SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Generic Name: Sildenafil Tablets 100 mg
Brand name: **Tiagra** 100 mg F.C. Tablet
Strength: Sildenafil 100 mg/tablet (as Sildenafil Citrate USP)
Dosage form: Tablet (Film Coated)
Distribution category of the Product: Prescription Only Medicine (POM)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains 140.8451 mg Sildenafil Citrate USP, is equivalent to 100 mg Sildenafil.
Each film coated tablet contains 0.86 mg lactose (as monohydrate).
For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablet (Film Coated)
Smooth well formed diamond shaped blue colored film coated tablet having logo 'R' on one side and bisect on other side.
Division of the Tablet: This tablet has score for dividing of the tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Tiagra is indicated in adult men with erectile dysfunction, which is the inability to achieve o maintain a penile erection sufficient for satisfactory sexual performance. In order for **Tiagra** to be effective, sexual stimulation is required.

4.2 Posology and method of administration

The usual dose is 50 mg once daily. It should be taken before 30-40 minutes of intercourse Depending on effectiveness & tolerance, the dose may be increased to a maximum recommended dose of 100 mg or decreased to 25 mg. The maximum dosing frequency is once per day. Some factors are associated with increased plasma levels of Sildenafil: age more than 65 years, hepatic problem, severe renal impairment and concomitant use of ketoconazole, itraconzole and erythromycin. Since higher plasma levels may increase both the efficacy and incidence of adverse events, a starting dose of 25 mg should be considered in these patients. **Tiagra** may take longer time to work if it is taken with a heavy meal.

4.3 Contraindications

Tiagra (Sildenafil) was shown to potentiate the hypotensive effects of nitrates and its administration to patients who are using organic nitrates, either regulatory and/or intermittently, in any form is therefore contraindicated.
Tiagra 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

4.4 Special warnings and precautions for use

There is a potential for cardiac risk of sexual activity in patients with preexisting cardiovascular disease. Therefore, treatments for erectile dysfunction, including Sildenafil, should not be generally used in men for whom sexual activity is inadvisable because of their underlying

concomitant use of these two drug classes can lower blood pressure significantly leading to symptomatic hypotension (e.g. dizziness, fainting). Consideration should be given to the following:
Patients should be stable on alpha-blocker therapy prior to initiating a PDE5 inhibitor.
Patients who demonstrate hemodynamic instability on alpha-blocker therapy alone are at increased risk of symptomatic hypotension with concomitant use of PDE5 inhibitors.
In those patients who are stable on alpha-blocker therapy, PDE5 inhibitors should be initiated at the lowest dose.
In those patients already taking an optimized dose of a PDE5 inhibitor, alpha-blocker therapy should be initiated at the lowest dose. Stepwise increase in alpha-blocker dose may be associated with further lowering of blood pressure when taking a PDE5 inhibitor.
Safety of combined use of PDE5 inhibitors and alpha-blockers may be affected by other variables, including intravascular volume depletion and other anti-hypertensive drugs.
Sildenafil has systemic vasodilatory properties and may augment the blood pressure lowering effect of other anti-hypertensive medications.
The film coating of the tablet contains lactose. Tiagra should not be administered to men with rare hereditary problems of galactose intolerance, total lactase deficiency or glucosegalactose malabsorption. This medicinal product contains less than 1 mmol sodium (23 mg) per tablet.
Patients on low sodium diets can be informed that this medicinal product is essentially 'sodium-free'

4.5 Interaction with other medicinal products and other forms of interaction

Effets of other medicinal products on Sildenafil
Sildenafil metabolism is principally mediated by the cytochrome P450 (CYP) isoforms 3A4 (major route) and 2C9 (minor route). Therefore, inhibitors of these isoenzymes may reduce sildenafil clearance and inducers of these isoenzymes may increase sildenafil clearance.
A reduction in sildenafil clearance when co-administered with CYP3A4 inhibitors (such as ketoconazole, erythromycin, cimetidine). Although no increased incidence of adverse events was observed in these patients, when sildenafil is administered concomitantly with CYP3A4 inhibitors, a starting dose of 25mg should be considered.
Co-administration of sildenafil with HIV protease inhibitor ritonavir is not advised and in any event the maximum dose of sildenafil should under no circumstances exceed 25mg within 48 hours.
Co-administration of the HIV protease inhibitor saquinavir, a CYP3A4 inhibitor, at steady state (1200 mg three times a day) with sildenafil (100 mg single dose) resulted in a 140% increase in sildenafil C_{max} and a 210% increase in sildenafil AUC. Sildenafil had no effect on saquinavir pharmacokinetics. Stronger CYP3A4 inhibitors such as ketoconazole and itraconazole would be expected to have greater effects.
When a single 100 mg dose of sildenafil was administered with erythromycin, a moderate CYP3A4 inhibitor, at steady state (500 mg twice daily for 5 days), there was a 182% increase in sildenafil systemic exposure (AUC). There was no evidence of an effect of azithromycin (500 mg daily for 3 days) on the AUC, C_{max}, t_{max}, elimination rate constant, or subsequent half-life of sildenafil or its principal circulating metabolite. Cimetidine (800 mg), a cytochrome P450 inhibitor and non-specific CYP3A4 inhibitor, caused a 56% increase in plasma sildenafil concentrations when co-administered with sildenafil (50 mg).
Grapefruit juice is a weak inhibitor of CYP3A4 gut wall metabolism and may give rise to modest increases in plasma levels of sildenafil.
Single doses of antacid (magnesium hydroxide/aluminium hydroxide) did not affect the bioavailability of sildenafil.

4.6 Pregnancy and lactation

Sildenafil connect is not indicated for use by women.
There are no adequate and well-controlled studies in pregnant or breast-feeding women.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.
As 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.

4.8 Undesirable effects

The most commonly reported adverse reactions in clinical studies among sildenafil treated patients were headache, flushing, dyspepsia, nasal congestion, dizziness, nausea, hot flush, visual disturbance, cyanopsia and blurred vision.
Very Common (≥ 1/10): Headache
Common *(≥ 1/100 and <1/10)*: Dizziness, Visual colour distortions**, Visual disturbance, Vision blurred, Flushing, Hot flush, Nasal congestion, Nausea, Dyspepsia.
Uncommon (≥ 1/1,000 and <1/100)*:** Rhinitis, Hypersensitivity, Somnolence, Hypoaesthesia, Lacrimation disorders, Eye pain, Photophobia, Photopsia, Ocular hyperaemia, Visual brightness, Conjunctivitis, Vertigo, Tinnitus, Tachycardia, Palpitations, Hypertension, Hypotension, Epistaxis, Sinus congestion, Gastro oesophageal reflux disease, Vomiting, Abdominal pain upper, Dry mouth, Rash, Myalgia, Pain in extremity, Haematuria, Chest pain, Fatigue, Feeling hot, Heart rate increased
Rare *(≥ 1/10,000 and <1/1,000)*: Cerebrovascular accident, Transient ischaemic attack, Seizure*, Seizure recurrence*, Syncope, Non-arteritic anterior ischaemic optic neuropathy (NAION)**, Retinal vascular occlusion*, Retinal haemorrhage, Arteriosclerotic retinopathy, Retinal disorder, Glaucoma, Visual field defect, Diplopia, Visual acuity reduced, Myopia, Asthenopia, Vitreous floaters, Iris disorder, Mydriasis, Halo vision, Eye oedema, Eye swelling, Eye disorder, Conjunctival hyperaemia, Eye irritation, Abnormal sensation in eye, Eyelid oedema, Scleral discoloration, Deafness, Sudden cardiac death*, Myocardial infarction, Ventricular arrhythmia*, Atrial fibrillation, Unstable angina, Throat tightness, Nasal oedema, Nasal dryness, Hypoaesthesia oral, Stevens-Johnson Syndrome (SJS)**, Toxic Epidermal Necrolysis (TEN)*, Penile haemorrhage, Priapism*, Haematospermia, Erection increased, Irritability.
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*****Reported during post-marketing surveillance only
**Visual colour distortions: Chloropsia, Chromatopsia, Cyanopsia, Erythropsia and Xanthopsia
***Lacrimation disorders: Dry eye, Lacrimal disorder and Lacrimation increased

4.9 Overdose

In studies with healthy volunteers of single doses up to 800 mg, adverse events were similar to those seen at lower doses but incidence rates and severities were 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 it is not eliminated in the urine.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Urologicals; Drugs used in erectile dysfunction.
ATC Code: G04B E03.
Sildenafil works by helping to relax the blood vessles of penis. The physiologic mechanism of erection of the penis involves release of Nitric Oxide (NO) in the corpus cavernosum during sexual stimulation. NO 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 has no direct relaxant effect on isolated human corpus cavernosum, but enhances the effect of Nitric Oxide (NO) by inhibiting phosphodiesterase type 5 (PDE5), which is responsible for degradation of cGMP in the corpus

5.2 Pharmacokinetic properties

Sildenafil is rapidly absorbed after oral administration, with absolute bioavailability of about 40%. Its pharmacokinetics is dose-proportional over the recommended dose range. It is eliminated primarily by hepatic metabolism (mainly cytochrome P450 3a4) and is converted to an active metabolite with properties similar to the parent. Both Sildenafil and its metabolite have a terminal half-life of about 4 hours.

5.3 Preclinical safety data

Not Available

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core Tablet Excipients:
Microcrystalline Cellulose (Type PH 102) USP-NF
Dibasic Calcium Phosphate Anhydrous USP
Croscarmellose Sodium USP-NF
Magnesium Stearate USP-NF

Film Coating Excipients:
Hypromellose (12 -18 cps)
Triacetin USP
Lactose monohydrate USP-NF
Talc USP
Titanium Dioxide USP
FD & C blue no. 2 lake Pharma grade
Purified Water USP/BP

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Do not store above 30°C, Store in a dry place. Protect from moisture.

6.5 Nature and contents of container

Alu.-Alu. blister pack.
Each strip contains 4 tablets.
Each trade pack contains 4 tablets (i.e. 1 × 4 = 4 tablets).

6.6 Special precautions for disposal and other handling

No special requirements. Any unused product or waste should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESS

Name : RENATA LIMITED
Address : PLOT # 1, MILK VITA ROAD,
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8. MARKETING AUTHORISATION NUMBER(S)

TAN 22 HM 240

9. DATE OF FIRST AUTHORISATION

19th July, 2022

10. DATE OF REVISION OF THE TEXT