SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

Generic Name: Tadalafil Tablets USP 20 mg

Brand Name: Talis-20

2. Qualitative and quantitative composition

Each Film coated Tablet contains:

Tadalafil USP..... 20 mg

Excipients..... q.s.

Color: Yellow Oxide of Iron

Excipient(s) with known effect:

Each film-coated tablet contains 240.00 mg of lactose (as monohydrate) & 1.0 mg of Sodium Lauryl Sulphate.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Solid, oral dosage form-Film-coated tablets

Description:

Yellow, almond shaped, film-coated tablets debossed with 'T20' on side and plain on other side.

4. Clinical particulars

4.1. Therapeutic Indication

Treatment of erectile dysfunction in adult males.

In order for Tadalafil to be effective for the treatment of erectile dysfunction, sexual stimulation is required. Tadalafil Tablets is not indicated for use by women.

4.2 Posology and method of administration

Posology

Erectile dysfunction in adult Men.

In general, the recommended dose is 10 mg taken prior to anticipated sexual activity and with or without food. In those patients in whom Tadalafil 10 mg does not produce an adequate effect, 20 mg might be tried. It may be taken at least 30 minutes prior to sexual activity.

The maximum dose frequency is once per day.

Tadalafil 10 and 20 mg is intended for use prior to anticipated sexual activity and it is not recommended for continuous daily use. In patients who anticipate a frequent use of Tadalafil 20 mg tablets (i.e., at least twice weekly) a once daily regimen with the lowest doses of Tadalafil 20 mg

tablets might be considered suitable, based on patient choice and the physician's judgment.
In these patients, the recommended dose is 5mg taken once a day at approximately the same time of day. The dose may be decreased to 2.5 mg once a day based on individual tolerability.
The appropriateness of continued use of the daily regimen should be reassessed periodically. Benign prostatic hyperplasia in adult men (Tadalafil 20 mg only).
The recommended dose is 5 mg, taken at approximately the same time every day with or without food. For adult men being treated for both benign prostatic hyperplasia and erectile dysfunction the recommended dose is also 5 mg taken at approximately the same time every day. Patients who are unable to tolerate tadalafil 5 mg for the treatment of benign prostatic hyperplasia should consider an alternative therapy as the efficacy of tadalafil 2.5 mg for the treatment of benign prostatic hyperplasia has not been demonstrated.

Special Populations

Elderly Men

Dose adjustments are not required in elderly patients.

Men with Renal Impairment

Dose adjustments are not required in patients with mild to moderate renal impairment. For patients with severe renal impairment, 10 mg is the maximum recommended dose.
Once-a-day dosing of 2.5 or 5 mg tadalafil both for the treatment of erectile dysfunction or benign prostatic hyperplasia is not recommended in patients with severe renal impairment.

Men with Hepatic Impairment

For the treatment of erectile dysfunction using on-demand Tadalafil 20 mg tablets the recommended dose of Tadalafil-5 is 10 mg taken prior to anticipated sexual activity and with or without food. There is limited clinical data on the safety of Tadalafil 20 mg tablets in patients with severe hepatic impairment (Child-Pugh class C); if prescribed, a careful individual benefit/risk evaluation should be undertaken by the prescribing physician. There are no available data about the administration of doses higher than 10mg of tadalafil to patients with hepatic impairment.
Once-a-day dosing both for the treatment of erectile dysfunction and benign prostatic hyperplasia has not been evaluated in patients with hepatic impairment; therefore, if prescribed, a careful individual benefit/risk evaluation should be undertaken by the prescribing physician.

Men with Diabetes

Dose adjustments are not required in diabetic patients.

Paediatric population

There is no relevant use of Tadalafil 20 mg tablets in the paediatric population with regard to the treatment of erectile dysfunction.

Method of administration:

Tadalafil Tablets is for oral use.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. In clinical studies, tadalafil was shown to augment the hypotensive effects of nitrates. This is thought to result from the combined effects of nitrates and tadalafil on the nitric oxide/cGMP pathway. Therefore, administration of Tadalafil to patients who are using any form of organic nitrate is contraindicated.

Tadalafil, must not be used in men with cardiac disease for whom sexual activity is inadvisable. Physicians should consider the potential cardiac risk of sexual activity in patients with pre-existing cardiovascular disease.

The following groups of patients with cardiovascular disease were not included in clinical trials and the use of tadalafil is therefore contraindicated:

• Patients with myocardial infarction within the last 90 days.

• Patients with unstable angina or angina occurring during sexual intercourse.

• Patients with New York Heart Association class 2 or greater heart failure in the last 6 months.

• Patients with uncontrolled arrhythmias, hypotension (<90/50mmHg), or uncontrolled hypertension.

• Patients with a stroke within the last 6 months.

Tadalafil 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 co-administration of PDE5 inhibitors, including tadalafil, with guanylate cyclase stimulators, such as riociguat, is contraindicated as it may potentially lead to symptomatic hypotension.

4.4 Special warnings and precautions for use

Before treatment with Tadalafil

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-nerve-sparing prostatectomy.

Cardiovascular

Serious cardiovascular events, including myocardial infarction, sudden cardiac death, unstable angina pectoris, ventricular arrhythmia, stroke, transient ischaemic attacks, chest pain, palpitations and tachycardia, have been reported either post marketing and/or in clinical trials. Most of the patients in whom these events have been reported had pre-existing cardiovascular risk factors. However, it is not possible to definitively determine whether these events are related directly to these risk factors, to Tadalafil, to sexual activity, or to a combination of these or other factors.

In patients who are taking alpha$_1$ blockers, concomitant administration of Tadalafil may lead to symptomatic hypotension in some patients (see section 4.5). The combination of tadalafil and doxazosin is not recommended.

Vision

Visual defects, including Central Serous Chorioretinopathy (CSCR) and cases of NAION have been reported in connection with the intake of Tadalafil and other PDE5 inhibitors. Most cases of CSCR resolved spontaneously after stopping tadalafil. Analyses of observational data suggest an increased risk of acute NAION in men with erectile dysfunction following exposure to tadalafil or other PDE5 inhibitors. As this may be relevant for all patients exposed to tadalafil, the patient should be advised that in case of sudden visual defect, visual acuity impairment and/or visual distortion, he should stop taking Tadalafil and consult a physician immediately.

Decreased or sudden hearing loss

Cases of sudden hearing loss have been reported after the use of tadalafil. Although other risk factors were present in some cases (such as age, diabetes, hypertension and previous hearing loss history) patients should be advised to stop taking tadalafil and seek prompt medical attention in the event of sudden decrease or loss of hearing.

Hepatic impairment

There is limited clinical data on the safety of single-dose administration of Tadalafil in patients with severe hepatic insufficiency (Child-Pugh class C). If Tadalafil is prescribed, a careful individual benefit/risk evaluation should be undertaken by the prescribing physician.

Priapism and anatomical deformation of the penis

Patients who experience erections lasting 4 hours or more should be instructed to seek immediate medical assistance. If priapism is not treated immediately, penile tissue damage and permanent loss of potency may result.

Tadalafil, 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 anaemia, multiple myeloma, or leukaemia).

Use with CYP3A4 inhibitors

Caution should be exercised when prescribing Tadalafil to patients using potent CYP3A4 inhibitors (ritonavir, saquinavir, ketoconazole, itraconazole, and erythromycin), as increased tadalafil exposure (AUC) has been observed if the medicinal products are combined.

Tadalafil and other treatments for erectile dysfunction

The safety and efficacy of combinations of Tadalafil and other PDE5 inhibitors or other treatments for erectile dysfunction have not been studied. The patients should be informed not to take Tadalafil in such combinations.

Children and adolescents:

Children and adolescents under the age of 18 do not indicate Tadalafil Tablets for use.

Excipient with known effect:

Lactose

Tadalafil contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

Sodium Lauryl Sulphate

This medicine contains sodium lauryl sulphate. It may cause stomach upset or diarrhoea. It may also affect absorption of other medicines taken at the same time.

4.5 Interaction with other medicinal products and other forms of interaction

Cytochrome P450 Inhibitors:

Azole Antifungals (e.g. ketoconazole):

Ketoconazole (200 mg daily), increased Tadalafil (10 mg) single dose exposure (AUC) 2-fold and C_{max} by 15 %, relative to the AUC and C_{max} values for Tadalafil alone. Ketoconazole (400 mg daily) increased Tadalafil (20 mg) single dose exposure (AUC) 4-fold and C_{max} by 22 %.

Protease inhibitors (e.g. ritonavir):

Ritonavir (200 mg twice daily), which is an inhibitor of CYP3A4, CYP2C9, CYP2C19, and

CYP2D6, increased Tadalafil (20 mg) single dose exposure (AUC) 2-fold with no change in C_{max}. Ritonavir (500 mg or 600 mg twice daily) increased Tadalafil (20 mg) single-dose exposure (AUC) by 32 % and decreased C_{max} by 30 %.

Cytochrome P450 Inducers:

Endothelin-1 receptor antagonists (e.g. bosentan) Bosentan (125 mg twice daily), a substrate of CYP2C9 and CYP3A4 and a moderate inducer of CYP3A4, CYP2C9 and possibly CYP2C19, reduced Tadalafil (40 mg once per day) systemic exposure by 42 % and C_{max} by 27 % following multiple dose co-administration. The efficacy of Tadalafil in patients already on bosentan therapy has not been conclusively demonstrated. Tadalafil did not affect the exposure (AUC and C_{max}) of bosentan or its metabolites.

The safety and efficacy of combinations of Tadalafil and other endothelin-1 receptor antagonists have not been studied.

Antimicrobial medicinal products (e.g. rifampicin):

A CYP3A4 inducer, rifampicin (600 mg daily), reduced Tadalafil AUC by 88 % and C_{max} by 46 %, relative to the AUC and C_{max} values for Tadalafil alone (10 mg).

Effects of Tadalafil on other medicinal products:

Nitrates:

In clinical studies, Tadalafil (5, 10 and 20 mg) was shown to augment the hypotensive effects of nitrates. This interaction lasted for more than 24 hours and was no longer detectable when 48 hours had elapsed after the last Tadalafil dose. Therefore, administration of Tadalafil to patients who are using any form of organic nitrate is contraindicated.

Anti-hypertensives (including Calcium channel blockers):

The co-administration of doxazosin (4 and 8 mg daily) and Tadalafil (5 mg daily dose and 20 mg as a single dose) increases the blood pressure-lowering effect of this alpha-blocker in a significant manner.

This effect lasts at least twelve hours and may be symptomatic, including syncope. Therefore, this combination is not recommended.

In interaction studies performed in a limited number of healthy volunteers, these effects were not reported with alfuzosin or tamsulosin.

In clinical pharmacology studies, the potential for Tadalafil (10 and 20 mg) to augment the hypotensive effects of antihypertensive medicinal products was examined. Major classes of antihypertensive medicinal products were studied either as monotherapy or as part of combination therapy. In patients taking multiple antihypertensive medicinal products whose hypertension was not well controlled, greater reductions in blood pressure were observed compared

to patients whose blood pressure was well controlled, where the reduction was minimal and similar to that in healthy subjects.

In patients receiving concomitant antihypertensive medicinal products, Tadalafil 20 mg may induce a blood pressure decrease, which (with the exception of doxazosin -see above) is, in general, minor and not likely to be clinically relevant.

Riociguat:

Preclinical studies showed an additive systemic blood pressure lowering effect when PDE5 inhibitors were combined with riociguat. In clinical studies, riociguat has been shown to augment the hypotensive effects of PDE5 inhibitors. There was no evidence of favourable clinical effect of the combination in the population studied. Concomitant use of riociguat with PDE5 inhibitors, including Tadalafil, is contraindicated.

Alcohol:

Alcohol concentrations were not affected by co-administration with Tadalafil (10 mg or 20 mg). In addition, no changes in Tadalafil concentrations were seen after co-administration with alcohol. Tadalafil (20 mg) did not augment the mean blood pressure decrease produced by alcohol (0.7 g/ kg or approximately 180 ml of 40 % alcohol [vodka] in an 80 kg male), but in some subjects, postural dizziness and orthostatic hypotension were observed. The effect of alcohol on cognitive function was not augmented by Tadalafil (10 mg).

CYP1A2 substrates (e.g. theophylline):

When Tadalafil 10 mg was administered with theophylline (a non-selective phosphodiesterase inhibitor) there was no pharmacokinetic interaction. The only pharmacodynamic effect was a small (3.5 bpm) increase in heart rate.

CYP2C9 substrates (e.g.R-warfarin):

Tadalafil (10 mg and 20 mg) had no clinically significant effect on exposure (AUC) to S-warfarin or R-warfarin (CYP2C9 substrate), nor did Tadalafil affect changes in prothrombin time induced by warfarin.

Acetylsalicylic acid:

Tadalafil (10 mg and 20 mg) did not potentiate the increase in bleeding time caused by acetyl salicylic acid.

P-glycoprotein substrates (e.g. digoxin):

Tadalafil (40 mg once per day) had no clinically significant effect on the pharmacokinetics of digoxin.

Oral contraceptive pill:

At steady-state, Tadalafil (40 mg once per day) increased ethinylestradiol exposure (AUC) by 26 % and C_{max} by 70 % relative to oral contraceptive administered with placebo. There was no statistically significant effect of Tadalafil on levonorgestrel which suggests the effect of ethinylestradiol is due to inhibition of gut sulphation by Tadalafil. The clinical relevance of this finding is uncertain.

Terbutaline:

A similar increase in AUC and C_{max} seen with ethinylestradiol may be expected with oral administration of terbutaline, probably due to inhibition of gut sulphation by Tadalafil. The clinical relevance of this finding is uncertain.

4.6 Pregnancy, Breastfeeding and Fertility:

Tadalafil is not indicated for use by women.

Pregnancy

There are limited data from the use of tadalafil in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. As a precautionary measure, it is preferable to avoid the use of Tadalafil during pregnancy.

Breastfeeding

Available pharmacodynamic/toxicological data in animals have shown excretion of tadalafil in milk. A risk to the suckling child cannot be excluded. Tadalafil should not be used during breast feeding.

Fertility

Effects were seen in dogs that might indicate impairment of fertility. Two subsequent clinical studies suggest that this effect is unlikely in humans, although a decrease in sperm concentration was seen in some men.

4.7 Effects on ability to drive and use machines

It has negligible influence on the ability to drive or use machines. Although the frequency of reports of dizziness in placebo and tadalafil arms in clinical trials was similar, patients should be aware of how they react to tadalafil tablets 20 mg before driving or using machines.

4.8 Undesirable effects

- Allergic reactions including skin rashes (frequency common).
- Chest pain does not use nitrates, but seek immediate medical assistance (frequency common).
- Priapism, a prolonged and possibly painful erection after taking Tadalafil Tablets (frequency uncommon). If you have such an erection, which lasts continuously for more than 4 hours you should contact a doctor immediately.
- Sudden loss of vision (rarely reported).

The following side effects have been very commonly reported in patients taking Tadalafil Tablets (may affect more than 1 in 10 people): headache, flushing, nasal and sinus congestion (blocked nose), nausea, indigestion (including abdominal pain or discomfort), muscle aches, back pain and pain in the extremity (including limb discomfort).

Other side effects have been reported:

Common (may affect up to 1 in 10 people):

- Blurred vision, low blood pressure, nosebleed, vomiting, increased or abnormal uterine bleeding, swelling of the face, acid reflux, migraine, irregular heartbeat and fainting.

Uncommon (may affect up to 1in 100 people):

- Seizures, passing memory loss, hives, excessive sweating, penile bleeding, presence of blood in semen and/or urine, high blood pressure, fast heart rate, sudden cardiac death and ringing in the ears.

PDE5 inhibitors are also used for the treatment of erectile dysfunction in men. Some side effects have been rarely reported:

- Partial, temporary or permanent decrease e or loss of vision in one or both eyes and serious allergic reaction which causes swelling of the face or throat. Sudden decrease or loss of hearing has also been reported.

Some side effects have been reported in men taking Tadalafil for the treatment of erectile dysfunction. These events were not seen in clinical studies for pulmonary arterial hypertension and therefore frequency is unknown:

- Swelling of the eyelids, eye pain, red eyes, heart attack and stroke.

Most but not all of those men reporting fast heart rate, irregular heartbeat, heart attack, stroke and sudden cardiac death had known heart problems before taking Tadalafil. It is not possible to determine whether these events were related directly to Tadalafil.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to the Botswana Medicines Regulatory Authority (BOMRA) through physicians or pharmacists.

4.9 Overdose

Single doses of up to 500 mg have been given to healthy subjects, and multiple daily doses up to 100 mg have been given to patients with erectile dysfunction. Adverse reactions were similar to those seen at lower doses.

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

5. Pharmacological properties

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Urologicals, drugs used in erectile dysfunction**.**

ATC code: G04BE08

Tadalafil is a potent and selective inhibitor of phosphodiesterase type 5 (PDE5), the enzyme responsible for the degradation of cyclic guanosine monophosphate (cGMP). Pulmonary arterial hypertension is associated with impaired release of nitric oxide by the vascular endothelium and consequent reduction of cGMP concentrations within the pulmonary vascular smooth muscle. PDE5 is the predominant phosphodiesterase in the pulmonary vasculature. Inhibition of PDE5 by Tadalafil increases the concentrations of cGMP resulting in relaxation of the pulmonary vascular smooth muscle cell and vasodilation of the pulmonary vascular bed.

5.2 Pharmacokinetic properties Pharmacokinetic Properties: Absorption:

Tadalafil is readily absorbed after oral administration and the mean maximum observed plasma concentration (C_{max}) is achieved at a median time of 4 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 after a single 10 mg administration) had no clinically relevant effects on the rate and extent of absorption.

Distribution:

The mean volume of distribution is approximately 771 at steady state, 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 3.4 l/h at steady state and the mean terminal half-life is 16 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, embryotoxicity, or foetotoxicity 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.

There was no impairment of fertility in male and female rats. In dogs given tadalafil daily for 6 to 12 months at doses of 25 mg/kg/day (resulting in at least a 3-fold greater exposure [range 3.7-18.6] than seen in humans given a single 20 mg dose) and above, there was regression of the seminiferous tubular epithelium that resulted in a decrease in spermatogenesis in some dogs.

6. Pharmaceutical particulars

6.1 List of excipients

Lactose Monohydrate, Low substituted Hydroxypropyl Cellulose, Hydroxypropyl cellulose, Sodium Lauryl Sulphate, Microcrystalline cellulose, Magnesium Stearate, Instacoat Aqua III A03G30218 & Purified Water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 30°C.

Keep out of the sight and reach of children.

6.5 Nature and contents of container

1 x 4's / 3 x 10's Alu-PVC/PE/PVDC (triplex) blister pack

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder

UMEDICA LABORATORIES PVT. LTD.

302, Dalamal House, 3rd floor, J. Bajaj Road,

Nariman point. Mumbai-400021, INDIA.

Phone: +91 – 22 – 62455050, 40028503;

Email: exports@umedicalabs.com

8. Marketing authorization number(s)

Zimbabwe-2025/31/6961

Botswana-To be assigned

9. Date of first authorization/renewal of the authorization

New registration in Botswana.

10. Date of revision of the text

22/06/2026