PROFESSIONAL INFORMATION

SCHEDULING STATUS

S6

1 NAME OF THE MEDICINE

SOVENOR® 5 (transdermal patches)

SOVENOR® 10 (transdermal patches)

SOVENOR® 20 (transdermal patches)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each SOVENOR® 5 contains 5 mg buprenorphine in a medicine-containing matrix that releases a nominal 5 µg of buprenorphine per hour over 7 days.

Each SOVENOR® 10 contains 10 mg buprenorphine in a medicine-containing matrix that releases a nominal 10 µg of buprenorphine per hour over 7 days.

Each SOVENOR® 20 contains 20 mg buprenorphine in a medicine-containing matrix that releases a nominal 20 µg of buprenorphine per hour over 7 days.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Transdermal patches.

SOVENOR® 5: A square, transdermal patch with rounded corners on rigid aluminium removable protective layer with a beige coloured backing layer. In the centre is posted a buprenorphine-containing adhesive matrix, printed with “SOVENOR® 5 mg, 5 mcg/h”.

SOVENOR® 10: A rectangular, transdermal patch with rounded corners on rigid aluminium removable protective layer with a beige coloured backing layer. In the centre is posted a buprenorphine-containing adhesive matrix, printed with “SOVENOR® 10 mg, 10 mcg/h”.

SOVENOR® 20: A square, transdermal patch with rounded corners on rigid aluminium removable protective layer with a beige coloured backing layer. In the center is posted a buprenorphine-containing adhesive matrix, printed with “SOVENOR® 20 mg, 20 mcg/h”.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

SOVENOR® is indicated for the treatment of chronic musculoskeletal pain of the joints and the lower back, when that pain is of moderate to severe intensity sufficient to require an opioid to obtain adequate analgesia.

4.2 Posology and method of administration

Posology

SOVENOR® Patch should be worn continuously for 7 days.

Patients aged 18 years and over:

The lowest SOVENOR® dose available, SOVENOR® 5 (5 µg/h) should be used as the initial dose in all patients.

Titration

During initiation, titration, and treatment with SOVENOR®, patients may continue their existing NSAID or paracetamol regimen as needed.

During the titration process, the dose may be adjusted every 3-days (72 hours). Thereafter, the 7-day dosing interval should be maintained.

Changes in SOVENOR® dosage may be individually titrated based on the need for supplemental analgesia and the patient’s analgesic response to SOVENOR®.

To increase the dose, a larger patch should replace the patch that is currently being worn, or a combination of patches should be applied in different places to achieve the desired dose. It is recommended that no more than two patches be applied at the same time, regardless of patch strength.

Titration should continue every 3 - 7 days until adequate analgesia is achieved.

If adequate pain control cannot be achieved with SOVENOR®, therapy with SOVENOR® should be discontinued and the patient converted to an appropriate analgesic regimen as determined by a physician.

Special populations

Paediatric population

The safety and efficacy of SOVENOR® in patients under 18 years of age has not been established.

Renal impairment

No special dose adjustment of SOVENOR® is necessary in patients with renal impairment.

Hepatic impairment

There is no need for dosage adjustment when using SOVENOR® in patients with mild to moderate hepatic impairment.

Patients with severe hepatic impairment may accumulate buprenorphine during SOVENOR® treatment. SOVENOR® should not be used in such patients (see section 4.3).

Method of administration

In order to minimise the potential of skin reactions (see Section 4.4).

SOVENOR® should be applied to non-irritated, intact skin of the upper outer arm, upper chest, upper back or the side of the chest. SOVENOR® should be applied to a relatively

hairless or nearly hairless skin site. If none are available, the hair at the site should be clipped, not shaven.

Application sites should be rotated whenever a transdermal patch is replaced or added.

Application sites should be re-used at no less than 3-week intervals.

If the application site must be cleaned, it should be done with clear water only. Soaps, alcohol, oils, lotions, or abrasive devices should not be used. The skin must be dry before the transdermal patch is applied.

SOVENOR® should be pressed firmly in place at the application site, making sure contact is complete, especially around the edges. If the edges of the patch begin to peel off, the edges may be taped down with suitable skin tape. If a transdermal patch falls off, a new one should be applied. Bathing, showering, or swimming should not affect the system.

While wearing SOVENOR®, patients should be advised to avoid exposing the SOVENOR® site to direct external heat sources such as heating pads, electric blankets, heat lamps, hot water bottles etc., as an increase in absorption of buprenorphine may occur. The effects of the use of SOVENOR® in hot tubs and saunas have not been studied.

Application directions

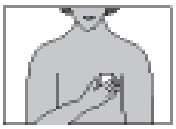
Open the pouch just before applying the patch by cutting the pouch along the dotted line with scissors. Be careful not to damage the transdermal patches with the scissors.

Take off the thin cover sheet.



Attach the patch to the upper arm, upper chest, upper back, or sides of the chest.





Press the patch with the hand for approximately 30 seconds and check that it is properly attached.

The patch should not be used if the seal is broken.

Discontinuation

After removal of SOVENOR®, plasma concentrations decrease gradually. This should be considered when therapy with SOVENOR® is to be followed by other opioids. As a general rule, a subsequent opioid should not be administered within 24 hours after removal of SOVENOR®.

4.3 Contraindications

SOVENOR® is contraindicated in:

- patients with known hypersensitivity to buprenorphine or to any of the excipients (see section 6.1), including previous history of application site reactions, suggestive of contact dermatitis with buprenorphine transdermal patches;
- patients suffering from delirium tremens;
- patients with severe hepatic impairment;
- patients suffering from myasthenia gravis.

SOVENOR® should not be used in patients with head injury, intracranial lesions or increased intracranial pressure, shock or a reduced level of consciousness of uncertain origin.

4.4 Special warnings and precautions for use

SOVENOR® should be used with caution in patients with impaired respiratory function and in patients concurrently receiving serotonergic agents including monoamine oxidase inhibitors (MAOIs) or who have received MAOIs within the previous two weeks (see section 4.5).

SOVENOR® should be used with caution in patients with constipation.

Caution should be exercised in patients suffering from sleep apnoea.

SOVENOR® may lower the seizure threshold in patients with a history of seizure disorder.

Severe febrile illness may increase the rate of buprenorphine absorption from SOVENOR®.

Respiratory depression

The primary risk of opioid excess is respiratory depression.

Opioids may cause sleep-related breathing disorders including central sleep apnoea (CSA) and sleep-related hypoxaemia. Opioid use may increase the risk of CSA in a dose-dependent manner in some patients. Opioids may also cause worsening of pre-existing sleep apnoea (see section 4.8). In patients who present with CSA, consider decreasing the total opioid dosage.

CNS depressants co-administration

Concomitant use of buprenorphine and sedative medicines such as benzodiazepines or related medicines 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 opioids concomitantly with sedative medicines, the lowest effective dose should be used, and the duration of treatment should be as short as possible. It is unknown if such severity can be expected from transdermal formulations of buprenorphine.

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).

Serotonin syndrome

Concomitant administration of buprenorphine and other serotonergic agents, such as MAOIs, selective serotonin re-uptake inhibitors (SSRIs), serotonin norepinephrine re-uptake inhibitors (SNRIs) or tricyclic antidepressants may result in serotonin syndrome, a potentially life-threatening condition (see section 4.5).

Caution is also advised in patients who have received MAOIs within the previous two weeks. If concomitant treatment with other serotonergic agents is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. Symptoms of serotonin syndrome may include mental-status changes, autonomic instability, neuromuscular abnormalities, and/or gastrointestinal symptoms.

Medicine dependence, tolerance and potential for abuse

For all patients, prolonged use of SOVENOR® may lead to medicine 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 online, 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.

Significant respiratory depression has been associated with buprenorphine, particularly by the intravenous route. A number of deaths have occurred when addicts have intravenously abused buprenorphine, usually with benzodiazepines concomitantly. Additional overdose deaths due to ethanol and benzodiazepines in combination with buprenorphine have been reported (see section 4.5).

Caution should be exercised when prescribing SOVENOR® to patients known to have, or suspected of having, problems with drug or alcohol abuse or serious mental illness.

Medicine 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 SOVENOR®.

Medicine 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.

Withdrawal syndrome, when it occurs, is generally mild, begins after 2 days and may last up to 2 weeks. The opioid medicine 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 medicine 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.
SOVENOR® should not be used at higher doses than recommended.

Skin reactions at application site

To minimise the risk of occurrence of application site skin reactions, it is important to follow the posology instructions (see section 4.2).
Application site reactions with SOVENOR® are usually presented by a mild or moderate skin inflammation (contact dermatitis), and their typical appearance may include erythema, oedema, pruritus, rash, small blisters (vesicles), and painful/burning sensation at the application site. Most commonly the cause is skin irritation (irritant contact dermatitis), and these reactions resolve spontaneously after SOVENOR® removal. SOVENOR® may also cause skin sensitisation and subsequent allergic contact dermatitis (immune mediated, type

IV hypersensitivity reaction). Allergic contact dermatitis may develop with a significant delay (it may take months after SOVENOR® treatment initiation) and may manifest with symptoms similar to irritant contact dermatitis, or with more intense symptoms, such as “burn” -like lesions with bullae and discharge, which may spread outside the application site and which may not resolve rapidly after SOVENOR® removal. Patients and caregivers should be instructed accordingly to monitor the application sites for such reactions. If allergic contact dermatitis is suspected, relevant diagnostic procedures should be performed to determine if sensitisation has occurred and its actual cause (buprenorphine and/or other ingredients of the patch). If allergic contact dermatitis has been confirmed, treatment should be discontinued (see section 4.3). Continued SOVENOR® treatment in individuals experiencing allergic contact dermatitis may lead to complications, including blistering of the skin, open wound, bleeding, ulceration, and subsequent infections. Mechanical injuries during patch removal (e.g. laceration) are also possible in patients with fragile skin. Chronic inflammation may lead to long-lasting sequelae, such as post inflammatory hyper- and hypopigmentation, as well as dry and thick scaly skin lesions, which may closely resemble scars.

Endocrine system

Opioids may influence the hypothalamic-pituitary-adrenal or -gonadal axes. Some changes that can be seen include an increase in serum prolactin and decreases in plasma cortisol and testosterone. Clinical symptoms may be manifest from these hormonal changes.

SOVENOR® is not recommended for analgesia in the immediate post-operative period or in other situations characterised by rapidly varying analgesic requirement.

SOVENOR® produces morphine-like effects, including euphoria and physical dependence. Administration of SOVENOR® to persons who are physically dependent on full μ-opioid agonists may precipitate an abstinence syndrome.

4.5 Interaction with other medicines and other forms of interaction

Caution in the use of SOVENOR® in patients taking MAOIs or who have received MAOIs within the previous two weeks is appropriate.

SOVENOR® should be used with caution in patients who are concurrently taking other central nervous system (CNS) depressants or other medicines that may cause respiratory depression, hypotension, profound sedation, or potentially result in coma and death. Such medicines include sedatives or hypnotics, general anaesthetics, other opioid analgesics, phenothiazines, centrally acting anti-emetics, benzodiazepines and alcohol.

Buprenorphine should be used cautiously when co-administered with serotonergic medicinal products, such as MAOIs, SSRIs, SNRIs or tricyclic antidepressants as the risk of serotonin syndrome, a potentially life-threatening condition, is increased (see section 4.4).

Reductions in hepatic blood flow induced by some general anaesthetics (e.g. halothane) and other medicines may result in a decreased rate of hepatic elimination of the medicine buprenorphine.

Buprenorphine, as in SOVENOR®, is primarily metabolised by glucuronidation and to a lesser extent (about 30 %) by CYP3A4. Concomitant treatment with CYP3A4 inhibitors may lead to elevated plasma concentrations with intensified efficacy of buprenorphine.

A medicine interaction study with the CYP3A4 inhibitor ketoconazole did not produce clinically relevant increases in mean maximum (C_{max}) or total (AUC) buprenorphine exposure following SOVENOR® with ketoconazole as compared to SOVENOR® alone.

The interaction between buprenorphine and CYP3A4 enzyme inducers has not been studied. Co-administration of buprenorphine and enzyme inducers (e.g. phenobarbitone, carbamazepine, phenytoin and rifampicin) could lead to increased clearance which might result in reduced efficacy.

4.6 Fertility, pregnancy and lactation

SOVENOR® should not be used during pregnancy or lactation.

Pregnancy

Buprenorphine, as contained in SOVENOR®, has been shown to cross the placenta in humans.

Prolonged used of SOVENOR® during pregnancy can result in neonatal opioid withdrawal syndrome.

Breastfeeding

Buprenorphine, as contained in SOVENOR®, has been detected in newborn blood, urine and meconium and also in mother's milk at low concentrations.

Fertility

No human data on the effect of buprenorphine on fertility are available. In animal studies, no effect on fertility has been observed with buprenorphine (see section 5.3).

4.7 Effects on ability to drive and use machines

SOVENOR® may impair the ability to drive and operate machinery.

4.8 Undesirable effects

a) Summary of safety profile

Serious adverse reactions that may be associated with SOVENOR® therapy in clinical use are similar to those observed with other opioid analgesics, including respiratory depression (especially when used with other CNS depressants) and hypotension (see section 4.4).

b) Tabulated list of adverse reactions

The following side effects have been reported during the use of SOVENOR®:

The table lists adverse reactions reported from 9 completed studies with SOVENOR®. The reactions are listed as MeDRA preferred term by system organ class and absolute 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); not known (cannot be estimated from the available data).

Immune System disorders	
Uncommon	allergic reaction (including oropharyngeal swelling and swollen tongue)
Very rare	anaphylactic response
Metabolism and nutrition disorders	
Common	anorexia
Rare	dehydration*
Psychiatric disorders	
Common	confusional state, depression*, insomnia, nervousness, anxiety
Uncommon	affect lability, agitation, euphoric mood, hallucination, decreased libido, nightmare, aggression
Rare	psychotic disorder
Very rare	depersonalisation, medicine dependence (see section 4.4)
Nervous system disorders	
Very common	dizziness, headache*, somnolence*
Common	Tremor
Uncommon	concentration impairment, abnormal co-ordination, dysarthria, dysgeusia, hypoaesthesia, memory impairment, migraine, syncope*, paraesthesia
Very rare	Convulsions
Not known	hyperalgesia, sleep apnoea syndrome
Eye disorders	
Uncommon	dry eye, blurred vision

Rare	Miosis
Ear and labyrinth disorders	
Uncommon	tinnitus, vertigo
Cardiac disorders	
Uncommon	palpitations, tachycardia
Rare	angina pectoris
Vascular disorders	
Uncommon	flushing, hypertension*
Rare	vasodilatation, orthostatic hypotension
Very rare	Hypotension
Respiratory, thoracic and mediastinal disorders	
Common	dyspnoea*
Uncommon	cough, hiccups, wheezing
Rare	asthma aggravated*, hyperventilation, hypoxia, respiratory failure, rhinitis
Very rare	respiratory depression
Gastrointestinal disorders	
Very Common	constipation*, nausea*, vomiting*
Common	abdominal pain*, diarrhoea*, dry mouth, dyspepsia*
Uncommon	Flatulence
Rare	dysphagia, ileus
Not known	diverticulitis*
Hepatobiliary disorders	
Not known	biliary colic*
Skin and subcutaneous tissue disorders	
Very Common	pruritus*

Common	rash*, sweating*
Uncommon	dry skin, urticaria, dermatitis contact
Rare	face oedema
Musculoskeletal and connective tissue disorders	
Uncommon	muscle spasm, myalgia
Renal and urinary disorders	
Uncommon	urinary incontinence, urinary retention, urinary hesitation
Reproductive system and breast disorders	
Rare	sexual dysfunction
General disorders and administration site conditions	
Very Common	application site reaction†
Common	asthenic conditions (including muscle weakness), peripheral oedema
Uncommon	oedema, pyrexia*, rigors*, withdrawal syndrome, chest pain, application site dermatitis**
Rare	influenza-like illness
Not known	withdrawal syndrome neonatal, tolerance
Investigations	
Uncommon	alanine amino-transferase increased, weight decreased
Injury and poisoning	
Uncommon	accidental injury (including fall)

* At least one serious case

†Includes: application site erythema, application site oedema, application site pruritus, application site rash.

** In some cases late onset local allergic reactions occurred with marked signs of inflammation. In such cases treatment with SOVENOR® should be terminated.

Adverse events identified through post marketing experience

Rare	Increased risk of abdominal pain, including pancreatitis has been reported

c) **Description of selected adverse reactions**

Mechanical injuries during patch removal (e.g. laceration) are also possible in patients with fragile skin. Chronic inflammation may lead to long-lasting sequelae, such as post inflammatory hyper- and hypopigmentation, as well as dry and thick scaly skin lesions, which may closely resemble scars. In such cases treatment with SOVENOR® should be terminated (see sections 4.3 and 4.4).

After discontinuation of SOVENOR®, withdrawal symptoms are uncommon. This may be due to the very slow dissociation of buprenorphine from the opioid receptors and to the gradual decrease of buprenorphine plasma concentrations (usually over a period of 30 hours after removal of the last patch).

Reporting suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Alternatively report to: ZADrugSafety@mundipharma.co.za

4.9 Overdose

The manifestations of SOVENOR® overdose is an extension of its pharmacological actions.

Respiratory depression has been absent in some cases of buprenorphine overdose.

Respiratory depression, including apnoea, may occur in other overdose situations. Additional symptoms include sedation, drowsiness, nausea, vomiting, cardiovascular collapse and marked miosis.

Remove any SOVENOR® in contact with the patient and dispose of it properly.

Establish and maintain a patent airway, assist and control respiration as indicated, and maintain adequate body temperature and fluid balance. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated.

A specific opioid antagonist such as naloxone may reverse the effects of buprenorphine, although naloxone may be less effective in reversing the effects of buprenorphine than other μ-opioid agonists. Treatment with continuous intravenous naloxone should begin with the usual doses but high doses may be required.

Maintenance of adequate ventilation is essential when managing a SOVENOR® overdose and more important than specific antidote treatment with a narcotic antagonist such as naloxone.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A 2.7 Narcotic analgesics

ATC code: N02 AE01

Buprenorphine is an opioid analgesic that is an agonist to the μ-opioid receptor and an antagonist at the kappa-opioid receptor.

5.2 Pharmacokinetic properties

Each buprenorphine base transdermal patch provides a steady delivery of buprenorphine for up to 7 days. Steady state is achieved during the first application. After removal of buprenorphine base transdermal patch, buprenorphine concentrations initially decline at a rate of approximately 50 % in 12 hours. Thereafter, mean elimination half-lives have been reported to be between 30 and 45 hours.

Absorption

The absorption does not vary significantly across the specified application sites. Mean exposure (AUC) at each of the application sites is within approximately ± 11 % of the mean exposure for the four sites.

Following buprenorphine base transdermal patch application, buprenorphine diffuses from the patch through the skin.

Buprenorphine metabolism in the skin following buprenorphine base transdermal patch application is negligible.

Distribution

Buprenorphine is approximately 96 % bound to plasma proteins.

Biotransformation

Norbuprenorphine, is the only known active metabolite of buprenorphine.

5.3 Preclinical safety data

Systemic toxicity and dermal toxicity

In single- and repeat-dose toxicity studies in rats, rabbits, guinea pigs, dogs and minipigs, buprenorphine base transdermal patch caused minimal or no adverse systemic events, whereas skin irritation was observed in all species examined. Toxicological data available did not indicate a sensitising potential of the additives of the transdermal patches.

Genotoxicity and carcinogenicity

A standard battery of genotoxicity tests indicated that buprenorphine is non-genotoxic. In long-term studies in rats and mice there was no evidence of any carcinogenic potential relevant to humans.

Reproductive and developmental toxicity

No effect on fertility or general reproductive performance was observed in rats treated with buprenorphine. No embryo-foetal toxicity effects were observed in rats or rabbits. In a rat pre- and post-natal development toxicity study with buprenorphine there was pup mortality and decreased pup body weight at maternal doses that produced a reduction in food consumption and clinical signs.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Levulinic acid, oleyl oleate, polyacrylate (dry solids), polyethylene terephthalate (PET) and povidone (PVP).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

SOVENOR® 5: 24 months

SOVENOR® 10: 36 months

SOVENOR® 20: 36 months

6.4 Special precautions for storage

Store at or below 25 °C. Store in original package.

6.5 Nature and contents of container

One transdermal patch packed into a heat sealed protective pouch composed of composite material: either paper, LDPE film, aluminium and ethylene copolymer (Composite 1); or paper, PET, polyethylene, aluminium and ethylene copolymer (Composite 2).

Two or four individually sealed pouches are packed into one outer carton.

6.6 Special precautions for disposal

No special requirements

7 HOLDER OF CERTIFICATE OF REGISTRATION

Mundipharma (Pty) Ltd

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Park Lane

Century City, Cape Town

7441

South Africa

8 REGISTRATION NUMBERS

South Africa: S6

SOVENOR® 5 Patch: 41/2.7/0589

SOVENOR® 10 Patch: 41/2.7/0590

SOVENOR® 20 Patch: 41/2.7/0591

Namibia: NS4

SOVENOR® 5 Patch: 12/2.7/0253

SOVENOR® 10 Patch: 12/2.7/0254

SOVENOR® 20 Patch: 12/2.7/0255

Botswana: S1B

SOVENOR® 5 Patch: BOT1402610B

SOVENOR® 10 Patch: BOT1402611B

SOVENOR® 20 Patch: BOT1402612B

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17 April 2009

10 DATE OF REVISION OF THE TEXT

18 July 2025

® = SOVENOR is a registered trademark