PROFESSIONAL INFORMATION

SCHEDULING STATUS

S5

1 NAME OF THE MEDICINE

VICTONEX 0,5 mg, film coated tablet

VICTONEX 1 mg, film coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

VICTONEX 0,5 mg, film coated tablet

Each film coated tablet contains 0,855 mg of varenicline tartrate equivalent to 0,5 mg of varenicline free base

VICTONEX 1 mg, film coated tablet

Each film coated tablet contains 1,710 mg of varenicline tartrate equivalent to 1 mg of varenicline free base

Sugar free

'for full list of excipients, see section 6.1'

3 PHARMACEUTICAL FORM

Film coated tablets

VICTONEX 0,5 mg, film coated tablet

Pink, capsular, biconvex, film coated tablets debossed with 'H' on one side and 'V23' on the other side.

VICTONEX 1 mg, film coated tablet

Yellow, capsular, biconvex, film coated tablets debossed with 'H' on one side and 'V24' on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

VICTONEX is indicated as an aid to smoking cessation in patients committed to stop smoking, in addition to a behaviour modification programme, for 12 weeks.

4.2 Posology and method of administration

All smoking cessation therapies are more likely to succeed in patients who are motivated to stop smoking and who are provided with additional advice and continuous support.

Patients should be treated with VICTONEX for 12 weeks.

Posology

The recommended dose of VICTONEX is 1 mg twice daily

following a 1-week titration as follows:

Day 1 -3	0,5 mg once daily in the evening
Day 4 -7	0,5 mg twice daily
Day 8 -End of treatment	1 mg twice daily

The patient should set the date to stop smoking. VICTONEX dosing should start 1 – 2 weeks before this date.

Patients who do not succeed in stopping smoking during 12 weeks of initial therapy, or who relapse after treatment, should be encouraged to make another attempt once factors contributing to the failed attempt have been identified and addressed.

For patients who have successfully stopped smoking at the end of 12 weeks, an additional course of 12 weeks of treatment with VICTONEX at 1 mg twice daily may be considered for the maintenance of abstinence.

A gradual approach to quitting smoking with VICTONEX should be considered for patients who are not able or willing to quit abruptly. Patients should reduce smoking during the first 12 weeks of treatment and quit

by the end of that treatment period. Patients should then continue taking VICTONEX for an additional 12 weeks for a total of 24 weeks of treatment.

Patients who cannot tolerate adverse reactions of VICTONEX may have the dose lowered temporarily or permanently.

Dose tapering of VICTONEX is not required at the end of treatment.

Special populations

Patients with renal insufficiency

No dosage adjustment is necessary for patients with mild (estimated creatinine clearance > 50 mL/min and ≤ 80 mL/min) to moderate (estimated creatinine clearance ≥ 30 mL/min and ≤ 50 mL/min) renal impairment. For patients with severe renal impairment, the recommended dose of VICTONEX is 1 mg once daily. Dosing should begin at 0,5 mg once daily for the first 3 days, then increased to 1 mg once daily. There is insufficient clinical experience with VICTONEX in patients with end-stage renal disease (see section 5.2).

Patients with hepatic impairment

No dosage adjustment is necessary for patients with hepatic impairment (see section 5.2).

Use in elderly patients

No dosage adjustment is necessary for elderly patients (see section 5.2).

Because elderly patients are more likely to have decreased renal function, medical practitioners should consider the renal status of an elderly patient.

Paediatric population

Safety and effectiveness of VICTONEX in paediatric patients have not been established; therefore, VICTONEX is not recommended for use in patients under 18 years of age (see section 5.2).

Method of administration

For oral use and the tablets should be swallowed whole with water.

VICTONEX can be taken with or without food.

4.3 Contraindications

Hypersensitivity to varenicline or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Effect of smoking cessation

Physiological changes resulting from smoking cessation, with or without treatment with VICTONEX, may alter the pharmacokinetics or pharmacodynamics of some medicines, for which dosage adjustment may be necessary (examples include theophylline, warfarin and insulin). However, in post-marketing data there were cases of increased international normalised ratio (INR). INR should be monitored more frequently, and the warfarin dose adjusted while using VICTONEX, and after discontinuation of VICTONEX (see section 4.5).

Neuropsychiatric symptoms and suicidality

Serious neuropsychiatric symptoms have been reported in patients being treated with varenicline. These post-marketing reports have included changes in behaviour or thinking, changes in mood (including depression and mania), aggressive behaviour, psychosis, hallucinations, paranoia, delusions, homicidal ideation, hostility, agitation, anxiety, and panic, as well as suicidal ideation, suicide attempt, and completed suicide (see section 4.8 – post-marketing experience). Some reported cases may have been complicated by the symptoms of nicotine withdrawal in patients who stopped smoking.

Depressed mood may be a symptom of nicotine withdrawal. Depression, including suicidal ideation, has been reported in smokers undergoing a smoking cessation attempt without medication. However, some of these symptoms have occurred in patients taking varenicline who continued to smoke. When symptoms

were reported, most were during varenicline treatment, but some were following discontinuation of varenicline therapy. These events have occurred in patients with and without pre-existing psychiatric disease; some patients have experienced worsening of their psychiatric illnesses. All patients being treated with VICTONEX should be observed for neuropsychiatric symptoms or worsening of pre-existing psychiatric illness.

Advise patients and caregivers that the patient should stop taking VICTONEX and contact a medical practitioner immediately if agitation, depressed mood, changes in behaviour or thinking that are not typical for the patient are observed, or if the patient develops suicidal ideation or suicidal behaviour. In many post-marketing cases, resolution of symptoms after discontinuation of varenicline was reported, although in some cases the symptoms persisted, therefore, ongoing monitoring and supportive care should be provided until symptoms resolve.

Medical practitioners should be aware of the possible emergence of serious neuropsychiatric symptoms in patients attempting to quit smoking with or without treatment. If serious neuropsychiatric symptoms occur whilst on VICTONEX, patients should discontinue VICTONEX immediately and contact a medical practitioner for re-evaluation of treatment.

History of psychiatric disorders

Smoking cessation, with or without pharmacotherapy, has been associated with exacerbation of underlying psychiatric illness (e.g. depression). varenicline smoking cessation studies have provided data in patients with a history of psychiatric disorders (see section 5.1). In a smoking cessation clinical trial, neuropsychiatric adverse events were reported more frequently in patients with a history of psychiatric disorders compared to those without a history of psychiatric disorders, regardless of treatment (see section 5.1). Care should be taken with patients with a history of psychiatric illness and patients should be advised accordingly.

Seizures

In clinical trials and post-marketing experience there have been reports of seizures in patients with or without a history of seizures, treated with varenicline. VICTONEX should be used cautiously in patients with a history of seizures or other conditions that potentially lower the seizure threshold.

Treatment discontinuation

At the end of treatment, discontinuation of varenicline was associated with an increase in irritability, urge to smoke, depression, and/or insomnia in up to 3 % of patients. The prescriber should inform the patient accordingly and discuss or consider the need for dose tapering.

Angioedema and hypersensitivity reactions

There have been post-marketing reports of hypersensitivity reactions including angioedema in patients treated with varenicline (see section 4.8 –post-marketing experience). Clinical signs included swelling of the face, mouth (tongue, lips, and gums), extremities, and neck (throat and larynx). There were reports of life-threatening angioedema requiring urgent medical attention due to respiratory compromise. Patients should be instructed to discontinue VICTONEX and immediately seek medical care if they experience these symptoms.

Serious skin reactions

There have been post-marketing reports of serious skin reactions, including Stevens-Johnson Syndrome and Erythema Multiforme in patients using varenicline (see section 4.8 – post-marketing experience). As these skin reactions can be life-threatening, patients should be instructed to stop taking VICTONEX and contact their medical practitioner immediately at the first appearance of a skin rash with mucosal lesions or any other signs of seizures or other conditions that potentially lower the seizure threshold.

Cardiovascular effects

In a smoking cessation trial of patients with stable cardiovascular disease, cardiovascular events were reported more frequently in patients treated with varenicline. A meta-analysis of 15 clinical trials, which included the smoking cessation trial of patients with stable cardiovascular disease, had similar results. Cardiovascular events occurred primarily in patients with known cardiovascular disease. Patients should be instructed to notify their medical practitioners of new or worsening cardiovascular symptoms and to seek immediate medical attention if they experience signs and symptoms of myocardial infarction or stroke.

4.5 Interaction with other medicines and other forms of interaction

Based on varenicline characteristics and clinical experience to date, VICTONEX has no clinically meaningful medicine interactions. No dosage adjustment of VICTONEX or co-administered medicine listed below is recommended.

In vitro studies demonstrate that varenicline does not inhibit cytochrome P450 enzymes (IC50 > 6 400 ng/mL). The P450 enzymes tested for inhibition were: 1A2, 2A6, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1, and 3A4/5. Also, in human hepatocytes *in vitro*, VICTONEX was shown to not induce the activity of cytochrome P450 enzymes 1A2 and 3A4. Therefore, VICTONEX is unlikely to alter the pharmacokinetics of compounds that are primarily metabolised by cytochrome P450 enzymes.

Furthermore, since metabolism of VICTONEX represents less than 10 % of its clearance, active substances known to affect the cytochrome P450 system are unlikely to alter the pharmacokinetics of VICTONEX and therefore a dose adjustment of VICTONEX would not be required.

In vitro studies demonstrate that varenicline does not inhibit human renal transport proteins at therapeutic concentrations. Therefore, medicines that are cleared by renal secretion (e.g. metformin – see below) are unlikely to be affected by VICTONEX.

In vitro studies demonstrate that active renal secretion of varenicline is mediated by the human organic cation transporter, OCT2. Co-administration with inhibitors of OCT2 does not require a dose adjustment of VICTONEX as the increase in systemic exposure to varenicline is not expected to be clinically meaningful (see cimetidine interaction below). Furthermore, since metabolism of VICTONEX represents less than 10

% of its clearance, medicines known to affect the cytochrome P450 system are unlikely to alter the pharmacokinetics of VICTONEX (see section 5.2) and therefore a dose adjustment of VICTONEX would not be required.

Metformin

Varenicline (1 mg twice daily) did not affect the pharmacokinetics of metformin (500 mg twice daily), which is a substrate of the organic cation transporter, OCT2. Metformin had no effect on varenicline pharmacokinetics.

Cimetidine

Co-administration of an OCT2 inhibitor, cimetidine (300 mg four times daily), with varenicline (2 mg single dose) increased the systemic exposure of varenicline by 29 % due to a reduction in varenicline renal clearance. No dosage adjustment is recommended based on concomitant cimetidine administration.

Digoxin

Varenicline (1 mg twice daily) did not alter the steady-state pharmacokinetics of digoxin administered as a 0,25 mg daily dose.

Warfarin

Varenicline (1 mg twice daily) did not alter the pharmacokinetics of a single 25 mg dose of (R, S)-warfarin. Prothrombin time (INR) was not affected by varenicline. Smoking cessation itself may result in changes to warfarin pharmacokinetics. However, in post-marketing data there were cases of increased INR. INR should be monitored more frequently, and the warfarin dose adjusted while using VICTONEX, and after discontinuation of VICTONEX (see section 4.4).

Alcohol

There are limited clinical data on any potential interaction between alcohol and VICTONEX. There have been post marketing reports of increased intoxicating effects of alcohol in patients treated with varenicline. A causal relationship between these events and VICTONEX use has not been established. Some cases described unusual and sometimes aggressive behaviour and were often accompanied by amnesia for the events. Advise patients to reduce the amount of alcohol they consume while taking VICTONEX until they know whether VICTONEX affects their tolerance for alcohol.

Use with other therapies for smoking cessation

Bupropion

Varenicline (1 mg twice daily) did not alter the steady-state pharmacokinetics of bupropion (150 mg twice daily). However, the incidence of nausea was doubled with co-administration.

Nicotine replacement therapy (NRT)

When varenicline (1 mg twice daily) and NRT (transdermal 21 mg/day) were co-administered to smokers (N=24) for 12 days, there was a statistically significant decrease in average systolic blood pressure (mean 2,6 mmHg) measured on the final day of the study. In this study, the incidence of nausea, headache, vomiting, dizziness, dyspepsia, and fatigue was greater for the combination than for NRT alone.

Safety and efficacy of VICTONEX in combination with other smoking cessation therapies have not been studied.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Where therapy is initiated, treatment should be timed such that the course is completed before conception occurs.

Pregnancy

The safety of VICTONEX in human pregnancy has not been established. The use of VICTONEX in pregnant women is not recommended.

Varenicline was not teratogenic in rats and rabbits at oral doses up to 15 and 30 mg/kg/day, respectively (36 and 50-times the maximum recommended human daily exposure based on AUC at 1 mg BD, respectively).

Breastfeeding

The safety of VICTONEX during lactation has not been established. Mothers on VICTONEX should therefore not breastfeed their infants.

Fertility

There are no clinical data on the effects of varenicline on fertility.

Non-clinical data revealed no hazard for humans based on standard male and female fertility studies in the rat (see section 5.3).

4.7 Effects on ability to drive and use machines

VICTONEX may have minor or moderate influence on the ability to drive and use machines. VICTONEX may cause dizziness, somnolence and transient loss of consciousness, and therefore may influence the ability to drive and use machines.

Patients should be advised to use caution driving or operating machinery until they know how quitting smoking and/or VICTONEX may affect them.

4.8 Undesirable effects

Summary of the safety profile

Smoking cessation with or without treatment is associated with varioussymptoms. For example, dysphoric or depressed mood, insomnia, irritability, frustration or anger, anxiety, difficulty concentrating, restlessness,

decreased heart rate, increased appetite or weight gain have been reported in patients attempting to stop smoking. No attempt has been made in either the design or the analysis of the VICTONEX studies to distinguish between adverse events associated with study drug treatment or those possibly associated with nicotine withdrawal. In patients treated with the recommended dose of 1 mg twice daily following an initial titration period the adverse event most commonly reported was nausea (28,6 %). In the majority of cases nausea occurred early in the treatment period, was mild to moderate in severity.

Tabulated summary of adverse reactions

SYSTEM ORGAN CLASS	**FREQUENCY**	**ADVERSE REACTION**
Infections and infestations	Frequent	Nasopharyngitis, bronchitis, sinusitis
	Less frequent	Fungal infection, viral infection
Blood and lymphatic system disorders	Less frequent	Decreased platelet count
Metabolism and nutrition disorders	Frequent	Weight increased, decreased appetite, increased appetite
	Less frequent	Hyperglycaemia, diabetes mellitus, polydipsia
Psychiatric disorders	Frequent	Abnormal dreams, insomnia
	Less frequent	Suicidal ideation, aggression, panic reaction, thinking abnormal, restlessness, mood swings, depression*, anxiety*, hallucinations*, libido increased, libido decreased, psychosis, somnambulism, abnormal behaviour, dysphoria, bradyphrenia
	Frequent	Headache, somnolence, dizziness, dysgeusia

Nervous system disorders	Less frequent	Seizure, tremor, lethargy, hypoaesthesia, cerebrovascular accident, hypertonia, dysarthria, coordination abnormal, hypogeusia, circadian rhythm sleep disorder
	Frequency unknown	Transient loss of consciousness
Eye disorders	Less frequent	Conjunctivitis, eye pain, scotoma, scleral discolouration, mydriasis, photophobia, myopia, lacrimation increased
Ear and labyrinth disorders	Less frequent	Tinnitus
Cardiac disorders	Less frequent	Myocardial infarction, angina pectoris, tachycardia, palpitations, heart rate increased, atrial fibrillation, electrocardiogram ST segment depression, electrocardiogram T wave amplitude decreased
Vascular disorders	Less frequent	Blood pressure increased, hot flush
Respiratory, thoracic and mediastinal disorders	Frequent	Dyspnoea, cough
	Less frequent	Upper respiratory tract inflammation, respiratory tract congestion, dysphonia, rhinitis allergic, throat irritation, sinus congestion, upper- airway cough syndrome, rhinorrhoea, laryngeal pain, snoring
Gastrointestinal disorders	Frequent	Nausea, gastrooesophageal reflux disease, vomiting, constipation, diarrhoea, abdominal distension, abdominal pain, toothache,

		dyspepsia, flatulence, dry mouth, stomach discomfort.
	Less frequent	Haematochezia, gastritis, change of bowel habit, eructation, aphthous stomatitis, gingival pain, haematemesis, abnormal faeces, tongue coated
Skin and subcutaneous tissue disorders	Frequent	Rash, pruritus
	Less frequent	Erythema, acne, hyperhidrosis, night sweats, severe cutaneous reactions, including Stevens Johnson Syndrome and Erythema Multiforme, angioedema
Musculoskeletal and connective tissue disorders	Frequent	Arthralgia, myalgia, back pain
	Less frequent	Muscle spasms, musculoskeletal chest pain, joint stiffness, costochondritis
Renal and urinary disorders	Less frequent	Pollakiuria, nocturia, glycosuria, polyuria
Reproductive system and breast disorders	Less frequent	Menorrhagia, vaginal discharge, sexual dysfunction
General disorders and administration site conditions	Frequent	Chest pain, fatigue
	Less frequent	Chest discomfort, influenza like illness, pyrexia, asthenia, malaise, feeling cold, cyst
Investigations	Frequent	Liver function test abnormal
	Less frequent	Semen analysis abnormal, C-reactive protein increased, blood calcium decreased

Post-marketing experience

The following adverse events have been reported during post-approval use of varenicline. Because these events are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to medicine exposure.

There have been reports of depression, mania, psychosis, hallucinations, paranoia, delusions, homicidal ideation, aggression, hostility, anxiety, and panic, as well as suicidal ideation, suicide attempt, completed suicide, mood swings, nightmares, insomnia, aggressiveness, suicidal tendency, irritability, abnormal dreaming, abnormal behaviour, psychotic reaction NOS, personality disorder, depressed mood, impaired concentration, agitation, sleepiness, emotional disorder, increased appetite, aggressive reaction, disturbed sleep, reaction, memory loss, forgetfulness, absence of appetite, anger, nervousness, mood disorder, abnormal mental state, drowsiness, confusion, abnormal thinking, sleeplessness, sleep disorder, sleep difficulty, impulsive behaviour, abnormal hunger, emotional lability, disorientation, aggravated depression, depressed state, depressed reaction, completed suicide, acute stress reaction, thoughts of self-harm, irrational thinking, suicide, marked restlessness, nervous tension, narcolepsy, mental impairment, mental disorder, memory impairment, memory disturbance, manic reaction, lethargy, lack of motivation, jitteriness, intentional self-injury, hypersomnia, auditory hallucination, flat effect, feeling strange, feeling high, feeling detached, euphoria, dissociative disorder, delirium, character change, bipolar disorder, loss of appetite, impaired appetite, decreased appetite, apathy, anti-social behaviour and acute stress disorder in patients attempting to quit smoking while taking varenicline (see section 4.4).

Smoking cessation with or without treatment is associated with nicotine withdrawal symptoms and the exacerbation of underlying psychiatric illness.

Not all patients had known pre-existing psychiatric illness and not all had discontinued smoking.

There have been reports of hypersensitivity reactions, including angioedema. Clinical signs included swelling of the face, mouth (tongue, lips, and gums), extremities, and neck (throat and larynx) (see section 4.4).

There have also been reports of serious skin reactions, including Stevens Johnson Syndrome and Erythema Multiforme in patients taking varenicline (see section 4.4).

There have been reports of seizures, feeling abnormal and crying.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of VICTONEX 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 or to the Holder of certificate of registration through the mail: pvg.cdma@heterogroups.com.

4.9 Overdose

No cases of overdose were reported in pre-marketing clinical trials. In case of overdose, standard supportive measures should be instituted as required.

Varenicline has been shown to be dialyzed in patients with end stage renal disease (see section 5.2), however, there is no experience in dialysis following overdose.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other nervous system drugs; Drugs used in addictive disorders; Drugs used in nicotine dependence, ATC code: N07BA03

Category and class: A 34 Other

Mechanism of action

Varenicline binds with high affinity and selectivity at the α4β2 neuronal nicotinic acetylcholine receptors, where it acts as a partial agonist a compound that has both agonist activity, with lower intrinsic efficacy than nicotine, and antagonist activities in the presence of nicotine.

Electrophysiology studies in vitro and neurochemical studies *in vivo* have shown that varenicline binds to the α4β2 neuronal nicotinic acetylcholine receptors and stimulates receptor-mediated activity, but at a significantly lower level than nicotine. Nicotine competes for the same human α4β2 nAChR binding site for which varenicline has higher affinity. Therefore, varenicline can effectively block nicotine's ability to fully activate α4β2 receptors and the mesolimbic dopamine system, the neuronal mechanism underlying reinforcement and reward experienced upon smoking. Varenicline is highly selective and binds more potently to the α4β2 receptor subtype (Ki=0.15 nM) than to other common nicotinic receptors (α3β4 Ki=84 nM, α7 Ki= 620 nM, α1βγδ Ki= 3,400 nM), or to non-nicotinic receptors and transporters (Ki > 1μM, except to 5-HT3 receptors: Ki=350 nM).

Pharmacodynamic effects

The efficacy of varenicline in smoking cessation is a result of varenicline's partial agonist activity at the α4β2 nicotinic receptor where its binding produces an effect sufficient to alleviate symptoms of craving and withdrawal (agonist activity), while simultaneously resulting in a reduction of the rewarding and reinforcing effects of smoking by preventing nicotine binding to α4β2 receptors (antagonist activity).

Clinical efficacy and safety

Smoking cessation therapies are more likely to succeed for patients who are motivated to stop smoking and who are provided with additional advice and support.

The efficacy of varenicline in smoking cessation was demonstrated in 3 clinical trials involving chronic cigarette smokers (≥ 10 cigarettes per day).

Two thousand six hundred nineteen (2619) patients received varenicline 1 mg BID (titrated during the first week), 669 patients received bupropion 150 mg BID (also titrated) and 684 patients received placebo.

5.2 Pharmacokinetic properties

Absorption

Maximum plasma concentrations of varenicline occur typically within 3 – 4 hours after oral administration. Following administration of multiple oral doses to healthy volunteers, steady-state conditions were reached within 4 days. Absorption is virtually complete after oral administration and systemic availability is high. Oral bioavailability of varenicline is unaffected by food or time-of-day dosing.

Distribution

Varenicline distributes into tissues, including the brain. Apparent volume of distribution averaged 415 L (% CV= 50) at steady state. Plasma protein binding of varenicline is low (≤ 20 %) and independent of both age and renal function.

Biotransformation

Varenicline undergoes minimal metabolism with 92 % excreted unchanged in the urine and less than 10 % excreted as metabolites. Minor metabolites in urine include varenicline N carbamoylglucuronide and hydroxyvarenicline. In circulation, varenicline comprises 91 % of medicine-related material. Minor circulating metabolites include varenicline N-carbamoylglucuronide and N-glucosylvarenicline.

Elimination

The elimination half-life of varenicline is approximately 24 hours. Renal elimination of varenicline is primarily through glomerular filtration along with active tubular secretion via the organic cationic transporter, OCT2 (see section 4.5).

Linearity/Non-linearity

Varenicline exhibits linear kinetics when given as single (0,1 to 3 mg) or repeated 1 to 3 mg/day doses.

Pharmacokinetics in special patient populations

There are no clinically meaningful differences in varenicline pharmacokinetics due to age, race, gender, smoking status, or use of concomitant medicines, as demonstrated in specific pharmacokinetic studies and in population pharmacokinetic analyses.

Hepatic impairment

Due to the absence of significant hepatic metabolism, varenicline pharmacokinetics should be unaffected in patients with hepatic impairment (see section 4.2).

Renal insufficiency

Varenicline pharmacokinetics were unchanged in subjects with mild renal impairment (estimated creatinine clearance > 50 mL/min and ≤ 80 mL/min). In patients with moderate renal impairment (estimated creatinine clearance ≥ 30 mL/min and ≤ 50 mL/min), varenicline exposure increased 1,5-fold compared with subjects with normal renal function (estimated creatinine clearance > 80 mL/min). In subjects with severe renal impairment (estimated creatinine clearance < 30 mL/min), varenicline exposure was increased 2,1-fold. In subjects with end-stage-renal disease (ESRD), varenicline was removed by haemodialysis. No dosing adjustment is necessary for patients with mild to moderate renal impairment and a reduced dosing frequency of 1 mg once daily is recommended for patients with severe renal impairment (see section 4.2). Dosing should begin at 0,5 mg once daily for the first 3 days, and then increased to 1 mg once daily.

Elderly

No dosage adjustment is necessary for elderly patients (see section 4.2). A combined single and multiple-dose pharmacokinetic study demonstrated that the pharmacokinetics of 1 mg varenicline given once or twice daily to 16 healthy elderly male and female smokers (aged 65 – 75 yrs) for 7 consecutive days was similar to that of younger subjects. For elderly patients with reduced renal function please refer to section 4.2.

Paediatric population

Because the safety and effectiveness of varenicline in paediatric patients have not been established, varenicline is not recommended for use in patients under 18 years of age (see section 4.2).

5.3 Preclinical safety data

Not applicable

6.PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose

Anhydrous dibasic calcium phosphate,

Croscarmellose Sodium

Ferric oxide

Colloidal Silicon Dioxide

Magnesium stearate

Opadry pink

Opadry yellow

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 °C.

Protect from moisture

HDPE bottles and blister strips are enclosed in an outer carton.

Keep the blister strips in outer carton until required for use.

Keep the HDPE container tightly closed.

6.5 Nature and contents of container

HDPE bottle:

White opaque high-density polyethylene (HDPE) bottle, closed with a child resistant plastic cap with pulp liner, containing desiccant 2,0 gramme silica gel canister.

Pack sizes: 56 tablets.

Blister strips:

Clear transparent, thermoformable, and rigid PVC film laminated with ACLAR Plain Peel-Push Through foil /Hard tampered plain aluminium foil with HSL coating on bright side.

Pack size: 14 tablets per blister, 15 blisters packed in a box

Not all pack sizes may be marketed

7. Name and business address of the holder of the certificate of registration

Hetero Drugs South Africa (Pty) Ltd.

Waterfall corporate campus,

Building no. 2, first floor,

74 Waterfall Drive, Midrand 2066.

Tel.: 0126441220.

8. REGISTRATION NUMBER

VICTONEX 0,5 mg: 57/34/0875.873

VICTONEX 1 mg: 57/34/0876.874

9. DATE OF FIRST AUTHORISATION

26 NOVEMBER 2025

10. DATE OF REVISION OF TEXT

N/A

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