

PACKAGE INSERT - OLTAD

1. NAME OF THE MEDICINAL PRODUCT

Oltad 20mg, film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 20mg film-coated tablet contains 20mg tadalafil

Excipient with known effect: lactose

- Each 20 mg film-coated tablet contains 245.5mg of lactose monohydrate

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

The 20mg tablets are yellow, round, convex film-coated tablets, plain on both sides, with diameter of nucleus 10.3mm

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Oltad is indicated for:

Treatment of erectile dysfunction in adult males. In order for tadalafil to be effective for the treatment of erectile dysfunction, sexual stimulation is required.

Oltad 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 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 (i.e., at least twice weekly), a once daily regimen with the lowest doses of tadalafil might be considered suitable, based on patient choice and the physician's judgement.

In these patients, the recommended dose is 5 mg 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.

Special population:

Elderly patients

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, 10mg is the maximum recommended dose. Once-a-day dosing of tadalafil is not recommended in patients with severe renal impairment.

Men with hepatic impairment

The recommended dose of Tadalafil is 10 mg taken prior to anticipated sexual activity and with or without food. There is limited clinical data on the safety of Tadalafil 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 10 mg of tadalafil to patients with hepatic impairment. Once-a-day dosing 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 in the paediatric population with regard to the treatment of erectile dysfunction.

The safety and efficacy of tadalafil in individuals below 18 years of age has not yet been established. No data are available.

Method of administration

Tablets for oral use.

4.3. Contraindications

- Hypersensitivity to the active substance or to any of the excipients
- 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. (See section [DRUG INTERACTIONS](#))
- 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.
- [Tadalafil is contraindicated in the following groups of patients with cardiovascular disease:](#)
 - 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 (see section [WARNINGS AND PRECAUTIONS](#)).
- 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 (see [DRUG INTERACTIONS](#)).

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 (see section [CONTRAINDICATIONS](#)).
- 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 [in patients receiving tadalafil](#). 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 α_1 blockers, concomitant administration of tadalafil may lead to symptomatic hypotension in some patients (see [DRUG INTERACTIONS](#)). The combination of tadalafil and [Alpha blockers](#) is not recommended.

Vision

Visual defects and cases of NAION have been reported in connection with the intake of tadalafil and other PDE5 inhibitors. The patient should be advised that in case of sudden visual defect, he should stop taking tadalafil and consult a physician immediately (see [CONTRAINDICATIONS](#)).

Renal and hepatic impairment

Due to increased tadalafil exposure (AUC), limited clinical experience and the lack of ability to influence clearance by dialysis, once-a-day dosing of tadalafil is not recommended in patients with severe renal impairment.

There is limited [information](#) on the safety of single-dose administration of tadalafil as treatment of erectile dysfunction or benign prostatic hyperplasia in patients with severe hepatic insufficiency (Child-Pugh class C). Once-a-day administration either for the treatment of erectile dysfunction or benign prostatic hyperplasia has not been evaluated in patients with hepatic insufficiency. If tadalafil is prescribed, a careful individual benefit/risk evaluation should be undertaken by the prescribing physician.

Priapism and anatomical deformation of the penis

Priapism has been reported in men treated with PDE5 inhibitors. 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 inducers or 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 (see DRUG INTERACTIONS).

For patients chronically taking potent inducers of CYP3A4, such as rifampicin, the use of tadalafil is not recommended (see DRUG INTERACTIONS).

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.

Prostacyclin and its analogues

The efficacy and safety of tadalafil co-administered with prostacyclin or its analogues has not been studied in controlled clinical studies. Therefore, caution is recommended in case of co-administration.

Bosentan

The efficacy of tadalafil in patients already on bosentan therapy has not been conclusively demonstrated.

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

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

Effects of Other Substances on tadalafil

Cytochrome P450 inhibitors

Tadalafil is principally metabolised by CYP3A4.

- A selective inhibitor of CYP3A4, ketoconazole (200mg daily), increased tadalafil (10mg) exposure (AUC) 2-fold and C_{max} by 15%, relative to the AUC and C_{max} values for tadalafil alone.
- Ketoconazole (400mg daily) increased tadalafil (20mg) exposure (AUC) 4-fold and C_{max} by 22%.
- Ritonavir, a protease inhibitor (200mg twice daily), which is an inhibitor of CYP3A4, CYP2C9, CYP2C19, and CYP2D6, increased tadalafil (20mg) 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 %.
- Although specific interactions have not been studied, other protease inhibitors, such as saquinavir, and other CYP3A4 inhibitors, such as erythromycin, clarithromycin, itraconazole, and grapefruit juice, should be co-administered with caution, as they would be expected to increase plasma concentrations of tadalafil. Consequently, the incidence of the adverse reactions might be increased.

Transporters

The role of transporters (for example, p-glycoprotein) in the disposition of tadalafil is not known. Therefore, there is the potential of drug interactions mediated by inhibition of transporters.

Cytochrome P450 inducers

Antimicrobial medicinal products (e.g. rifampicin)

A CYP3A4 inducer, rifampicin (600 mg daily), reduced tadalafil AUC by 88%, relative to the AUC values for tadalafil alone (10mg). This reduced exposure can be anticipated to decrease the efficacy of tadalafil; the magnitude of decreased efficacy is unknown.

Other inducers of CYP3A4, such as phenobarbital, phenytoin, and carbamazepine, may also decrease plasma concentrations of tadalafil.

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.

Effects of tadalafil on Other Medicinal Products

Nitrates

Augment the hypotensive effects of nitrates. Therefore, concomitant use of any form of organic nitrate is contraindicated. Thus, in a patient prescribed any dose of tadalafil (2.5-20mg), where nitrate administration is deemed medically necessary in a life-threatening situation, at least 48 hours should have elapsed after the last dose of tadalafil before nitrate administration is considered. In such circumstances, nitrates should only be administered under close medical supervision with appropriate haemodynamic monitoring.

Anti-hypertensives (including calcium channel blockers)

Augment blood pressure-lowering effect of doxazosin significantly when co-administered with tadalafil. This effect lasts at least twelve hours and may be symptomatic, including syncope. Therefore, this combination is not recommended (see WARNINGS AND PRECAUTIONS). Although these effects were not reported with alfuzosin or tamsulosin, caution should be exercised when using tadalafil in patients treated with any alpha-blockers, and notably in the elderly. Treatments should be initiated at minimal dosage and progressively adjusted.

Tadalafil had no clinically significant interaction with major classes of anti-hypertensive medicinal products including calcium channel blockers (amlodipine), ACE-inhibitors (enalapril), beta-adrenergic receptor blockers (metoprolol), thiazide diuretics (bendroflumazide), and angiotensin II receptor blockers (various types and doses, alone or in combination with thiazides, calcium channel blockers, beta blockers and/or alpha blockers).

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

No difference in adverse events was reported in patients taking tadalafil with or without anti-hypertensive medicinal products. However, appropriate clinical advice should be given to patients regarding a possible decrease in blood pressure when they are treated with anti-hypertensive medicinal products.

CYP1A2 substrates (e.g. theophylline)

When tadalafil 10mg was administered with theophylline (a non-selective phosphodiesterase inhibitor) in a clinical pharmacology study, there was no pharmacokinetic interaction. The only pharmacodynamic effect was a small (3.5 bpm) increase in heart rate. Although this effect is minor and was of no clinical significance in this study, it should be considered when co-administering these medicinal products.

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.

Alcohol

Alcohol concentrations (mean maximum blood concentration 0.08%) were not affected by co-administration with tadalafil (10mg or 20mg). In addition, no changes in tadalafil concentrations were seen 3 hours after co-administration with alcohol. Alcohol was administered in a manner to maximise the rate of alcohol absorption (overnight fast with no food until 2 hours after alcohol). Tadalafil (20mg) did not augment the mean blood pressure decrease produced by alcohol (0.7g/kg or approximately 180ml of 40% alcohol [vodka] in an 80 kg male) but, in some subjects, postural dizziness and orthostatic hypotension were observed. When tadalafil was administered with lower doses of alcohol (0.6g/kg), hypotension was not observed and dizziness occurred with similar frequency to alcohol alone. The effect of alcohol on cognitive function was not augmented by tadalafil (10mg).

Cytochrome P450 metabolised medicinal products

Tadalafil is not expected to cause clinically significant inhibition or induction of the clearance of medicinal products metabolised by CYP450 isoforms. Studies have confirmed that tadalafil does not inhibit or induce CYP450 isoforms, including CYP3A4, CYP1A2, CYP2D6, CYP2E1, CYP2C9 and CYP2C19.

CYP2C9 substrates (e.g. R-warfarin)

Tadalafil (10mg and 20mg) 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.

Aspirin

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

P-glycoprotein substrates (e.g. digoxin)

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

Antidiabetic medicinal products

Specific interaction studies with antidiabetic medicinal products were not conducted.

Riociguat

Riociguat: augment hypotensive effects of PDE5 inhibitor. No evidence of favourable clinical effect of the combination has been reported. Concomitant use of riociguat with PDE5 inhibitors, including tadalafil, is contraindicated (see CONTRAINDICATIONS).

4.6. Fertility, pregnancy and lactation

Pregnancy

As a precautionary measure, it is preferable to avoid the use of tadalafil during pregnancy.

Breast-feeding

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 reported in dogs that might indicate impairment of fertility. Literature suggests that this effect is unlikely in humans, although a decrease in sperm concentration was reported in some men.

4.7. Effects on ability to drive and use machines

Tadalafil 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 before driving or using machines.

4.8. Undesirable effects

Summary of the safety profile of tadalafil in erectile dysfunction

The most commonly reported adverse reactions in patients taking tadalafil for the treatment of erectile dysfunction were headache, dyspepsia, back pain and myalgia, in which the incidences increase with increasing dose of tadalafil. The adverse reactions reported were transient, and generally mild or moderate. The majority of headaches reported with tadalafil once-a-day dosing are experienced within the first 10 to 30 days of starting treatment.

Tabulated summary of adverse reactions

Very common, Common, Uncommon, Rare, Very Rare and Not known side effects presented below.

Very common	Common	Uncommon	Rare
<i>Immune system disorders</i>			
		Hypersensitivity reactions	Angioedema ²
<i>Nervous system disorders</i>			
	Headache	Dizziness	Stroke ¹ (including haemorrhagic events), Syncope, Transient ischaemic

			attacks ¹ , Migraine ² , Seizures, Transient amnesia
<i>Eye disorders</i>			
		Blurred vision, Sensations described as eye pain	Visual field defect, Swelling of eyelids, Conjunctival hyperaemia, Non-arteritic anterior ischaemic optic neuropathy (NAION) ² , Retinal vascular occlusion ²
<i>Ear and labyrinth disorders</i>			
		Tinnitus	Sudden hearing loss
<i>Cardiac disorders¹</i>			
		Tachycardia, Palpitations	Myocardial infarction, Unstable angina pectoris ³ , Ventricular arrhythmia ³
<i>Vascular disorders</i>			
	Flushing	Hypotension ³ , Hypertension	
<i>Respiratory, thoracic and mediastinal disorders</i>			
	Nasal congestion	Dyspnoea, Epistaxis	
<i>Gastrointestinal disorders</i>			
	Dyspepsia, Gastro-oesophageal reflux	Abdominal pain	
<i>Skin and subcutaneous tissue disorders</i>			
		Rash, Hyperhydrosis (sweating)	Urticaria, Stevens-Johnson syndrome ² , Exfoliative dermatitis ²
<i>Renal and urinary disorders</i>			
		Haematuria	
<i>Musculoskeletal, connective tissue and bone disorders</i>			
	Back pain, Myalgia, Pain in extremity		
<i>Reproductive system and breast disorders</i>			
		Penile haemorrhage, Haemospermia	Prolonged erections, Priapism ²
<i>General disorders and administration site conditions</i>			
		Chest pain ¹	Facial oedema ² , Sudden cardiac death ^{1,2}

¹ Most of the patients had pre-existing cardiovascular risk factors (see [Warnings and Precautions](#)).

² Postmarketing surveillance reported adverse reactions not observed in placebo-controlled clinical trials.

³ More commonly reported when tadalafil is given to patients who are already taking antihypertensive medicinal products.

Description of selected adverse reactions

A slightly higher incidence of ECG abnormalities, primarily sinus bradycardia, has been reported in patients treated with tadalafil once a day as compared with placebo. Most of these ECG abnormalities were not associated with adverse reactions.

Other special populations

Data in patients over 65 years of age receiving tadalafil in clinical trials, either for the treatment of erectile dysfunction or the treatment of benign prostatic hyperplasia, are limited. In clinical trials with tadalafil 5mg taken once a day for the treatment of benign prostatic hyperplasia, dizziness and diarrhoea were reported more frequently in patients over 75 years of age.

4.9. Overdose

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

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: Urologicals, 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 (ED) in the absence of sexual stimulation.

Erectile dysfunction

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.

The effect of PDE5 inhibition on cGMP concentration in the corpus cavernosum is also observed in the smooth muscle of the prostate, the bladder and their vascular supply. The resulting vascular relaxation increases blood perfusion which may be the mechanism by which symptoms of benign prostatic hyperplasia are reduced. These vascular effects may be complemented by inhibition of bladder afferent nerve activity and smooth muscle relaxation of the prostate and bladder.

Pharmacodynamic effects

Tadalafil is a selective inhibitor of PDE5. PDE5 is an enzyme found in the smooth muscle of the corpus cavernosum, prostate and bladder as well as in vascular and visceral smooth muscle, skeletal muscle, platelets, kidney, lung, cerebellum and pancreas. The effect of tadalafil is more potent on PDE5 than on other phosphodiesterases.

5.2 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 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 it 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 litres 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 2.5L/h at steady state 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).

Linearity/non-linearity

Tadalafil pharmacokinetics in healthy subjects are linear with respect to time and dose. Over a dose range of 2.5 to 20mg, exposure (AUC) increases proportionally with dose. Steady state plasma concentrations are attained within 5 days of once-daily dosing. Pharmacokinetics determined with a population approach in patients with erectile dysfunction is similar to pharmacokinetics in subjects without erectile dysfunction.

Special Populations

Elderly

Healthy elderly subjects (65 years or over) had a lower oral clearance of tadalafil, resulting in 25% higher exposure (AUC) relative to healthy subjects aged 19 to 45 years. This effect of age is not clinically significant and does not warrant a dose adjustment.

Renal Insufficiency

It was reported that tadalafil exposure (AUC) approximately doubled in patients with mild (creatinine clearance of 51 to 80ml/min) or moderate (creatinine clearance of 31 to 50ml/min) renal impairment and in patients with end-stage renal disease on dialysis when they were administered a single dose tadalafil (5-20mg). In haemodialysis patients, C_{max} was reported to be 41% higher than that reported in healthy individuals. Haemodialysis contributes negligibly to tadalafil elimination.

Hepatic Insufficiency

Tadalafil exposure (AUC) in subjects with mild and moderate hepatic impairment (Child-Pugh class A and B) is comparable to exposure in healthy subjects when a dose of 10mg is administered.

There is limited clinical data on the safety of tadalafil in patients with severe hepatic insufficiency (Child-Pugh class C). If Oltad is 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. There are no available data about the administration of once-a-day dosing of tadalafil to patients with hepatic impairment. If Oltad is prescribed once-a-day, a careful individual benefit/risk evaluation should be undertaken by the prescribing physician.

Patients with severe hepatic cirrhosis (Child-Pugh Class C) have not been studied and therefore dosing of tadalafil in these patients is not recommended.

Patients with Diabetes

Tadalafil exposure (AUC) in patients with diabetes was approximately 19% lower than the AUC value for healthy subjects. This difference in exposure does not warrant a dose adjustment.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core:

- Lactose monohydrate,
- Hydroxypropylcellulose,
- Croscarmellose sodium,
- Sodium laurilsulphate,
- Cellulose microcrystalline ,
- Magnesium stearate,

Film coating

- Hypromellose
- Lactose monohydrate
- Triacetin
- Titanium dioxide (E171)
- Talc
- Iron oxide yellow (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 30°C in the original package.

6.5 Nature and contents of container

PVC/PE/PVDC-Alu blisters in carton boxes of 4 and 8 tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Manufacturer

Medochemie Ltd (Far East) Ltd, (Oral Facility), No. 40 Street 6 Vietnam Singapore Industrial Park II, Binh Duong Industry Service Urban Comple, Hoa Phu ward, Thu Dau Mot city, Vietnam

8. Product registration HOLDER

KOMEDIC SDN BHD, No. 4 Jalan PJS 11/14, Bandar Sunway, 46150 Petaling Jaya, Selangor, MALAYSIA

9. MARKETING AUTHORISATION NUMBER(S)

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11. DATE OF REVISION OF THE TEXT

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