Summary of product characteristics

1. NAMEOFTHEMEDICINALPRODUCT

1.1 ProductName **:Exxgraa Tablets**
1.2 GenericName **:Sildenafil Citrate Tablets 100mg**
1.3 Strength **:**100mg/Tablets
1.4 PharmaceuticalForm **:**Film Coated Tablets
1.5 Packaging **:**1×4 Diamond shape tablets in ALU-PVC Blisterpack mono carton With pack insert, such 10 mono-cartons in a shrink.

2. QUALITY AND QUANTITATIVE

COMPOSITIONBatchsize:3.00 Lac.

Sr. No.	Ingredients	Specification	Qty/ Tablets (mg)	Qty/ 3LacBatch(Kg)	Function
	DRYMIXING				
1.	Sildenafil Citrate	BP	140	42.00	Active
2.	MCC	USP	20	6.00	Anti-caking
3.	DiCalciumPhosphate	USP	138.24	41.474	DietarySup plement
4.	MaizeStarch	USP	200.74	60.224	Dis-integrant
5.	MaizeStarch**	USP	23.4	7.02	Dis-integrant
	BINDER				
6.	PVPK30	USP	67.5	2.250	Binder
7.	IsoPropylAlcohol	USP	65	19.500	Solvent
8.	MaizeStarch	USP	12.5	3.750	Dis-integrant
9.	MethylParaben	USP	0.41	0.124	Preservative
10.	PropylParaben	USP	0.21	0.063	Preservative
11.	Purifiedwater	USP	112.5	33.75	Solvent
	LUBRICATION				
12.	Talcum	USP	54.6	16.380	Lubricant
13.	ColloidalSiliconDioxide	USP	6	1.800	Lubricant
14.	MagnesiumStearate	USP	64.6	19.125	Lubricant
15.	CrossCarmelloseSodium	USP	54	16.200	Dis-integrant
16.	SodiumStarchGlycolate	USP	53.4	16.020	SuspendingAgent
	COATING				
17.	MethyleneDichloride	IH	629.88	188.964	Solvent
18.	UltraCoat U Witch 30 Blue	IH	54.45	16.335	CoatingAgent
19.	IsoPropylAlcohol	USP	629.88	188.964	Solvent
20.	Novomix WhiteGlow	IH	0.81	0.243	ColoringAgent
21.	PVPK30	USP	4.2	1.26	Binder
Totalaverageweight pertablet			**632.00mg**		

***Calculation:**

Molecular weight of Sildenafil Citrate ($C_{28}H_{38}N_6O_{11}S$) is 666.703

g/molMolecularweight of Sildenafil($C_{22}H_{30}N_6O_4S$)is 474.58 g/mol

SterileSildenafilCitrate $= \frac{\text{MolecularweightofSildenafilCitrate}_x}{\text{MolecularweightofSildenafil}}$ LabelClaim

$$= \frac{666.703}{474.58} \times 100$$

= 140.48 mg

Therefore,

Sildenafil Citrate equivalent to Sildenafil on100%assay

baseTherefore,140.48mgofSildenafilCitrateequivalenttoSildenafil100mg

3. PHARMACEUTICALFORMVISUALDESCRIPTION:

Filmcoatedtablet

4. CLINICALPARTICULARS

4.1 THERAPEUTICINDICATIONS:

Treatment of men with erectile dysfunction, which is the inability to achieve or maintain a penileerectionsufficient forsatisfactorysexual performance.

4.2 Posologyandmethodofadministration

The usual starting dose of Sildenafil is 50 mg once daily. It should be taken before 30-40 minutes ofintercourse. Depending on effectiveness and tolerance; the dose may be increased to a minimumrecommendeddoseof100mgordecreasedto25mg.Themaximumdosingfrequencyisonceperday. Somefactorsareassociatedwithincreasedplasmalevelsof Sildenafil:age>65,hepaticimpairment,severeren alimpairmentandconcomitantuseofketoconazole,itraconazoleanderythromycin. Since higher plasma levels may increase both the efficacy and incidence of adverseevents, a starting dose of 25 mg should be considered in these patients. Sildenafil may takes longertimeto work ifyou takeit with aheavymeal.

4.3 Contraindications

Sildenafil was shown to potentiate the hypotensive effects of nitrate and its administration to patientswhoareusingorganicnitrates,eitherregularlyandorintermittentlyinanyformisthereforecontraindica ted.

4.4 Specialwarningsandprecautionsforuse

A medical history and physical examination should be undertaken to diagnose erectile dysfunction anddeterminepotential underlyingcauses, beforepharmacological treatment isconsidered.

Cardiovascularriskfactors

Prior to initiating any treatment for erectile dysfunction, physicians should consider the cardiovascularstatus of their patients, since there is a degree of cardiac risk associated with sexual activity.
Sildenafilhasvasodilatorproperties,resultinginmildandtransientdecreasesinbloodpressure.Priortoprescrib ingsildenafil,physiciansshouldcarefullyconsiderwhethertheirpatientswithcertainunderlyingconditionsco uldbeadverselyaffectedbysuchvasodilatoryeffects,especiallyincombination with sexual activity. Patients with increased susceptibility to vasodilators include thosewithleftventricularoutflowobstruction(e.g.,aorticstenosis,hypertrophicobstructivecardiomyopathy) , or those with the rare syndrome of multiple system atrophy manifesting as severelyimpairedautonomic control of bloodpressure.

Sildenafilpotentiatesthe hypotensive effectofnitrates.

Serious cardiovascular events, including myocardial infarction, unstable angina, sudden cardiac death,ventriculararrhythmia,cerebrovascularhaemorrhage,transientischaemicattack,hypertensionandhyp otensionhavebeenreportedpost-marketingintemporal associationwith the useof Sildenafil.

Most, but not all, of these patients had pre-existing cardiovascular risk factors. Many events werereported to occur during or shortly after sexual intercourse and a few were reported to occur shortlyafter the use of Sildenafil without sexual activity. It is not possible to determine whether these eventsarerelated directlyto thesefactors or to otherfactors.

Priapism

Agents for the treatment of erectile dysfunction, including sildenafil, should be used with caution inpatients with anatomical deformation of the penis (such as angulation, cavernosal fibrosis or Peyronie'sdisease),orinpatientswhohaveconditionswhichmaypredisposethemtopriapism(suchassicklecellanaemia, multiple myelomaor leukaemia).

Concomitantusewithothertreatmentsforerectiledysfunction

The safety and efficacy of combinations of sildenafil with other treatments for erectile dysfunction havenotbeen studied. Thereforethe useof suchcombinations is not recommended.

Effectsonvision

Cases of visual defectshave been reported spontaneously inconnectionwith the intake of sildenafiland other PDE5 inhibitors. Cases of non-arteritic anterior ischaemic optic neuropathy, a rare condition,have been reported spontaneously and in an observational study in connection with the intake ofsildenafil and other PDE5 inhibitors. Patients should be advised that in case of sudden visual defect,theyshould stop taking Sildenafiland consult a physicianimmediately.

Concomitantusewith ritonavir

Co-administrationofsildenafilwith ritonavirisnotadvised.

Concomitantusewithalpha-blockers

Caution is advised when sildenafil is administered to patients taking an alpha-blocker, as the co-administration may lead to symptomatic hypotension in a few susceptible individuals. This is mostlikely to occur within 4 hours post sildenafil dosing. In order to minimize the potential for developingpostural hypotension, patients should be hemodynamically stable on alpha blocker therapy prior toinitiating sildenafil treatment. Initiation of sildenafil at a dose of 25 mg should be considered. Inaddition,physicians shouldadvisepatientswhat todoin theevent ofpostural hypotensivesymptoms.

4.3Interactionwithothermedicinalproductsandotherformsofinteraction

Effects of other medicinal products on

sildenafilInvitro studies:

Sildenafil metabolism is principally mediated by the cytochrome P450 (CYP) isoforms 3A4 (majorroute) and 2C9 (minor route). Therefore, inhibitors of these isoenzymes may reduce sildenafilclearance.

Invivostudies:

Population pharmacokinetic analysis of clinical trial data indicated a reduction in sildenafil clearancewhenco-administeredwithCYP3A4inhibitors(suchasketoconazole,erythromycin,cimetidine).

Although no increased incidence of adverse events was observed in these patients, when sildenafil isadministeredconcomitantlywithCYP3A4 inhibitors, astartingdoseof25mgshouldbeconsidered.

Sildenafilhadnoeffectonritonavirpharmacokinetics.Basedonpharmacokineticresultsco-administration of sildenafil with ritonavir is not advised and in any event the maximum dose ofsildenafilshould under no circumstances exceed 25 mgwithin 48hours.

SildenafilhadnoeffectonHIVproteaseinhibitorsaquinavirpharmacokinetics.

When a single 100 mg dose of sildenafil was administered with erythromycin, a specific CYP3A4inhibitor, at steady state (500 mg twice daily. for 5 days), there was a 182% increase in sildenafilsystemic exposure (AUC). In normal healthy male volunteers, there was no evidence of an effect ofazithromycin (500 mg daily for 3 days) onthe AUC, Cmax, tmax, elimination rate constant,orsubsequenthalf-lifeofsildenafiloritsprincipalcirculatingmetabolite.Cimetidine(800mg),acytochrome P450 inhibitor and non-specific CYP3A4 inhibitor, caused a 56% increase in plasmasildenafilconcentrations whenco-administered withsildenafil (50mg) tohealthyvolunteers.

Grapefruit juice is a weak inhibitor of CYP3A4 gut wall metabolism and may give rise to modestincreasesin plasmalevels of sildenafil.

Single doses of antacid (magnesium hydroxide/aluminium hydroxide) did not affect the bioavailabilityofsildenafil.

Althoughspecificinteractionstudieswerenotconductedforallmedicinalproducts,populationpharmacokinetic analysis showed no effect of concomitant medication on sildenafil pharmacokineticswhen grouped as CYP2C9 inhibitors (such as tolbutamide, warfarin, phenytoin), CYP2D6 inhibitors(suchasselectiveserotoninreuptakeinhibitors,tricyclicantidepressants),thiazideandrelateddiuretics, loop and potassium sparing diuretics, angiotensin converting enzyme inhibitors, calciumchannelblockers,beta-adrenoreceptorantagonistsorinducersofCYP450metabolism(suchasrifampicin,barbiturates).

4.6 Fertility,pregnancyandlactation

Sildenafilisnot indicatedforuse bywomen.

4.7 Effectsonabilitytodriveandusemachines

No studies on the effects on the ability to drive and use machines have been performed. As dizzinessand altered vision were reported in clinical trials with sildenafil, patients should be aware of how theyreactto Sildenafil, beforedrivingor operatingmachinery.

4.8 Undesirableeffects

Like all medicines, Sildenafil can cause side effects although not everybody gets them. The side effectsof Sildenafil are usually mild to moderate and of a short duration. All medicines including Sildenafilcancauseallergicreactions.Contactwithdoctorsimmediatelyifexperiencesanyofthefollowing

symptoms after taking Sildenafil: sudden wheeziness, difficulty in breathing or dizziness, swelling ofthe eyelids, face, lips or throat. Common side effect includes headache, facial flushing, indigestion,effectson vision, lightsensitivity, blurred vision orreduced stuffynoseanddizziness.

4.9 Overdose

In single dose volunteer studies of doses up to 800 mg with sildenafil tablets, adverse reactions weresimilar to those seen at lower doses, but the incidence rates and severities were increased. Doses of 200mg did not result in increased efficacy but the incidence of adverse reactions (headache, flushing,dizziness,dyspepsia, nasal congestion, alteredvision) was increased.

In cases of overdose, standard supportive measures should be adopted as required. Renal dialysis is notexpected to accelerate clearance as sildenafil is highly bound to plasma proteins and not eliminated intheurine.

5. Pharmacologicalproperties

5.1 Pharmacodynamicproperties

Pharmacotherapeuticgroup: Drugsusedinerectiledysfunction

ATC-code:G04BE03

Sildenafil is an oral therapy for erectile dysfunction. In the natural setting, i.e. with sexual stimulation,itrestores impaired erectile function byincreasing bloodflow to thepenis.

The physiological mechanism responsible for erection of the penis involves the release of nitric oxide(NO) in the corpus cavernosum during sexual stimulation. Nitric oxide then activates the enzymeguanylatecyclase, which results in increased levels of cyclic guanosine monophosphate (cGMP),producingsmooth muscle relaxationin thecorpuscavernosumand allowinginflow ofblood.

Sildenafil is a potent and selective inhibitor of cGMP specific phosphodiesterase type 5 (PDE5) in thecorpus cavernosum, where PDE5 is responsible for degradation of cGMP. Sildenafil has a peripheralsiteofactiononerections.Sildenafilhasnodirectrelaxanteffectonisolatedhumancorpuscavernosum but potently enhances the relaxant effect of NO on this tissue. When the NO/cGMPpathway is activated, as occurs with sexual stimulation, inhibition of PDE5 by sildenafil results inincreased corpus cavernosum levels of cGMP. Therefore sexual stimulation is required in order forsildenafilto produceits intendedbeneficial pharmacological effects.

5.2 Pharmacokinetic

propertiesAbsorption

Sildenafil is rapidly absorbed. Maximum observed plasma concentrations are reached within 30 to 120minutes(median60minutes)oforaldosinginthefastedstate.Themeanabsoluteoralbioavailabilityis41% (range25-63%).

When sildenafil is taken with food, the rate of absorption is reduced with a mean delay in tmax of 60minutesand amean reduction in Cmaxof 29%.

Distribution

The mean steady state volume of distribution (Vd) for sildenafil is 105 l, indicating distribution into thetissues. After a single oral dose of 100 mg, the mean maximum total plasma concentration of sildenafilisapproximately440ng/ml(CV40%).Sincesildenafil(anditsmajorcirculatingN-desmethylmetabolite)is96%boundtoplasmaproteins,thisresultsinthemeanmaximumfreeplasmaconcentrationforsildenafilof18ng/ml(38nM).Proteinbindingisindependentoftotaldrugconcentrations.

In healthy volunteers receiving sildenafil tablets (100 mg single dose), less than 0.0002% (average 188mg)oftheadministereddosewas present inejaculate90 minutes afterdosing.

Biotransformation

Sildenafil is cleared predominantly by the CYP3A4 (major route) and CYP2C9 (minor route) hepaticmicrosomalisoenzymes.Themajorcirculatingmetaboliteresultsfrom N-demethylationofsildenafil.

This metabolite has a phosphodiesterase selectivity profile similar to sildenafil and an in vitro potencyfor PDE5 approximately 50% that of the parent drug. Plasma concentrations of this metabolite areapproximately 40% of those seen for sildenafil. The N-desmethyl metabolite is further metabolised,witha terminal half-life ofapproximately4h.

Elimination

The total body clearance of sildenafil is 41 l/h with a resultant terminal phase half-life of 3-5 h. Aftereither oral or intravenous administration, sildenafil is excreted as metabolites predominantly in thefaeces(approximately80%ofadministeredoraldose)andtoalesserextentintheurine(approximately13%of administered oral dose).

Pharmacokineticsinspecialpatientgroups

Elderly:

Healthy elderlyvolunteers(65yearsorover)hadareducedclearanceofsildenafil,resultinginapproximately 90% higher plasma concentrations of sildenafil and the active N-desmethyl metabolitecompared to those seen in healthy younger volunteers (18-45 years). Due to age-differences in plasmaprotein binding, the corresponding increase in free sildenafil plasma concentration was approximately40%.

Renalinsufficiency:

Involunteerswithmildtomoderaterenalimpairment(creatinineclearance=30-80ml/min),thepharmacokineticsofsildenafilwerenotalteredafterreceivinga50mgsingleoraldose.Themean AUC and Cmax of the N-desmethyl metabolite increased 126% and 73% respectively, compared toage-matched volunteers with no renal impairment. However, due to high inter-subject variability, thesedifferences were not statistically significant. In volunteers with severe renal impairment (creatinineclearance <30 ml/min), sildenafil clearance was reduced, resulting in meanincreases in AUC andCmaxof100%and88%respectivelycomparedtoage-matchedvolunteerswithnorenalimpairment.In addition, N-desmethyl metabolite AUC and Cmax values were significantly increased 79% and200%respectively.

Hepaticinsufficiency:

In volunteers with mild to moderate hepatic cirrhosis (Child-Pugh A and B) sildenafil clearance wasreduced, resulting in increases in AUC (84%) and Cmax (47%) compared to age-matched volunteerswith no hepatic impairment. The pharmacokinetics of sildenafil in patients with severely impairedhepaticfunction has notbeen studied.

5.3 Preclinicalsafetydata

Non-clinical data revealed no special hazard for humans based on conventional studies of safetypharmacology,repeateddosetoxicity,genotoxicity,carcinogenicpotential,andtoxicitytoreproduction .

6. Pharmaceuticalparticulars

6.1 Listof Excipients

Sr.No.	Excipients
1.	MCC
2.	DiCalciumPhosphate
3.	MaizeStarch
BINDER	
4.	PVPK30
5.	IsoPropylAlcohol
LUBRICATION	
6.	Talcum
7.	ColloidalSiliconDioxide
8.	MagnesiumStearate
9.	CrossCarmelloseSodium
10.	Sodiumstarchglycolate
COATING	
11.	MethyleneDichloride
12	UltraCoat U Witch 30 Blue
13.	Isoproyl Alcohol
14.	Novomix WhiteGlow
15.	PVPK30

6.2 Incompatibilities:

NotApplicable

6.3 ShelfLife:

3years

6.4 Specialprecautionsforstorage:

Storeat atemperaturenot exceeding30°Cin adryplace. Protectfrom light.

7. MANUFACTURER

WINTECHPHARMACEUTICALSLTD.

Office No. 2 & 3, 3rd floor, Broadway shopping Centre,Dr. Ambedkar Road, Dadar T.T. Mumbai- 400 014,

IndiaTel:(+9122)42123456 (100 lines)
Fax:42123400

8. DISTRIBUTEDBY:

EXXONPHARMANIGERIALTD

Address: Arcee textile mill compound, Aswani road,BlockA, Plot2B, oshodi Industrial scheme, Isolo, Lagos Nigeria.

9. DATEOFREVISIONOFTHETEXT

April, 2026

10. DOSIMETRY(IFAPPLICABLE)

NotApplicable