**COMMON TECHNICAL DOSSIER (CTD) – Module 1**

**EDSAVE 20 (Tadalafil Tablets USP 20mg)**

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## SUMMARY OF THE PRODUCT CHARACTERISTICS (SmPC)

### 1. NAME OF THE MEDICINAL PRODUCTS

**EDSAVE 20** (Tadalafil Tablets USP 20mg)

### 2. QUALITY AND QUANTITATIVE COMPOSITION

Each Film Coated Tablet Contains:

Tadalafil USP 20mg

For the full list of excipients please refer section 6.1 below

### 3. PHARMACEUTICAL FORM

Film Coated Tablets

### 4. CLINICAL PARTICULARS

#### 4.1 Therapeutics Indications

Tadalafil tablets are indicated for erectile dysfunction, benign prostatic hyperplasia, and pulmonary arterial hypertension.

#### 4.2 Posology and method of administration

**Erectile dysfunction**

Adults: Initially 10 mg (max. per dose 20 mg), to be taken at least 30 minutes before sexual activity, subsequent doses adjusted according for response, the effect of intermittent dosing may persist for longer than 24 hours, continuous daily use not recommended; maximum 1 dose per day.

**Benign prostatic hyperplasia**

Adults: 5 mg once daily

**Pulmonary arterial hypertension**

Adults: 40 mg once daily

**Method of Administration:** Oral

Tadalafil tablets are for oral use in men only. Swallow the tablet whole with some water. The tablets can be taken with or without food.

## 4.3 Contraindication

Hypersensitivity to drug or its composition. Acute myocardial infarction in past 30 days, history of non-arteritic anterior ischemic optic neuropathy, hypotension {avoid if systolic blood pressure below 90 mmHg). When used for benign prostatic hyperplasia or erectile dysfunction Mild to severe heart failure, patients in whom vasodilation or sexual activity are inadvisable, recent stroke, uncontrolled arrhythmias, uncontrolled hypertension, unstable angina.

## 4.4 Special warning and precaution for use

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

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. Tadalafil has vasodilator properties, resulting in mild and transient decreases in blood pressure, and as such potentiates the hypotensive effect of nitrates.

The evaluation of erectile dysfunction should include a determination of potential underlying causes and the identification of appropriate treatment following an appropriate medical assessment. It is not known if Tadalafil is effective in patients who have undergone pelvic surgery or radical non-nerves paring prostatectomy.

## 4.5 Interaction with other medicinal products and other forms of interaction

- Alpha blockers cause significant hypotensive effects when given with phosphodiesterase type - 5 inhibitors. Patient should be stabilized on first drug then second drug should be added at the lowest recommended dose.
- Anti-androgens, Anti-epileptics, Mitotane, Rifamycins are predicted to decrease the exposure to phosphodiesterase type-5 inhibitors.

- Anti-arrhythmics, Antifungals, Calcium channel blockers, Crizotinib, HIV-protease inhibitors, Imatinib, Letermovir, Macrolides (erythromycin), Neurokinin-1 receptor antagonists, Nilotinib are predicted to increase the exposure to Tadalafil.
- Cobicistat, Idelalisib, Macrolides (clarithromycin), is predicted to increase the exposure to Tadalafil. Use with caution or avoid.

**4.6 Pregnancy, Lactation and Fertility**

Tadalafil is not indicated for use by women.

**4.7 Effects on ability to drive and use machine**

Some men taking Tadalafil in clinical studies have reported dizziness. Check carefully how you react to the tablets before driving or using machines.

**4.8 Undesirable effects**

**Common or very common:** Flushing, gastrointestinal discomfort, headaches, myalgia, nasal congestion, pain.

**Uncommon:** Arrhythmias, chest pain, dizziness, dyspnea, eye pain, fatigue, gastro oesophageal reflux disease, hemorrhage, hypertension, hypotension, nausea oedema, palpitations, skin reactions, tinnitus, vision disorders, vomiting.

**Rare or very rare:** Acute coronary syndrome, angioedema, cerebrovascular insufficiency, eye erythema, eye swelling haematospermia, hyperhidrosis, memory loss, optic neuropathy, priapism, retinal occlusion, seizure, Stevens- Johnson syndrome, sudden cardiac death, sudden hearing loss, syncope.

**4.9 Overdose**

In cases of overdose, standard supportive measures should be adopted as required. Haemodialysis contributes negligibly to Tadalafil elimination.

**5. PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Urological, Drugs used in erectile dysfunction.

ATC Code: G04BE08.

Mechanism of action:

Tadalafil is a selective, reversible inhibitor of cyclic guanosine monophosphate (cGMP)-specific phosphodiesterase type 5 (PDE5). When sexual stimulation causes the local release of nitric oxide, inhibition of PDE5 by Tadalafil produces increased levels of cGMP in the corpus cavernosum. This results in smooth muscle relaxation and inflow of blood into the penile tissues, thereby producing an erection. Tadalafil has no effect in the treatment of erectile dysfunction in the absence of sexual stimulation.

Pharmacodynamic effects:

Studies in vitro have shown that tadalafil is a selective inhibitor of PDE5. PDE5 is an enzyme found in corpus cavernosum smooth muscle, vascular and visceral smooth muscle, skeletal muscle, platelets, kidney, lung, and cerebellum. The effect of tadalafil is more potent on PDE5 than on other phosphodiesterase. Tadalafil is > 10,000-fold more potent for PDE5 than for PDE1, PDE2, and PDE4, enzymes which are found in the heart, brain, blood vessels, liver, and other organs. Tadalafil is > 10,000-fold more potent for PDE5 than for PDE3, an enzyme found in the heart and blood vessels. This selectivity for PDE5 over PDE3 is important because PDE3 is an enzyme involved in cardiac contractility. Additionally, tadalafil is approximately 700-fold more potent for PDE5 than for PDE6, an enzyme which is found in the retina and is responsible for photo transduction. Tadalafil is also > 10,000-fold more potent for PDE5 than for PDE7 through PDE10.

## 5.2 Pharmacokinetic properties

Absorption

Tadalafil is readily absorbed after oral administration and the mean maximum observed plasma concentration (Cmax) is achieved at a median time of 2 hours after dosing. Absolute bioavailability of tadalafil following oral dosing has not been determined.

The rate and extent of absorption of tadalafil are not influenced by food, thus tadalafil may be taken with or without food. The time of dosing (morning versus evening) had no clinically relevant effects on the rate and extent of absorption.

Distribution

The mean volume of distribution is approximately 63 l, indicating that tadalafil is distributed into tissues. At therapeutic concentrations, 94 % of tadalafil in plasma is bound to proteins. Protein binding is not affected by impaired renal function.

Less than 0.0005 % of the administered dose appeared in the semen of healthy subjects.

Biotransformation

Tadalafil is predominantly metabolised by the cytochrome P450 (CYP) 3A4 isoform. The major circulating metabolite is the methylcatechol glucuronide. This metabolite is at least 13,000-fold less potent than tadalafil for PDE5. Consequently, it is not expected to be clinically active at observed metabolite concentrations.

Elimination

The mean oral clearance for tadalafil is 2.5 l/h and the mean half-life is 17.5 hours in healthy subjects. Tadalafil is excreted predominantly as inactive metabolites, mainly in the faeces (approximately 61 % of the dose) and to a lesser extent in the urine (approximately 36 % of the dose)

## 5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, and toxicity to reproduction.

There was no evidence of teratogenicity, embryo toxicity or foeto toxicity in rats or mice that received up to 1000 mg/kg/day tadalafil. In a rat prenatal and postnatal development study, the no observed effect dose was 30 mg/kg/day. In the pregnant rat the AUC for calculated free drug at this dose was approximately 18 times the human AUC at a 20 mg dose.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of Excipients

Sodium Lauryl Sulphate, Lactose Monohydrate, Croscarmellose Sodium, Microcrystalline Cellulose, Hydroxypropyl Cellulose, Magnesium Stearate, Isopropyl Alcohol, Hypromellose, Titanium Dioxide, Purified Talc, Triacetin, Ferric Oxide Red, Ferric Oxide Yellow & Purified Water.

### 6.2 Incompatibilities

None

### 6.3 Shelf Life

24 months

### 6.4 Special Precautions for storage

Store below 30°C in a dry place. Protect from light.

### 6.5 Nature and contents of container

Nature: 1 blister strip of 10 film coated tablets packed in a carton along with pack insert.

Contents of container: 1x10's

### 6.6 Special precautions for disposal

No special requirements.

## 7. ADDRESS OF THE MANUFACTURER

M/s. FOURRTS (INDIA) LABORATORIES PVT.LIMITED,
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**8. Marketing Authorization Number:**

NAFDAC Reg No: B4 – 9857B

**9. Date of first Authorization / Renewal of the authorization:**

Renewal of Authorization: 31.05.2019

**10. Date of revision of the text:**

25th October 2023