For the use of a Registered Medical Practitioner only

PRESCRIBING INFORMATION

TALIS 20

(Tadalafil Tablets USP 20 mg)

COMPOSITION

Each film coated tablet contains :
Tadalafil USP 20mg

List of excipients
Poloxamer (188), Hydroxy Propyl cellulose, Lactose Monohydrate, Crospovidone, Microcrystalline cellulose, Colloidal Anhydrous Silica, Magnesium Stearate, (Film coating Opadry II 31F82689 (Hypromellose, Lactose Monohydrate, Titanium dioxide, Macrogol, Talc, Iron oxide Yellow))

DESCRIPTION

TALIS 20 is a Yellow colored, oval shaped, biconvex, film coated tablets plain on both the sides.

TALIS 20 contains Tadalafil which is a selective, reversible inhibitor of cyclic guanosine monophosphate (cGMP)-specific phosphodiesterase type 5 (PDE5).

PHARMACODYNAMIC AND PHARMACOKINETIC PROPERTIES

- Pharmacodynamics

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.

The effect of PDE5 inhibition on cGMP concentration in the corpus cavernosum is also reported 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 (BPH) 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. 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 phototransduction. Tadalafil is also >10,000-fold more potent for PDE5 than for PDE7 through PDE10.

- Pharmacokinetics

Tadalafil is readily absorbed after oral administration and the mean maximum observed plasma concentration (C_{max}) is reported to be 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.

The mean volume of distribution is approximately 63L, indicating that tadalafil is distributed into tissues. At therapeutic concentrations, 94% of tadalafil in plasma is reported to be bound to proteins. Protein binding is not affected by impaired renal function. Less than 0.0005% of the administered dose was reported to appear in the semen of healthy individuals.

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 reported metabolite concentrations.

Reportedly, the mean oral clearance for tadalafil is 2.5L/h and the mean half life is 17.5 hours in healthy individuals. Tadalafil is reported to be 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).

Tadalafil pharmacokinetics are reported to be linear with respect to time and dose. Over a dose range of 2.5mg 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 ED are reported to be similar to pharmacokinetics in subjects without ED.

Elderly

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

Renal impairment

It was reported that, tadalafil exposure (AUC) approximately doubled in patients with mild (creatinine clearance 51 to 80ml/min) or moderate (creatinine clearance 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 impairment

It was reported that tadalafil exposure (AUC) in patients with mild and moderate hepatic impairment (Child-Pugh Class A and B) is comparable to exposure in healthy individuals when a dose of 10mg is administered. There is limited information on the safety of tadalafil in patients with severe hepatic impairment (Child-Pugh Class C). There are no available information about the administration of once-a-day dosing of tadalafil to patients with hepatic impairment. If tadalafil is prescribed once-a-day, a careful individual benefit/risk evaluation should be undertaken by the prescribing physician.

Patients with diabetes

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

INDICATIONS

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

Treatment of the signs and symptoms of benign prostatic hyperplasia (BPH). If tadalafil is used with finasteride to initiate BPH treatment, such use is recommended for up to 26 weeks.

Treatment of erectile dysfunction and the signs and symptoms of benign prostatic hyperplasia (ED/BPH).

Tadalafil is not indicated for use by women.

DOSE AND METHOD OF ADMINISTRATION

For oral use. Tadalafil tablets can be taken with or without food.

Tablet should be swallowed whole and not divided.

Erectile Dysfunction in adult men

Tadalafil for Use as Needed

The recommended dose is 10mg taken prior to anticipated sexual activity. In those patients in whom tadalafil 10mg does not produce an adequate effect, the maximum dose is 20mg and the maximum dosing frequency is once per day. It may be taken from 30 minutes to 36 hours prior to sexual activity. Tadalafil 10mg and 20mg is intended for use prior to anticipated sexual activity and it is not recommended for continuous daily use.

Tadalafil for Once 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 starting dose is 2.5mg once a day, taken at approximately the same time every day, without regard to timing of sexual activity. The dose may be increased to 5mg once a day, based on individual efficacy and tolerability. The appropriateness of continued use of the daily regimen should be reassessed periodically.

Benign Prostatic Hyperplasia

The recommended dose is 5mg, taken at approximately the same time every day. When therapy for BPH is initiated with tadalafil and finasteride, the recommended dose of tadalafil is 5mg, taken at approximately the same time every day for up to 26 weeks.

Erectile Dysfunction and Benign Prostatic Hyperplasia

The recommended dose is 5 mg, taken at approximately the same time every day, without regard to timing of sexual activity.

Use in elderly men

Dose adjustments are not required in elderly patients.

Use in men with renal impairment

Tadalafil for Use as Needed

- Mild (creatinine clearance 51 to 80mL/min): No dose adjustment is required.
- Moderate (creatinine clearance 31 to 50mL/min): A starting dose of 5mg not more than once per day is recommended, and the maximum dose is 10mg not more than once in every 48 hours.
- Severe (creatinine clearance <30mL/min or on hemodialysis): The maximum dose is 5mg not more than once in every 72 hours.

Tadalafil for Once Daily Use

- Mild (creatinine clearance 51 to 80mL/min): No dose adjustment is required.
- Moderate (creatinine clearance 31 to 50mL/min): No dose adjustment is required.
- Severe (creatinine clearance <30mL/min or on hemodialysis): tadalafil for once daily use is not recommended.

Use in men with hepatic impairment

Tadalafil for Use as Needed

The recommended dose is 10mg taken prior to anticipated sexual activity. There is limited information 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 information about the administration of doses higher than 10mg of tadalafil to patients with hepatic impairment.

Tadalafil for Once Daily Use

Once-a-day dosing has not been extensively evaluated in patients with hepatic impairment; therefore, if prescribed, a careful individual benefit/risk evaluation should be undertaken by the prescribing physician.

Use in men with diabetes

Dose adjustments are not required in diabetic patients.

Paediatric population

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

Use in patients taking CYP3A4 Inhibitors

Tadalafil for Use as Needed

For patients taking concomitant potent inhibitors of CYP3A4, such as ketoconazole or ritonavir, the maximum recommended dose of tadalafil is 10mg, not to exceed once every 72 hours.

Tadalafil for Once Daily Use

For patients taking concomitant potent inhibitors of CYP3A4, such as ketoconazole or ritonavir, the maximum recommended dose of tadalafil is 2.5mg.

CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients.

Tadalafil was reported 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 DRUG INTERACTIONS).

Tadalafil should 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 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).

WARNINGS AND PRECAUTIONS

Before treatment with tadalafil

A medical history and physical examination should be undertaken to diagnose erectile dysfunction (ED) or benign prostatic hyperplasia and determine potential underlying causes, before pharmacological treatment is considered.

Prior to initiating any treatment for ED, 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 potentiate the hypotensive effect of nitrates (see CONTRAINDICATIONS).

The evaluation of ED 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.

Prior to initiating treatment with tadalafil for BPH, patients should be examined to rule out the presence of carcinoma of the prostate and carefully assessed for cardiovascular conditions.

Cardiovascular

Serious cardiovascular events, including myocardial infarction, sudden cardiac death, unstable angina pectoris, ventricular arrhythmia, stroke, transient ischemic 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 receiving concomitant anti-hypertensive medicinal products, tadalafil may induce a blood pressure decrease. When initiating daily treatment with tadalafil, appropriate clinical considerations should be given to a possible dose adjustment of the anti-hypertensive therapy.

In patients who are taking alpha1 blockers, such as doxazosin, concomitant administration of tadalafil may lead to symptomatic hypotension in some patients (see DRUG INTERACTIONS). Therefore, 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. 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, he should stop taking tadalafil and consult a physician immediately (see CONTRAINDICATIONS).

Decrease of sudden hearing loss

Decrease 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.

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 clinical data on the safety of single-dose administration of tadalafil in patients with severe hepatic impairment (Child-Pugh Class C). Once-a-day administration has not been evaluated in patients with hepatic impairment. 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 reported if the medicinal products are combined (see DOSE AND METHOD OF ADMINISTRATION and 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 ED have not been studied. The patients should be informed not to take tadalafil in such combinations.

Effects on ability to drive and use machines

Tadalafil has negligible influence on the ability to drive or use machines. Dizziness has been reported with tadalafil, patients should be aware of how they react to tadalafil before driving or using machines.

Lactose

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

DRUG INTERACTIONS

Interactions reported with tadalafil 10 mg and/or 20 mg are presented below.

Effects of other medicinal products on tadalafil

Cytochrome P450 inhibitors

Tadalafil is principally metabolised by CYP3A4. It was reported that, 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 reportedly increased tadalafil 20mg exposure (AUC) 4-fold and C_{max} by 22%. Ritonavir (500mg or 600mg twice daily at steady state), an inhibitor of CYP3A4, CYP2C9, CYP2C19 and CYP2D6, was reported to increase tadalafil 20mg single-dose exposure (AUC) by 32% with a 30% reduction in C_{max}, relative to the values for tadalafil 20mg alone. Ritonavir 200mg twice daily, also

reportedlyincreased tadalafil 20mg single-dose exposure (AUC) by 124% with no change in C_{max}, relative to the values for tadalafil 20mg alone. 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 coadministered with caution as they would be expected to increase plasma concentrations of tadalafil (see WARNINGS AND PRECAUTIONS). Consequently the incidence of the adverse reactions listed in section SIDE EFFECTS/UNDESIRABLE EFFECTS 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

A CYP3A4 inducer, rifampicin, reportedly reduced tadalafil AUC by 88%, relative to the AUC values for tadalafil 10mg alone. 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.

Effects of tadalafil on other medicinal products

Nitrates

Tadalafil (5, 10 and 20mg) was reported to augment the hypotensive effects of nitrates. Therefore, administration of tadalafil to patients who are using 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

Blood pressure-lowering effect of doxazosin has been reported to increase 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.

The hypotensive effects of antihypertensive medicinal products have been reported to be augmented by tadalafil. Tadalafil (10 mg except for studies with angiotensin II receptor blockers and amlodipine in which a 20mg dose was applied) had no clinically significant interaction with major classes of anti-hypertensive medicinal products including calcium channel blockers (amlodipine), ACE-inhibitors (enalapril), betaadrenergic receptor blockers (metoprolol), thiazide diuretics (bendrofluazide), 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.

Riociguat

An additive systemic blood pressure lowering effect was reported when PDE5 inhibitors were combined with riociguat. Riociguat has been reported to augment the hypotensive effects of PDE5 inhibitors. 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).

5-alpha reductase inhibitors (5-ARIs)

Caution should be exercised when tadalafil is co-administered with 5-ARIs.

CYP1A2 substrates (e.g. theophylline)

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

Ethinylestradiol and terbutaline

Tadalafil has been reported to produce an increase in the oral bioavailability of ethinylestradiol; a similar increase may be expected with oral administration of terbutaline, although the clinical consequence of this is uncertain.

Alcohol

Alcohol concentrations (mean maximum blood concentration 0.08%) were reportedly not affected by coadministration with tadalafil 10mg or 20mg. In addition, no changes in tadalafil concentrations were reported 3 hours after co-administration with alcohol. Alcohol was administered in a manner to maximize the rate of alcohol absorption (overnight fast with no food until 2 hours after alcohol). It was reported that tadalafil 20mg did not augment the mean blood pressure decrease produced by alcohol (0.7g/kg or approximately 180ml or 40% alcohol [vodka] in an 80-kg male) but in some patients, postural dizziness and orthostatic hypotension were reported. When tadalafil was administered with lower doses of alcohol (0.6g/kg), hypotension was not reported and dizziness was reported 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. It has been reported 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 reportedly 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

It was reported that tadalafil 10mg and 20mg did not potentiate the increase in bleeding time caused by aspirin.

Anti-diabetic medicinal products

There is no specific interaction studies reported with anti-diabetic medicinal products.

Digoxin

Co-administration of tadalafil 40mg once per day for 10 days did not reportedly have a significant effect on the steady-state pharmacokinetics of digoxin 0.25mg/day in healthy individuals.

SIDE EFFECTS/UNDESIRABLE EFFECTS

Summary of the safety profile

The most commonly reported adverse reactions in patients taking tadalafil for the treatment of ED or BPH 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

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

The table below lists the adverse reactions observed from spontaneous reporting and in placebo-controlled clinical trials (comprising a total of 8,022 patients on Cialis and 4,422 patients on placebo) for on-demand and once-a-day treatment of ED and the once-a-day treatment of BPH.

Frequency convention: Very common (≥1/10), Common (≥1/100 to <1/10), Uncommon (≥1/1,000 to <1/100), Rare (≥1/10,000 to <1/1,000), Very Rare (<1/10,000) and Not known (cannot be estimated from the available data).

Very common	Common	Uncommon	Rare
Immune system disorders			
		Hypersensitivity reactions	Angioedema[2]
Nervous system disorders			
	Headache	Dizziness	Stroke[1] (including haemorrhagic events), Syncope, Transient ischaemic attacks[1], Migraine[2], Seizures[2], Transient amnesia
Eye disorders			
		Blurred vision, Sensations described as eye pain	Visual field defect, Swelling of eyelids, Conjunctival hyperaemia, Non-arteritic anterior ischemic optic neuropathy (NAION)[2], Retinal vascular occlusion[2]
Ear and labyrinth disorders			
		Tinnitus	Sudden hearing loss[4]
Cardiac disorders[1]			
		Tachycardia, Palpitations	Myocardial infarction, Unstable angina pectoris[2], Ventricular arrhythmia[2]
Vascular disorders			
	Flushing	Hypotension[3], Hypertension	
Respiratory, thoracic and mediastinal disorders			
	Nasal congestion	Dyspnoea, Epistaxis	
Gastrointestinal disorders			
	Dyspepsia	Abdominal pain, Vomiting, Nausea, Gastro-oesophageal reflux	
Skin and subcutaneous tissue disorders			
	Rash		Urticaria, Stevens-Johnson syndrome[2], Exfoliative dermatitis[2], Hyperhydrosis (sweating)
Musculoskeletal, connective tissue and bone disorders			
	Back pain, Myalgia, Pain in extremity		
Renal and urinary disorders			
		Haematuria	
Reproductive system and breast disorders			
		Prolonged erections	Priapism, Penile haemorrhage, Haematospermia
General disorders and administration site conditions			
		Chest pain[1],	Facial oedema2,

		Peripheral oedema, Fatigue	Sudden cardiac death[1, 2]

[1] Most of the patients had pre-existing cardiovascular risk factors (see WARNINGS AND PRECAUTIONS).

[2] Post-marketing 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.

[4]Sudden decrease or loss of hearing has been reported in a small number of post-marketing and clinical trial cases with the use of all PDE5 inhibitors, including tadalafil.

Description of selected adverse reactions

ECG abnormalities, primarily sinus bradycardia, has been reported in patients treated with tadalafil once a day. Most of these ECG abnormalities were not reported to be 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 ED or BPH, are limited. In clinical trials with tadalafil taken on-demand for the treatment of ED, diarrhoea was reported more frequently in patients over 65 years of age. In clinical trials with tadalafil 5 mg taken once a day for the treatment of BPH, Dizziness and diarrhoea were reported more frequently in patients over 75 years of age.

USE IN SPECIAL POPULATIONS

Pregnancy and Lactation

Tadalafil is not indicated for use by women. There is no reported clinical experience on exposed pregnancies. No direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development have been reported in animals.

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.

OVERDOSE

Similar adverse events were reported with Tadalafil lower dose, single doses of up to 500 mg in healthy individuals and multiple daily doses of up to 100 mg in patients.

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

STORAGE

Store up to 30°C.

AVAILABILITY

TALIS 20 (Tadalafil) Tablet 20mg is available in blister packs. 02 tablets of 02 blisters are packed in show box along with package insert

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