPANE are enhanced,

- anti-dysrhythmics (e.g. mexiletine, quinidine), as codeine, as contained in STILPANE, delays the absorption of mexiletine. Mexiletine reduces the removal of caffeine, as contained in STILPANE, from the body. The pain-relieving activity of codeine, as contained in STILPANE, is likely to be significantly impaired by quinidine which impairs the breakdown of codeine,
- antibiotics (e.g. ciprofloxacin, enoxacin and pipemidic acid), as caffeine can stay in your body for longer when given with ciprofloxacin, enoxacin and pipemidic acid,
- medicines used to treat tuberculosis, including isoniazid, as severe liver damage can occur,
- anti-depressants (e.g. fluvoxamine, monoamine oxidase inhibitors and tricyclic anti-depressants), as the depressant effects may be enhanced and/or prolonged. Fluvoxamine also causes caffeine to stay in your body for longer. Tricyclic antidepressants may not work as well when given with meprobamate, as contained in STILPANE. You should not take STILPANE if you are also taking monoamine oxidase inhibitors (see Do not take STILPANE),
- medicines used to treat psychosis, anxiety and sleep disturbances (anti-psychotics, anxiolytics, hypnotics and other sedative medicines), as the risk for enhanced effects (sedation, breathing depression, blood pressure lowering etc.) can occur,
- anti-epileptics (e.g. phenytoin, carbamazepine, phenobarbital, primidone and lamotrigine), as phenytoin may not work as well if given together with meprobamate. Phenytoin causes caffeine to be removed from the body much quicker. If used together with paracetamol, the breakdown of paracetamol can increase, and possible liver damage can occur. Lamotrigine might not work as well if taken with paracetamol,
- gastrointestinal medicines (e.g. cimetidine), cimetidine may prevent the breakdown of codeine resulting in higher concentrations. Cimetidine prevents the removal of caffeine from the body and thus causes caffeine to stay in your body longer,

- lithium, as lithium toxicity can occur,
- methoxsalen, methoxsalen reduces the rate of removal of caffeine from the body in patients with psoriasis,
- oral contraceptives, as they decrease the rate of removal of caffeine from the body, thus caffeine stays in the body longer. Oral contraceptives may not work as well when given with meprobamate,
- corticosteroids, as they might not work as well when given with meprobamate,
- sympathomimetics (e.g. phenylpropanolamine, ephedrine that may be contained and cough and cold medicines), as concomitant use with caffeine can cause more side effects. Concomitant use of ephedrine and caffeine, as contained in STILPANE, may have an effect on your heart, blood pressure, metabolism, hormonal responses, glucose and insulin levels,
- domperidone and metoclopramide, as the absorption of paracetamol may be accelerated. Codeine works against the effects of metoclopramide and domperidone on gastrointestinal activity,
- cisapride, codeine works against the effects of cisapride on gastrointestinal activity,
- probenecid, removal of paracetamol from the body may be affected and concentrations changed when given with probenecid, paracetamol may stay in the body for longer,
- cholestyramine, as it reduces the absorption of paracetamol if given within 1 hour of paracetamol,
- sodium oxybate, as concomitant administration of codeine and sodium oxybate may cause increased central nervous system depression and/or airway depression and/or lowered blood pressure (hypotension),
- anti-coagulants (e.g. warfarin), since there is an increased risk of bleeding in patients taking regular doses of paracetamol,

- anti-virals (e.g. interferon alfa and zidovudine), as paracetamol enhances the antiviral effect of Interferon Alfa. Severe liver toxicity has occurred after the use of paracetamol in patients taking zidovudine and co-trimoxazole,
- phenothiazines, as sedation and blood pressure lowering effects may increase, it also increases the amount of opioid (such as codeine) required to produce satisfactory relief from pain. Phenothiazines are removed from the body quicker if given together with meprobamate,
- anaesthetics, as the combination may cause increased central nervous depression and/or airway depression and/or lowered blood pressure (hypotension),
- flucloxacillin, as concurrent intake with paracetamol has been associated acid accumulates in the body, especially in patients with risk factors,
- anti-histamines (e.g. hydroxyzine), as the combination can cause increased central nervous system depression and/or airway depression and/or lowered blood pressure (hypotension) as well as enhanced pain-relieving effects,
- Interference with laboratory tests: Opioids may interfere with gastric emptying studies.

STILPANE with food, drink and alcohol

Drinking alcohol together with STILPANE can enhance the blood pressure lowering, sedative, breathing and central nervous system depressant effects. Drinking alcohol with STILPANE may also lead to reduced judgment and coordination. You should not drink alcohol if you are taking STILPANE.

Pregnancy and breastfeeding

Do not take STILPANE when you are pregnant or breastfeeding your baby as safety has not been established.

If you are pregnant or breastfeeding, think you may be pregnant or planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before taking STILPANE.

Driving and using machines

Do not drive or operate machinery, because the use of STILPANE may lead to drowsiness and impaired concentration that may be aggravated by the simultaneous intake of alcohol or anti-depressants.

It is not always possible to predict to what extent STILPANE may interfere with your daily activities. You should ensure that you do not engage in the above activities until you are aware of the measure to which STILPANE affects you (see section 4).

3. How to take STILPANE

Do not share medicines prescribed for you with any other person.

For short term use only. Do not take STILPANE for longer than 10 days.

STILPANE should not be used in children under 12 years of age.

The usual dose for adults and children over 12 is:

Take two tablets orally three or four times a day as required.

DO NOT EXCEED THE RECOMMENDED DOSE.

Your doctor will tell you how long your treatment with STILPANE will last.

If you are an elderly or debilitated (weak) patient, your healthcare provider may decide to reduce your dose.

Always take STILPANE exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure. If you have the impression that the effect of STILPANE is too strong or too weak, talk to your doctor or pharmacist.

If you take more STILPANE than you should

In the event of overdosage, consult a doctor or pharmacist immediately. If neither is available, seek help at the nearest hospital or poison centre. Prompt treatment is essential. Evidence of liver damage is often delayed until after the time for effective treatment has lapsed. Symptoms of paracetamol overdosage in the first 24 hours are pallor, nausea, vomiting, loss of appetite (anorexia) and possibly abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion. Abnormal heartbeat has been reported.

Overdosage with STILPANE can cause severe and/or fatal low blood pressure, respiratory depression, shock, heart failure and death. Extremely high doses and increased sensitivity to STILPANE may lead to agitation, increased urine, repeated vomiting with extreme thirst, disorientation (confusion), hallucinations, very high body temperature (41 °C or above), abnormal heartbeat including increased heart rate, electrolyte disturbances, convulsions and death.

If you forget to take STILPANE

Do not take a double dose to make up for forgotten individual doses.

If you stop taking STILPANE

STILPANE should not be used for longer than 10 days. If you are taking more STILPANE for longer periods of time, you could develop tolerance, addiction or an increased sensitivity to pain (hyperalgesia). In this case, the dose should be reduced gradually to prevent the occurrence of withdrawal symptoms. Withdrawal syndrome is characterised by some or all of

the following: restlessness, watery eyes, runny nose, yawning, sweating, chills, muscle pain, pupils (of the eye) that are larger than usual and pounding or fluttering heartbeat. Other symptoms may also develop including irritability, agitation, anxiety, excessive movement of a part of the body, tremor, weakness, sleeplessness, loss of appetite, stomach cramps, nausea, vomiting, diarrhoea, increased blood pressure, increased breathing rate or heart rate.

If you notice any of these symptoms when you stop taking STILPANE, please contact your doctor.

4. Possible side effects

STILPANE can have side effects.

Not all side effects reported for STILPANE are included in this leaflet. Should your general health worsen while taking STILPANE or if you notice any side effects not mentioned in this leaflet, please inform your doctor, pharmacist or other healthcare provider for advice.

If any of the following happens, stop taking STILPANE and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Sensitivity reactions: medicine fever and abscesses/ulcers, allergic skin condition, itching of the nose and medicine sensitivity, bleeding, skin rash,
- swelling of the hands, feet, ankles, face, eyes, lips and mouth, tongue or throat, which may cause difficulty in swallowing or breathing,
- rash or itching,
- fainting,
- blistering of the skin, mouth, eyes and genitals as these may be due to a serious allergic reaction known as severe cutaneous adverse reactions (SCARs) such as Toxic Epidermal Necrolysis (TEN), Stevens-Johnson syndrome (SJS), acute

generalised exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS)/Drug-induced hypersensitivity syndrome (DIHS), fixed drug eruption (FDE).

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to STILPANE. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- Seeing and hearing things that are not real (hallucinations),
- convulsions and uncontrolled muscle movements,
- deepening coma,
- raised skull pressure, that can present with symptoms such as severe headache, blurred vision and vomiting,
- reduced body temperature (hypothermia),
- decreased, irregular or increased heartbeat, or other changes in the way your heart beats (bradycardia, tachycardia, cardiac dysrhythmias, extrasystoles, palpitations),
- decreased white blood cells (neutropenia, leucopenia, agranulocytosis) that can present with symptoms such as fever, chills, sore throat, fatigue, which may be signs of an infection,
- too few blood cells of all types (pancytopenia), which can cause weakness, bruising or make infections more likely,
- increased number of a certain type of white blood cell (eosinophilia), that can present with symptoms such as weight loss, fevers, night sweats, cough, chest pain, rash,
- serious reduction of blood cells (due to failure of the bone marrow) that can cause weakness, bruising or make infections more likely (aplastic anaemia),

- decreased number of red blood cells which can make the skin pale and cause weakness or breathlessness,
- constriction of air passages which causes difficulty breathing, coughing, wheezing and chest tightness (bronchospasm, dyspnoea and large doses may produce respiratory depression),
- decreased blood platelets (thrombocytopenia), that can present with symptoms such as unusual or unexplained bruising or bleeding,
- gastrointestinal bleeding and gastric ulceration, that can present with symptoms such as black tarry stools, vomiting of blood, upper stomach pain, indigestion,
- inflammation of the pancreas (pancreatitis), that can present with symptoms such as upper stomach pain, stomach pain that radiates to the back, tenderness when touching the stomach,
- yellowing of skin or the whites of your eyes as this could be signs of problems with your liver (hepatic dysfunction).

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

- Drowsiness, insomnia, headache,
- anxiety, restlessness,
- unsteady, shaky movements (ataxia),
- constipation, nausea, vomiting, abdominal pain.

Less frequent side effects:

- Difficulty in urination (micturition),

- muscle rigidity,
- sweating,
- light headedness when standing up (orthostatic hypotension),
- facial flushing,
- confusion, mood changes,
- pupil (eye) contraction (miosis),
- sleepiness (sedation), dizziness, faintness,
- excitement, cheerfulness (euphoria),
- weakness,
- dry mouth,
- diarrhoea,
- disturbance of vision.

Side effects with an unknown frequency:

- Low blood pressure (hypotension),
- balance disorder, a sensation that the environment is spinning (vertigo),
- spasm of the bile duct (may be associated with altered liver enzyme values),
- ringing in the ears (tinnitus),
- difficulty in complete or partial emptying of the bladder (urinary retention), colic/spasm of the ureter/kidney duct (ureteric spasm), painful urination (dysuria),
- stomach cramps,
- tremor,
- a general feeling of being unwell (malaise), tiredness,
- high blood sugar levels (hyperglycaemia),
- lack/loss of appetite (anorexia),
- sexual dysfunction, erectile dysfunction, decreased potency, decreased libido,

- pins and needles sensation (paraesthesia),
- fever, splenomegaly and lymphadenopathy,
- mental depression, nightmares, a state of unease or generalized dissatisfaction with life (dysphoria),
- visual aura that may precede a migraine headache (scintillating scotoma).

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

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to **SAHPRA:** via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088/ +27 (0)11 239-6200

By reporting side effects, you can help provide more information on the safety of STILPANE.

5. How to store STILPANE

Store all medicines out of reach of children.

Store at or below 25 °C, in a well-closed container.

Protect from light.

Keep in original packaging until required for use.

Do not store in a bathroom.

Do not use after the expiry date stated on the label.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What STILPANE contains

The active ingredients in each STILPANE tablet are:

Meprobamate	150 mg
Codeine phosphate	8 mg
Paracetamol	320 mg
Caffeine anhydrous	32 mg

The other ingredients are dye lake green (C.I No's: 47005, 42090, 15985), magnesium stearate, nipastat, povidone K25, sodium starch glycollate, starch, talc.

Preservative:

Nipastat 0,02 % *m/m*

Sugar free

What STILPANE looks like and the contents of the pack

STILPANE is a green, biconvex tablet, debossed "C26" on the one side and bisected on the other side.

100 tablets are packed in aluminium/PVC blister strips. The strips are packed, together with a leaflet into a unit carton.

500 tablets are packed into a white polypropylene (PP) securitainer, together with a foam insert and a leaflet and sealed with a white polyethylene cap.

1 000 tablets are packed into amber PVC jars together with a foam insert and a leaflet and sealed with a screwcap.

Not all packs and pack sizes are necessarily marketed.

Holder of Certificate of Registration

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Access to the corresponding Professional Information SAHPRA Repository of Professional Information and Patient Information Leaflets:

https://www.sahpra.org.za/pi-pil-repository/

Aspen Pharmacare:

E-mail: Medinfo@aspenpharma.com

Tel: 0800 118 088

Botswana: B9322890 1C

Namibia: NS3 10/2.9/0565

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