For the use only of Registered Medical Practitioner

1. Generic Name and Brand Name

Sildenafil & Dapoxetine Tablets
VICOGRA™ FORCE

2. Qualitative and Quantitative Composition:

Each film coated tablet contains:
Sildenafil Citrate I.P.
eq. to Sildenafil……50 mg
Dapoxetine Hydrochloride I.P.
eq. to Dapoxetine…….30 mg
Colours: Lake Brilliant Blue FCF & Titanium Dioxide I.P.

3. Dosage Form & strength

Refer section 1 & 2

4. Clinical particulars

4.1 Therapeutic indication

For the treatment of co-existing Erectile Dysfunction and Premature Ejaculation in men 18 to 64 years of age.

4.2 Posology and method of administration

Posology
Taken once per day on an as-needed basis 1 to 3 hours before sexual intercourse.
Method of administration: For oral use only.
Taken by mouth with a glass of water taken once per day on an as-needed basis 1 to 3 hours before sexual intercourse. Do not take the dose more than once per day

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.
Consistent with its known effects on the nitric oxide/cyclic guanosine monophosphate (cGMP) pathway, sildenafil was shown to potentiate the hypotensive effects of nitrates, and its co-administration with nitric oxide donors (such as amyl nitrite) or nitrates in any form is therefore contraindicated.
The co-administration of PDE5 inhibitors, including sildenafil, with guanylate cyclase stimulators, such as riociguat, is contraindicated as it may potentially lead to symptomatic hypotension.
Agents for the treatment of erectile dysfunction, including sildenafil, should not be used in men for whom sexual activity is inadvisable (e.g. patients with severe cardiovascular disorders such as unstable angina or severe cardiac failure).
Sildenafil is contraindicated in patients who have loss of vision in one eye because of non-arteritic anterior ischaemic optic neuropathy (NAION), regardless of whether this episode was in connection or not with previous PDE5 inhibitor exposure.
The safety of sildenafil has not been studied in the following sub-groups of patients and its use is therefore contraindicated: severe hepatic impairment, hypotension (blood pressure <90/50 mmHg), recent history of stroke or myocardial infarction and known hereditary degenerative retinal disorders such as retinitis pigmentosa (a minority of these patients have genetic disorders of retinal phosphodiesterases).
Significant pathological cardiac conditions such as:

• Heart failure (NYHA class II-IV)
• Conduction abnormalities such as AV block or sick sinus syndrome
• Significant ischemic heart disease
• Significant valvular disease
• A history of syncope.
A history of mania or severe depression.
Concomitant treatment with monoamine oxidase inhibitors (MAOIs), or within 14 days of discontinuing treatment with an MAOI. Similarly, an MAOI should not be administered within 7 days after Dapoxetine has been discontinued.
Concomitant treatment with thioridazine, or within 14 days of discontinuing treatment with thioridazine. Similarly, thioridazine should not be administered within 7 days after Dapoxetine has been discontinued.
Concomitant treatment with serotonin reuptake inhibitors [selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs)] or other medicinal/herbal products with serotonergic effects [e.g., L-tryptophan, triptans, tramadol, linezolid, lithium, St. John's Wort (*Hypericum perforatum*)] or within 14 days of discontinuing treatment with these medicinal/herbal products. Similarly, these medicinal/herbal products should not be administered within 7 days after Dapoxetine has been discontinued.
Concomitant treatment of potent CYP3A4 inhibitors such as ketoconazole, itraconazole, ritonavir, saquinavir, telithromycin, nefazadone, nelfinavir, atazanavir, etc.
Moderate and severe hepatic impairment.

4.4 Special warnings and precautions for use

Sildenafil

A medical history and physical examination should be undertaken to diagnose erectile dysfunction and determine potential underlying causes, before pharmacological treatment is considered.

Cardiovascular risk factors

Prior to initiating any treatment for erectile dysfunction, physicians should consider the cardiovascular status of their patients, since there is a degree of cardiac risk associated with sexual activity. Sildenafil has vasodilator properties, resulting in mild and transient decreases in blood pressure. Prior to prescribing sildenafil, physicians should carefully consider whether their patients with certain underlying conditions could be adversely affected by such vasodilatory effects, especially in combination with sexual activity. Patients with increased susceptibility to vasodilators include those with left ventricular outflow obstruction (e.g., aortic stenosis, hypertrophic obstructive cardiomyopathy), or those with the rare syndrome of multiple system atrophy manifesting as severely impaired autonomic control of blood pressure.
Sildenafil potentiates the hypotensive effect of nitrates.
Serious cardiovascular events, including myocardial infarction, unstable angina, sudden cardiac death, ventricular arrhythmia, cerebrovascular haemorrhage, transient ischaemic attack, hypertension and hypotension have been reported post-marketing in temporal association with the use of Sildenafil. Most, but not all, of these patients had pre-existing cardiovascular risk factors. Many events were reported to occur during or shortly after sexual intercourse and a few were reported to occur shortly after the use of Sildenafil without sexual activity. It is not possible to determine whether these events are related directly to these factors or to other factors.

Prolonged Erection and Priapism

Prolonged erection (greater than 4 hours) and priapism (painful erections greater than 6 hours in duration) have been reported infrequently since market approval of Sildenafil. In the event of an erection that persists longer than 4 hours, the patient should seek immediate medical assistance. If priapism is not treated immediately, penile tissue damage and permanent loss of potency could result.

Sildenafil should be used with caution in patients with anatomical deformation of the penis (such as angulation, cavernosal fibrosis or Peyronie's disease), or in patients who have conditions which may predispose them to priapism (such as sickle cell anemia, multiple myeloma, or leukemia). However, there are no controlled clinical data on the safety or efficacy of Sildenafil in patients with sickle cell or related anemias.

Concomitant use with other PDE5 inhibitors or other treatments for erectile dysfunction

The safety and efficacy of combinations of sildenafil with other PDE5 inhibitors, or other pulmonary arterial hypertension (PAH) treatments containing sildenafil (REVATIO), or other treatments for erectile dysfunction have not been studied. Therefore the use of such combinations is not recommended.

Effects on vision

Cases of visual defects have been reported spontaneously in connection with the intake of sildenafil and other PDE5 inhibitors. Cases of non-arteritic anterior ischaemic optic neuropathy, a rare condition, have been reported spontaneously and in an observational study in connection with the intake of sildenafil and other PDE5 inhibitors. Patients should be advised that in the event of any sudden visual defect, they should stop taking sildenafil and consult a physician immediately.

Concomitant use with ritonavir

Co-administration of sildenafil with ritonavir is not advised.

Concomitant use with alpha-blockers

Caution is advised when sildenafil is administered to patients taking an alpha-blocker, as the coadministration may lead to symptomatic hypotension in a few susceptible individuals. This is most likely to occur within 4 hours post sildenafil dosing. In order to minimise the potential for developing postural hypotension, patients should be hemodynamically stable on alpha-blocker therapy prior to initiating sildenafil treatment. Initiation of sildenafil at a dose of 25mg should be considered. In addition, physicians should advise patients what to do in the event of postural hypotensive symptoms.

Effect on bleeding

Studies with human platelets indicate that sildenafil potentiates the antiaggregatory effect of sodium nitroprusside in vitro. There is no safety information on the administration of sildenafil to patients with bleeding disorders or active peptic ulceration. Therefore, sildenafil should be administered to these patients only after careful benefit-risk assessment.

Women

Sildenafil is not indicated for use by women.

Counseling Patients about Sexually Transmitted Diseases

The use of Sildenafil offers no protection against sexually transmitted diseases. Counseling of patients about the protective measures necessary to guard against sexually transmitted diseases, including the Human Immunodeficiency Virus (HIV), may be considered.

Dapoxetine

General recommendations

Dapoxetine is only indicated in men with Premature Ejaculation who meet all the criteria listed in sections 4.1 and 5.1. Dapoxetine should not be prescribed to men who have not been diagnosed with Premature Ejaculation. Safety has not been established and there are no data on the ejaculation-delaying effects in men without Premature Ejaculation.

Other forms of sexual dysfunction

Before treatment, subjects with other forms of sexual dysfunction, including erectile dysfunction, should be carefully investigated by physicians. Dapoxetine should not be used in men with erectile dysfunction (ED) who are using PDE5 inhibitors.

Orthostatic hypotension

Before treatment initiation, a careful medical examination including history of orthostatic events should be performed by the physician. An orthostatic test should be performed before initiating therapy (blood

pressure and pulse rate, supine and standing). In case of a history of documented or suspected orthostatic reaction, treatment with Dapoxetine should be avoided.
Orthostatic hypotension has been reported in clinical trials. The prescriber should counsel the patient in advance that if he experiences possibly prodromal symptoms, such as lightheadedness soon after standing, he should immediately lie down so his head is lower than the rest of his body or sit down with his head between his knees until the symptoms pass. The prescriber should also inform the patient not to rise quickly after prolonged lying or sitting.

Suicide/suicidal thoughts

Antidepressants, including SSRIs, increased the risk compared to placebo of suicidal thinking and suicidality in short-term studies in children and adolescents with Major Depressive Disorder and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24. In clinical trials with Dapoxetine for the treatment of premature ejaculation, there was no clear indication of treatment-emergent suicidality in evaluation of possibly suicide-related adverse events evaluated by the Columbia Classification Algorhythm of Suicide Assessment (C-CASA), Montgomery-Asberg Depression Rating Scale, or Beck Depression Inventory-II.

Syncope

Patients should be cautioned to avoid situations where injury could result, including driving or operating hazardous machinery, should syncope or its prodromal symptoms such as dizziness or lightheadedness occur.
Possibly prodromal symptoms such as nausea, dizziness/lightheadedness, and diaphoresis were reported more frequently among patients treated with Dapoxetine compared to placebo.
In the clinical trials, cases of syncope characterized as loss of consciousness, with bradycardia or sinus arrest observed in patients wearing Holter monitors, were considered vasovagal in etiology and the majority occurred during the first 3 hours after dosing, after the first dose, or associated with study-related procedures in the clinic setting (such as blood draw and orthostatic maneuvers and blood pressure measurements). Possibly prodromal symptoms, such as nausea, dizziness, lightheadedness, palpitations, asthenia, confusion and diaphoresis generally occurred within the first 3 hours following dosing, and often preceded the syncope. Patients need to be made aware that they could experience syncope at any time with or without prodromal symptoms during their treatment with Dapoxetine. Prescribers should counsel patients about the importance of maintaining adequate hydration and about how to recognize prodromal signs and symptoms to decrease the likelihood of serious injury associated with falls due to loss of consciousness. If the patient experiences possibly prodromal symptoms, the patient should immediately lie down so his head is lower than the rest of his body or sit down with his head between his knees until the symptoms pass, and be cautioned to avoid situations where injury could result, including driving or operating hazardous machinery, should syncope or other CNS effects occur.

Patients with cardiovascular risk factors

Subjects with underlying cardiovascular disease were excluded from Phase 3 clinical trials. The risk of adverse cardiovascular outcomes from syncope (cardiac syncope and syncope from other causes) is increased in patients with underlying structural cardiovascular disease (e.g., documented outflow obstruction, valvular heart disease, carotid stenosis and coronary artery disease). There are insufficient data to determine whether this increased risk extends to vasovagal syncope in patients with underlying cardiovascular disease.

Use with recreational drugs

Patients should be advised not to use Dapoxetine in combination with recreational drugs.
Recreational drugs with serotonergic activity such as ketamine, methylenedioxymethamphetamine (MDMA) and lysergic acid diethylamide (LSD) may lead to potentially serious reactions if combined with Dapoxetine. These reactions include, but are not limited to, arrhythmia, hyperthermia, and serotonin

syndrome. Use of Dapoxetine with recreational drugs with sedative properties such as narcotics and benzodiazepines may further increase somnolence and dizziness.

Ethanol

Patients should be advised not to use Dapoxetine in combination with alcohol.

Combining alcohol with Dapoxetine may increase alcohol-related neurocognitive effects and may also enhance neurocardiogenic adverse events such as syncope, thereby increasing the risk of accidental injury; therefore, patients should be advised to avoid alcohol while taking Dapoxetine.

Medicinal products with vasodilatation properties

Dapoxetine should be prescribed with caution in patients taking medicinal products with vasodilatation properties (such as alpha adrenergic receptor antagonists and nitrates) due to possible reduced orthostatic tolerance.

Moderate CYP3A4 inhibitors

Caution is advised in patients taking moderate CYP3A4 inhibitors and the dose is restricted to 30 mg.

Potent CYP2D6 inhibitors

Caution is advised if increasing the dose to 60 mg in patients taking potent CYP2D6 inhibitors or if increasing the dose to 60 mg in patients known to be of CYP2D6 poor metabolizer genotype, as this may increase exposure levels, which may result in a higher incidence and severity of dose dependent adverse events.

Mania

Dapoxetine should not be used in patients with a history of mania/hypomania or bipolar disorder and should be discontinued in any patient who develops symptoms of these disorders.

Seizure

Due to the potential of SSRIs to lower the seizure threshold, Dapoxetine should be discontinued in any patient who develops seizures and avoided in patients with unstable epilepsy. Patients with controlled epilepsy should be carefully monitored.

Paediatric population

Dapoxetine should not be used in individuals below 18 years of age.

Depression and/or psychiatric disorders

Men with underlying signs and symptoms of depression should be evaluated prior to treatment with Dapoxetine to rule out undiagnosed depressive disorders. Concomitant treatment of Dapoxetine with antidepressants, including SSRIs and SNRIs, is contraindicated. Discontinuation of treatment for ongoing depression or anxiety in order to initiate Dapoxetine for the treatment of PE is not recommended. Dapoxetine is not indicated for psychiatric disorders and should not be used in men with these disorders, such as schizophrenia, or in those suffering with co-morbid depression, as worsening of symptoms associated with depression cannot be excluded. This could be the result of underlying psychiatric disorder or might be a result of medicinal product therapy. Physicians should encourage patients to report any distressing thoughts or feelings at any time and if signs and symptoms of depression develop during treatment, Dapoxetine should be discontinued.

Haemorrhage

There have been reports of bleeding abnormalities with SSRIs. Caution is advised in patients taking Dapoxetine, particularly in concomitant use with medicinal products known to affect platelet function (e.g., atypical antipsychotics and phenothiazines, acetylsalicylic acid, nonsteroidal anti-inflammatory drugs [NSAIDs], anti-platelet agents) or anticoagulants (e.g., warfarin), as well as in patients with a history of bleeding or coagulation disorders.

Renal impairment

Dapoxetine is not recommended for use in patients with severe renal impairment and caution is advised in patients with mild or moderate renal impairment.

Withdrawal effects

Abrupt discontinuation of chronically administered SSRIs used to treat chronic depressive disorders has been reported to result in the following symptoms: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia and hypomania.
A double-blind clinical trial in subjects with PE designed to assess the withdrawal effects of 62 days of daily or as needed dosing with 60 mg Dapoxetine showed mild withdrawal symptoms with a slightly higher incidence of insomnia and dizziness in subjects switched to placebo after daily dosing.
Eye disorders
The use of Dapoxetine has been associated with ocular effects such as mydriasis and eye pain. Dapoxetine should be used with caution in patients with raised intraocular pressure or those at risk of angle closure glaucoma.

4.5 Drug Interactions

Sildenafil

Nitrates
Administration of Sildenafil with nitric oxide donors such as organic nitrates or organic nitrites in any form is contraindicated. Consistent with its known effects on the nitric oxide/cGMP pathway, Sildenafil was shown to potentiate the hypotensive effects of nitrates.
Alpha-blockers
Use caution when co-administering alpha-blockers with Sildenafil because of potential additive blood pressure lowering effects. When Sildenafil is co-administered with an alpha-blocker, patients should be stable on alpha-blocker therapy prior to initiating Sildenafil treatment and Sildenafil should be initiated at the lowest dose.
Amlodipine
When Sildenafil 100 mg was co-administered with amlodipine (5 mg or 10 mg) to hypertensive patients, the mean additional reduction on supine blood pressure was 8 mmHg systolic and 7 mmHg diastolic.
Ritonavir and other CYP3A4 inhibitors
Co-administration of ritonavir, a strong CYP3A4 inhibitor, greatly increased the systemic exposure of sildenafil (11-fold increase in AUC). It is therefore recommended not to exceed a maximum single dose of 25 mg of Sildenafil in a 48-hour period.
Co-administration of erythromycin, a moderate CYP3A4 inhibitor, resulted in a 160% and 182% increases in sildenafil Cmax and AUC, respectively. Co-administration of saquinavir, a strong CYP3A4 inhibitor, resulted in 140% and 210% increases in sildenafil Cmax and AUC, respectively. Stronger CYP3A4 inhibitors such as ketoconazole or itraconazole could be expected to have greater effects than seen with saquinavir. A starting dose of 25 mg of Sildenafil should be considered in patients taking erythromycin or strong CYP3A4 inhibitors (such as saquinavir, ketoconazole, and itraconazole).
Alcohol
In a drug-drug interaction study sildenafil 50 mg given with alcohol 0.5 g/kg in which mean maximum blood alcohol levels of 0.08% was achieved, sildenafil did not potentiate the hypotensive effect of alcohol in healthy volunteers.

Dapoxetine

Potential for interaction with monoamine oxidase inhibitors
In patients receiving an SSRI in combination with a monoamine oxidase inhibitor (MAOI), there have been reports of serious, sometimes fatal, reactions including hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma. These reactions have also been reported in patients who have recently discontinued an SSRI and have been started on an MAOI. Some cases presented with features

resembling neuroleptic malignant syndrome. Animal data on the effects of combined use of an SSRI and MAOIs suggest that these medicinal products may act synergistically to elevate blood pressure and evoke behavioural excitation. Therefore, Dapoxetine should not be used in combination with an MAOI, or within 14 days of discontinuing treatment with an MAOI. Similarly, an MAOI should not be administered within 7 days after Dapoxetine has been discontinued.

Potential for interaction with thioridazine

Thioridazine administration alone produces prolongation of the QTc interval, which is associated with serious ventricular arrhythmias. Medicinal products such as Dapoxetine that inhibit the CYP2D6 isoenzyme appear to inhibit the metabolism of thioridazine and the resulting elevated levels of thioridazine are expected to augment the prolongation of the QTc interval. Dapoxetine should not be used in combination with thioridazine or within 14 days of discontinuing treatment with thioridazine. Similarly, thioridazine should not be administered within 7 days after Dapoxetine has been discontinued.

Medicinal/herbal products with serotonergic effects

As with other SSRIs, co-administration with serotonergic medicinal/herbal products (including MAOIs, L-tryptophan, triptans, tramadol, linezolid, SSRIs, SNRIs, lithium and St. John's Wort (*Hypericum perforatum)* preparations) may lead to an incidence of serotonin associated effects. Dapoxetine should not be used in combination with other SSRIs, MAOIs or other serotonergic medicinal/herbal products or within 14 days of discontinuing treatment with these medicinal/herbal products. Similarly, these medicinal/herbal products should not be administered within 7 days after Dapoxetine has been discontinued.

CNS active medicinal products

The use of Dapoxetine in combination with CNS active medicinal products (e.g., antiepileptics, antidepressants, antipsychotics, anxiolytics, sedative hypnotics) has not been systematically evaluated in patients with premature ejaculation. Consequently, caution is advised if the concomitant administration of Dapoxetine and such medicinal products is required.

4.6 Use in special populations (Pregnancy, Nursing woman, Pediatric use, Geriatric use)

Pregnancy and breast-feeding

Sildenafil & Dapoxetine Tablet should not be taken by women.

Driving and using machines

It has been demonstrated that Sildenafil & Dapoxetine does not affect the driving performance in adults. However, the response from each patient to the medicine may be different. Therefore, patient should check how this medicine affects you, before driving or operating machinery.

4.7 Effects on ability to drive and use machines

Dizziness and altered vision were reported in clinical trials with sildenafil, patients should be aware of how they react to this medicine, before driving or operating machinery. Minor or moderate influence on the ability to drive and use machines. Dizziness, disturbance in attention, syncope, blurred vision and somnolence have been reported in subjects receiving Dapoxetine in clinical trials. Therefore, patients should be warned to avoid situations where injury could result, including driving or operating hazardous machinery.

4.8 Undesirable effects

Sildenafil

The most common adverse reactions reported in clinical trials (>2%) are headache, flushing, dyspepsia, abnormal vision, nasal congestion, back pain, myalgia, nausea, dizziness, and rash.

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice. Sildenafil was administered to over 3700 patients (aged 19-87 years) during pre-marketing clinical trials worldwide. Over 550 patients were treated for longer than one year.
In placebo-controlled clinical studies, the discontinuation rate due to adverse reactions for Sildenafil (2.5%) was not significantly different from placebo (2.3%).
The following events occurred in <2% of patients in controlled clinical trials; a causal relationship to Sildenafil is uncertain. Reported events include those with a plausible relation to drug use; omitted are minor events and reports too imprecise to be meaningful:
Body as a Whole: face edema, photosensitivity reaction, shock, asthenia, pain, chills, accidental fall, abdominal pain, allergic reaction, chest pain, accidental injury.
Cardiovascular: angina pectoris, AV block, migraine, syncope, tachycardia, palpitation, hypotension, postural hypotension, myocardial ischemia, cerebral thrombosis, cardiac arrest, heart failure, abnormal electrocardiogram, and cardiomyopathy.
Digestive: vomiting, glossitis, colitis, dysphagia, gastritis, gastroenteritis, esophagitis, stomatitis, dry mouth, liver function tests abnormal, rectal hemorrhage, gingivitis.
Hemic and Lymphatic: anemia and leukopenia.
Metabolic and Nutritional: thirst, edema, gout, unstable diabetes, hyperglycemia, peripheral edema, hyperuricemia, hypoglycemic reaction, hypernatremia.
Musculoskeletal: arthritis, arthrosis, myalgia, tendon rupture, tenosynovitis, bone pain, myasthenia, synovitis.
Nervous: ataxia, hypertonia, neuralgia, neuropathy, paresthesia, tremor, vertigo, depression, insomnia, somnolence, abnormal dreams, reflexes decreased, hypesthesia.
Respiratory: asthma, dyspnea, laryngitis, pharyngitis, sinusitis, bronchitis, sputum increased, cough increased.
Skin and Appendages: urticaria, herpes simplex, pruritus, sweating, skin ulcer, contact dermatitis, exfoliative dermatitis.
Special Senses: sudden decrease or loss of hearing, mydriasis, conjunctivitis, photophobia, tinnitus, eye pain, ear pain, eye hemorrhage, cataract, dry eyes.
Urogenital: cystitis, nocturia, urinary frequency, breast enlargement, urinary incontinence, abnormal ejaculation, genital edema and anorgasmia.
Analysis of the safety database from controlled clinical trials showed no apparent difference in adverse reactions in patients taking Sildenafil with and without anti-hypertensive medication. This analysis was performed retrospectively, and was not powered to detect any pre-specified difference in adverse reactions.

Postmarketing Experience
The following adverse reactions have been identified during post approval use of Sildenafil. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. These events have been chosen for inclusion either due to their seriousness, reporting frequency, lack of clear alternative causation, or a combination of these factors.
Cardiovascular and cerebrovascular: Serious cardiovascular, cerebrovascular, and vascular events, including myocardial infarction, sudden cardiac death, ventricular arrhythmia, cerebrovascular hemorrhage, transient ischemic attack, hypertension, subarachnoid and intracerebral hemorrhages, and pulmonary hemorrhage have been reported post-marketing in temporal association with the use of Sildenafil. Most, but not all, of these patients had preexisting cardiovascular risk factors. Many of these events were reported to occur during or shortly after sexual activity, and a few were reported to occur shortly after the use of Sildenafil without sexual activity. Others were reported to have occurred hours to

days after the use of Sildenafil and sexual activity. It is not possible to determine whether these events are related directly to Sildenafil, to sexual activity, to the patient's underlying cardiovascular disease, to a combination of these factors, or to other factors.
Hemic and Lymphatic: Vaso-occlusive crisis: In a small, prematurely terminated study of sildenafil in patients with pulmonary arterial hypertension (PAH) secondary to sickle cell disease, vaso-occlusive crises requiring hospitalization were more commonly reported in patients who received sildenafil than in those randomized to placebo. The clinical relevance of this finding to men treated with Sildenafil for ED is not known.
Nervous: seizure, seizure recurrence, anxiety, and transient global amnesia.
Respiratory: epistaxis
Special senses:
Hearing: Cases of sudden decrease or loss of hearing have been reported postmarketing in temporal association with the use of PDE5 inhibitors, including Sildenafil. In some of the cases, medical conditions and other factors were reported that may have also played a role in the otologic adverse events. In many cases, medical follow-up information was limited. It is not possible to determine whether these reported events are related directly to the use of Sildenafil, to the patient's underlying risk factors for hearing loss, a combination of these factors, or to other factors.
Ocular: diplopia, temporary vision loss/decreased vision, ocular redness or bloodshot appearance, ocular burning, ocular swelling/pressure, increased intraocular pressure, retinal edema, retinal vascular disease or bleeding, and vitreous traction/detachment.
Non-arteritic anterior ischemic optic neuropathy (NAION), a cause of decreased vision including permanent loss of vision, has been reported rarely post-marketing in temporal association with the use of phosphodiesterase type 5 (PDE5) inhibitors, including Sildenafil. Most, but not all, of these patients had underlying anatomic or vascular risk factors for developing NAION, including but not necessarily limited to: low cup to disc ratio ("crowded disc"), age over 50, diabetes, hypertension, coronary artery disease, hyperlipidemia and smoking. It is not possible to determine whether these events are related directly to the use of PDE5 inhibitors, to the patient's underlying vascular risk factors or anatomical defects, to a combination of these factors, or to other factors.
Urogenital: prolonged erection, priapism, and hematuria.

Dapoxetine
Tabulated list of adverse reactions

Frequency of Adverse Reactions (MedDRA)				
System Organ Class	**Very common (> 1/10)**	**Common (≥ 1/100 to < 1/10)**	**Uncommon (≥ 1/1000 to < 1/100)**	**Rare (≥ 1/10000 to < 1/1000)**
Psychiatric disorders		Anxiety, Agitation, Restlessness, Insomnia, Abnormal dreams, Libido decreased	Depression, Depressed mood, Euphoric mood, Mood altered, Nervousness, Indifference, Apathy, Confusional state, Disorientation, Thinking abnormal, Hypervigilance, Sleep disorder, Initial insomnia, Middle insomnia, Nightmare, Bruxism, Loss of libido, Anorgasmia	

Nervous system disorders	Dizziness, Headache	Somnolence, Disturbance in attention, Tremor, Paraesthesia	Syncope, Syncope vasovagal, Dizziness postural, Akathisia, Dysgeusia, Hypersomnia, Lethargy, Sedation, Depressed level of consciousness	Dizziness exertional, Sudden onset of sleep
Eye disorders		Vision blurred	Mydriasis (see section 4.4), Eye pain, Visual disturbance	
Ear and labyrinth disorders		Tinnitus	Vertigo	
Cardiac disorders			Sinus arrest, Sinus bradycardia, Tachycardia	
Vascular disorders		Flushing	Hypotension, Systolic hypertension, Hot flush	
Respiratory, thoracic and mediastinal disorders		Sinus congestion, Yawning		
Gastrointestinal disorders	Nausea	Diarrhoea, Vomiting, Constipation, Abdominal pain, Abdominal pain upper, Dyspepsia, Flatulence, Stomach discomfort, Abdominal distension, Dry mouth	Abdominal discomfort, Epigastric discomfort	Defaecation urgency
Skin and subcutaneous tissue disorders		Hyperhidrosis	Pruritis, Cold sweat	
Reproductive system and breast disorders		Erectile dysfunction	Ejaculation failure, Male orgasmic disorder, Paraesthesia of genital male	
General disorders and administration site conditions		Fatigue, Irritability	Asthenia, Feeling hot, Feeling jittery, Feeling abnormal, Feeling drunk	
Investigations		Blood pressure increased	Heart rate increased, Blood pressure diastolic increased, Blood pressure orthostatic increased	

Adverse drug reactions reported in the 9-month long-term open-label extension trial were consistent with those reported in the double-blind studies and no additional adverse drug reactions were reported.

Description of selected adverse reactions

Syncope characterized as loss of consciousness, with bradycardia or sinus arrest observed in patients wearing Holter monitors, has been reported in clinical trials and is considered medicinal product-related.

The majority of cases occurred during the first 3 hours after dosing, after the first dose or associated with study-related procedures in the clinical setting (such as blood draw and orthostatic maneuvers and blood pressure measurements). Prodromal symptoms often preceded the syncope.
The occurrence of syncope and possibly prodromal symptoms appears dose dependent as demonstrated by higher incidence among patients treated with higher than recommended doses in

Other special populations
Caution is advised if increasing the dose to 60 mg in patients taking potent CYP2D6 inhibitors or if increasing the dose to 60 mg in patients known to be of CYP2D6 poor metabolizer genotype.
Withdrawal effects
Abrupt discontinuation of chronically administered SSRIs used to treat chronic depressive disorders has been reported to result in the following symptoms: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia and hypomania.
Results of a safety study showed a slightly higher incidence of withdrawal symptoms of mild or moderate insomnia and dizziness in subjects switched to placebo after 62 days of daily dosing.

4.9 Overdose
Sildenafil
In single dose volunteer studies of doses up to 800 mg, adverse reactions were similar to those seen at lower doses, but the incidence rates and severities were increased. Doses of 200 mg did not result in increased efficacy but the incidence of adverse reactions (headache, flushing, dizziness, dyspepsia, nasal congestion, and altered vision) was increased.
In cases of overdose, standard supportive measures should be adopted as required. Renal dialysis is not expected to accelerate clearance as sildenafil is highly bound to plasma proteins and not eliminated in the urine.

Dapoxetine
No case of overdose has been reported.
There were no unexpected adverse events in a clinical pharmacology study of Dapoxetine with daily doses up to 240 mg (two 120 mg doses given 3 hours apart). In general, symptoms of overdose with SSRIs include serotonin-mediated adverse reactions such as somnolence, gastrointestinal disturbances such as nausea and vomiting, tachycardia, tremor, agitation and dizziness.
In cases of overdose, standard supportive measures should be adopted as required. Due to high protein binding and large volume of distribution of Dapoxetine hydrochloride, forced diuresis, dialysis, hemoperfusion and exchange transfusion are unlikely to be of benefit. No specific antidotes for Dapoxetine are known.

5. Pharmacological properties
5.1 Pharmacodynamic Properties
Pharmacodynamic properties
Sildenafil
Pharmacotherapeutic group: Urologicals; Drugs used in erectile dysfunction.
Mechanism of action
Sildenafil is an oral therapy for erectile dysfunction. In the natural setting, i.e. with sexual stimulation, it restores impaired erectile function by increasing blood flow to the penis.
The physiological mechanism responsible for erection of the penis involves the release of nitric oxide (NO) in the corpus cavernosum during sexual stimulation. Nitric oxide then activates the enzyme guanylate

cyclase, which results in increased levels of cyclic guanosine monophosphate (cGMP), producing smooth muscle relaxation in the corpus cavernosum and allowing inflow of blood.
Sildenafil is a potent and selective inhibitor of cGMP specific phosphodiesterase type 5 (PDE5) in the corpus cavernosum, where PDE5 is responsible for degradation of cGMP. Sildenafil has a peripheral site of action on erections. Sildenafil has no direct relaxant effect on isolated human corpus cavernosum but potently enhances the relaxant effect of NO on this tissue. When the NO/cGMP pathway is activated, as occurs with sexual stimulation, inhibition of PDE5 by sildenafil results in increased corpus cavernosum levels of cGMP. Therefore, sexual stimulation is required in order for sildenafil to produce its intended beneficial pharmacological effects.

Pharmacodynamic effects
Studies in vitro have shown that sildenafil is selective for PDE5, which is involved in the erection process. Its effect is more potent on PDE5 than on other known phosphodiesterases. There is a 10-fold selectivity over PDE6 which is involved in the phototransduction pathway in the retina. At maximum recommended doses, there is an 80-fold selectivity over PDE1, and over 700-fold over PDE2, 3, 4, 7, 8, 9, 10 and 11. In particular, sildenafil has greater than 4,000-fold selectivity for PDE5 over PDE3, the cAMP-specific phosphodiesterase isoform involved in the control of cardiac contractility.

Dapoxetine
Pharmacotherapeutic group: Other Urologicals, ATC code: G04BX14
Mechanism of action
Dapoxetine is a potent selective serotonin reuptake inhibitor (SSRI) with an IC_{50} of 1.12 NM, while its major human metabolites, desmethylDapoxetine (IC_{50} < 1.0 NM) and didesmethylDapoxetine (IC_{50} = 2.0 NM) are equivalent or less potent (Dapoxetine-N-oxide (IC_{50} = 282 NM)).
Human ejaculation is primarily mediated by the sympathetic nervous system. The ejaculatory pathway originates from a spinal reflex Centre, mediated by the brain stem, which is influenced initially by a number of nuclei in the brain (medial preoptic and paraventricular nuclei).
The mechanism of action of Dapoxetine in premature ejaculation is presumed to be linked to the inhibition of neuronal reuptake of serotonin and the subsequent potentiation of the neurotransmitter's action at pre- and postsynaptic receptors.
In the rat, Dapoxetine inhibits the ejaculatory expulsion reflex by acting at a supraspinal level within the lateral paragigantocellular nucleus (LPGi). Post ganglionic sympathetic fibers that innervate the seminal vesicles, vas deferens, prostate, bulbourethral muscles and bladder neck cause them to contract in a coordinated fashion to achieve ejaculation. Dapoxetine modulates this ejaculatory reflex in rats.

5.2 Pharmacokinetic properties
Sildenafil
Absorption
Sildenafil is rapidly absorbed. Maximum observed plasma concentrations are reached within 30 to 120 minutes (median 60 minutes) of oral dosing in the fasted state. The mean absolute oral bioavailability is 41% (range 25-63%). After oral dosing of sildenafil AUC and Cmax increase in proportion with dose over the recommended dose range (25-100 mg).
When sildenafil is taken with food, the rate of absorption is reduced with a mean delay in tmax of 60 minutes and a mean reduction in Cmax of 29%.

Distribution
The mean steady state volume of distribution (Vd) for sildenafil is 105 l, indicating distribution into the tissues. After a single oral dose of 100 mg, the mean maximum total plasma concentration of sildenafil is approximately 440ng/mL (CV 40%). Since sildenafil (and its major circulating N-dimethyl metabolite) is

96% bound to plasma proteins, this result in the mean maximum free plasma concentration for sildenafil of 18ng/mL (38nM). Protein binding is independent of total drug concentrations.
In healthy volunteers receiving sildenafil (100mg single dose), less than 0.0002% (average 188 ng) of the administered dose was present in ejaculate 90 minutes after dosing.
Biotransformation
Sildenafil is cleared predominantly by the CYP3A4 (major route) and CYP2C9 (minor route) hepatic microsomal isoenzymes. The major circulating metabolite results from N-demethylation of sildenafil. This metabolite has a phosphodiesterase selectivity profile similar to sildenafil and an in vitro potency for PDE5 approximately 50% that of the parent drug. Plasma concentrations of this metabolite are approximately 40% of those seen for sildenafil. The N-dimethyl metabolite is further metabolised, with a terminal half-life of approximately 4 h.

Elimination
The total body clearance of sildenafil is 41 l/h with a resultant terminal phase half-life of 3-5 h. After either oral or intravenous administration, sildenafil is excreted as metabolites predominantly in the faeces (approximately 80% of administered oral dose) and to a lesser extent in the urine (approximately 13% of administered oral dose).

Dapoxetine
Absorption
Dapoxetine is rapidly absorbed with maximum plasma concentrations (C_{max}) occurring approximately 1-2 hours after tablet intake. The absolute bioavailability is 42% (range 15-76%), and dose proportional increases in exposure (AUC and C_{max}) are observed between the 30 and 60 mg dose strengths. Following multiple doses, AUC values for both Dapoxetine and the active metabolite desmethylDapoxetine (DED) increase by approximately 50% when compared to single dose AUC values.
Ingestion of a high fat meal modestly reduced the C_{max} (by 10%) and modestly increased the AUC (by 12%) of Dapoxetine and slightly delayed the time for Dapoxetine to reach peak concentrations. These changes are not clinically significant. Dapoxetine can be taken with or without food.

Distribution
More than 99% of Dapoxetine is bound *in vitro* to human serum proteins. The active metabolite desmethylDapoxetine (DED) is 98.5% protein bound. Dapoxetine has a mean steady state volume of distribution of 162 L.

Biotransformation
In vitro studies suggest that Dapoxetine is cleared by multiple enzyme systems in the liver and kidneys, primarily CYP2D6, CYP3A4, and Flavin monooxygenase (FMO1). Following oral dosing of ^{14}C-Dapoxetine, Dapoxetine was extensively metabolized to multiple metabolites primarily through the following biotransformation pathways: N-oxidation, N-demethylation, naphthyl hydroxylation, glucuronidation and sulfation. There was evidence of presystemic first-pass metabolism after oral administration.
Intact Dapoxetine and Dapoxetine-N-oxide were the major circulating moieties in the plasma. *In vitro* binding and transporter studies show that Dapoxetine-N-oxide is inactive. Additional metabolites including desmethylDapoxetine and didesmethylDapoxetine account for less than 3% of the total circulating drug –related materials in plasma. *In vitro* binding studies indicate that DED is equipotent to Dapoxetine and didesmethylDapoxetine has approximately 50% of the potency of Dapoxetine. The unbound exposures (AUC and C_{max}) of DED are approximately 50% and 23%, respectively, of the unbound exposure of Dapoxetine.

Elimination
The metabolites of Dapoxetine were primarily eliminated in the urine as conjugates. Unchanged active substance was not detected in the urine. Following oral administration, Dapoxetine has an initial (disposition) half-life of approximately 1.5 hours, with plasma levels less than 5% of peak concentrations by 24 hours' post-dose, and a terminal half-life of approximately 19 hours. The terminal half-life of DED is approximately 19 hours.

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Sildenafil

Carcinogenesis Sildenafil was not carcinogenic when administered to rats for 24 months at a dose resulting in total systemic drug exposure (AUCs) for unbound sildenafil and its major metabolite of 29- and 42-times, for male and female rats, respectively, the exposures observed in human males given the Maximum Recommended Human Dose (MRHD) of 100 mg. Sildenafil was not carcinogenic when administered to mice for 18-21 months at dosages up to the Maximum Tolerated Dose (MTD) of 10 mg/kg/day, approximately 0.6 times the MRHD on a mg/m2 basis.

Mutagenesis Sildenafil was negative in in vitro bacterial and Chinese hamster ovary cell assays to detect mutagenicity, and in vitro human lymphocytes and in vivo mouse micronucleus assays to detect clastogenicity.

Impairment of Fertility There was no impairment of fertility in rats given sildenafil up to 60 mg/kg/day for 36 days to females and 102 days to males, a dose producing an AUC value of more than 25 times the human male AUC.

Dapoxetine

A full assessment of the safety pharmacology, repeat dose toxicology, genetic toxicology, carcinogenicity, dependence/withdrawal liability, phototoxicity and developmental reproductive toxicology of Dapoxetine was conducted in preclinical species (mouse, rat, rabbit, dog and monkey) up to the maximum tolerated doses in each species. Due to the more rapid bioconversion in the preclinical species than in man, pharmacokinetic exposure indices (C_{max} and $AUC_{0\text{-}24\ hr}$) at the maximum tolerated doses in some studies approached those observed in man. However, the body weight normalized dose multiples were greater than 100-fold. There were no clinically relevant safety hazards identified in any of these studies.

In studies with oral administration, Dapoxetine was not carcinogenic to rats when administered daily for approximately two years at doses up to 225 mg/kg/day, yielding approximately twice the exposures (AUC) seen in human males given the Maximum Recommended Human Dose (MRHD) of 60 mg. Dapoxetine also did not cause tumors in Tg.rasH2 mice when administered at the maximum possible doses of 100 mg/kg for 6 months and 200 mg/kg for 4 months. The steady state exposures of Dapoxetine in mice following 6-months oral administration at 100 mg/kg/day were less than the single dose exposures observed clinically at 60 mg.

There were no effects on fertility, reproductive performance or reproductive organ morphology in male or female rats and no adverse signs of embryotoxicity or fetotoxicity in the rat or rabbit. Reproductive toxicity studies did not include studies to assess the risk of adverse effects after exposure during the peri-post-natal period.

7. Description

Vicogra Force is supplied for oral administration, as film coated tablet of Sildenafil Citrate equivalent to Sildenafil and Dapoxetine Hydrochloride equivalent to Dapoxetine. Each film coated tablet of Vicogra Force contains Sildenafil Citrate equivalent to Sildenafil 50 mg and Dapoxetine Hydrochloride equivalent to Dapoxetine 30 mg.

8. Pharmaceutical particulars

8.1 Incompatibilities

NA

8.2 Shelf Life

Refer Pack

8.3 Packaging Information

Refer Pack

8.4 Storage condition & handling instructions

Refer Pack

9. Patient Counseling Information

Read this entire leaflet carefully before you start taking this medicine because it contains important information for you.

• Keep this leaflet. You may need to read it again.
• If you have any further questions, ask your doctor, pharmacist or nurse.
• This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
• If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

What Sildenafil & Dapoxetine Tablet is and it is used for?

This product(Tablet) is a fixed dose combination of Sildenafil & Dapoxetine as active ingredients and it is Indicated for the treatment of sexual dysfunction characterized by sexual dysfunction and premature ejaculation. it should be taken in a dose and duration as directed by physician.

What you need to know before you use Sildenafil & Dapoxetine Tablets

Do not take Sildenafil & Dapoxetine Tablet

If you have allergy to drug Sildenafil & Dapoxetine or any of the other ingredients of this medicine.
have ever had any heart problems (e.g., angina, chest pain, heart failure, irregular heartbeats, heart attack or narrowing of the aortic valve)
• have ever had a stroke
• have low or high blood pressure
• have ever had severe vision loss
• have a rare inherited eye disease called retinitis pigmentosa
• have ever had any kidney problems
• have ever had any liver problems
• have ever had any blood problems, including sickle cell anemia or leukemia
• are allergic to sildenafil or any of the other ingredients of Sildenafil & Dapoxetine tablets
• have a deformed penis, Peyronie's disease, or ever had an erection that lasted more than 4 hours
• have stomach ulcers or any types of bleeding problems
• are taking any other medicines
• You have heart problems, such as heart failure or problems with the heart rhythm
• You have a history of fainting
• You have ever had mania (symptoms include feeling over–excited, irritable or not being able to think clearly) or severe depression

• You are taking:
• Medicines for depression called ‘monoamine oxidase inhibitors’ (MAOIs)
• Thioridazine used for schizophrenia
• Other medicines for depression
• Lithium - a medicine for bipolar disorder
• Linezolid - an antibiotic used to treat infections
• Tryptophan - a medicine to help you sleep
• St John’s wort - an herbal medicine
• Tramadol - used to treat serious pain
• Medicines used to treat migraines

Warnings and precautions

Tell your doctor or HCP if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription. This includes medicines, herbal remedies, health products or supplements that you have obtained without a prescription

Please discuss with your doctor if you are taking any of the following medicines before Sildenafil & Dapoxetine Tablet:

- Ketoconazole (an antifungal medicine)
- Erythromycin (an antibiotic)
- Diltiazem (to treat angina)
- Cyclosporine (to reduce the activity of your immune system, thus avoiding transplant rejection or reducing disease activity in autoimmune and allergic disorders, such as psoriasis, atopic dermatitis or rheumatoid arthritis)
- Ritonavir (to treat AIDS)
- Rifampicin (an antibiotic)
- Phenobarbital (used for treatment of epilepsy)
- Phenytoin (used for treatment of epilepsy)
- Rifampicin (used to treat tuberculosis and some other infections)
- Gemfibrozil (used for treatment of high lipid levels in plasma).

Combining alcohol with Dapoxetine may increase alcohol-related neurocognitive effects and may also enhance neurocardiogenic adverse events such as syncope, thereby increasing the risk of accidental injury; therefore, patients should be advised to avoid alcohol

Pregnancy and breast-feeding

Sildenafil & Dapoxetine Tablet should not be taken by women.

Driving and using machines

Dizziness and altered vision were reported in clinical trials with sildenafil, patients should be aware of how they react to this medicine, before driving or operating machinery. Minor or moderate influence on the ability to drive and use machines. Dizziness, disturbance in attention, syncope, blurred vision and somnolence have been reported in subjects receiving Dapoxetine in clinical trials. Therefore, patients should be warned to avoid situations where injury could result, including driving or operating hazardous machinery.

How to take Sildenafil & Dapoxetine Tablet?

Posology

Orally, once daily or as directed by the physician.

Method of administration: For oral use only.

Grapefruit juice or any other fruit juices should not be used for oral dispersion or administration.

Possible Side Effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Side-effects that may be experienced in adults and adolescents are:

Very common side effects (affects more than 1 user in 10):

• Feeling dizzy
• Headache
• Feeling sick

Common side effects (affects 1 to 10 users in 100):

• Feeling irritable, anxious, agitated or restless
• Feeling numb or having 'pins and needles'
• Difficulty getting or keeping an erection
• Sweating more than normal or flushing
• Diarrhoea, constipation or having wind
• Stomach pain, bloating or being sick
• Problems sleeping or strange dreams
• Feeling tired or sleepy, yawning
• Blocked nose (nasal congestion)
• A rise in blood pressure
• Difficulty concentrating
• Shaking or trembling
• Lower interest in sex
• Ringing in the ears
• Blurred vision
• Indigestion
• Dry mouth.

Uncommon side effects (affects 1 to 10 users in 1,000):

• Fainting or feeling dizzy upon standing
• Change in mood, feeling overly excited or feelings of paranoia
• Feeling confused, disoriented or unable to think clearly
• Slow or irregular heartbeat or increase in heart rate
• Loss of sex drive, problems reaching orgasm
• Feeling weak, sedated, lethargic or fatigued
• Feeling depressed, nervous or indifferent
• Feeling hot, jittery, abnormal or drunk
• Vision problems or dilated pupils
• Low or high blood pressure
• Feeling itchy or cold sweat
• Spinning sensation
• Abnormal taste
• Teeth grinding.

Rare side effects (affects 1 to 10 users in 10,000):

• Feeling dizzy following exertion
• Sudden onset of sleep
• Urgency of bowel action.

Very rare side effects (may affect up to 1 in 10,000 people):

• Hallucinations (seeing things which are not there)
• Disorientation
• Stuttering

Frequency not known: cannot be estimated from the available data
• Palpitations (feeling your heart beat)
• Tachycardia (fast heart beat)
• Allergic reactions the signs of which may include difficulty in breathing, dizziness, collapsing or losing consciousness, swelling of your face, lips, tongue or throat, and/or swelling and redness of the skin. If you notice any of these serious side effects, stop taking the medicine and seek urgent medical advice straight away.
• Vomiting

10. Details of manufacturer
Refer Pack for manufacturer details.

Marketed by:
Abbott Healthcare Pvt. Ltd.
Angel Space, Bldg. D-4, Gala No. 1 to 3 &
11 to 13 Ground Floor, 101 to 106 &
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12. Date of revision
Version 2.0, dated 02-Jan-26

For Product Complaints/Adverse events or Queries please write to **webmasterindia@abbott.com**