SUMMARY OF PRODUCT CHARACTERISTICS

1. Nameofthemedicinalproduct:OBEREMTABLETS4mg

Ondansetron Orally Disintegrating tablets USP4mg

2. Qualitativeandquantitativecomposition:

EachUncoatedtabletcontains:O

ndansetronUSP4mg

For the full list of excipients,see section 6.1

3. Pharmaceuticalform:

SolidDosageform(Tablets)

4. Clinicalparticulars:

4.1 Therapeuticindications:

Adults

Ondansetronhydrochlorideisindicatedforthemanagement ofnauseaandvomitinginducedbycytotoxicchemotherapyandradiotherapy,andforthepreventionandtreatmentofpost-operativenauseaandvomiting.

PaediatricPopulation

Ondansetronhydrochlorideisindicatedforthemanagementofchemotherapy-inducednauseaandvomiting(CINV)inchildrenaged≥6months,andforthepreventionandtreatmentofPONVin childrenaged≥1month.

4.2 Posologyandmethodof administration:

ChemotherapyandRadiotherapy

Adults:Theemetogenicpotentialofcancertreatmentvariesaccordingto thedosesandcombinationsofchemotherapyandradiotherapyregimensused.Therouteofadministration anddoseofOndansetronhydrochlorideshouldbeflexibleintherangeof8-32mgadayandselectedasshownbelow.

Emetogenicchemotherapyandradiotherapy:Ondansetronhydrochloridecanbegiveneither byrectal,oral(tablets orsyrup),intravenousorintramuscularadministration.

Formostpatientsreceivingemetogenicchemotherapy orradiotherapy,Ondansetronhydrochloride8mgshouldbeadministeredasaslowintravenousorintramuscularinjectionimmediatelybeforetreatment,followedby8mgorallytwelvehourly.

Toprotectagainstdelayedorprolongedemesisafterthefirst24hours,oralorrectaltreatmentwithOndanset

ronHydrochlorideshouldbecontinuedforuptofivedaysafteracourseoftreatment.
Highlyemetogenicchemotherapy:Forpatientsreceivinghighlyemetogenicchemotherapy,e.g..high-dosecisplatin,Ondansetronhydrochloridecanbegiveneitherbyrectal,intravenousorintramuscularadministration.
Ondansetronhydrochloridehasbeenshowntobeequallyeffectiveinthefollowingdoseschedulesoverthefirst24hoursofchemotherapy:
- Asingledoseof8mgbyslowintravenousorintramuscularinjectionimmediatelybeforechemotherapy.

- Adoseof8mgbyslowintravenousorintramuscularinjectionimmediatelybeforechemotherapy,followedbytwofurtherintravenousorintramusculardosesof8mgtwotofourhours apart,orbyaconstantinfusionof1mg/hour forupto24hours.
- Asingledoseof32mgdilutedin50-l00mlofsalineorothercompatibleinfusionfluidandinfusedovernotless than15minutesimmediatelybeforechemotherapy.

Theselectionofdoseregimenshouldbedeterminedbytheseverityoftheemetogenicchallenge.Theefficacyofondansetronhydrochlorideinhighlyemetogenicchemotherapymaybeenhancedbytheadditionofa singleintravenousdoseofdexamethasonesodiumphosphate,20mgadministeredprior tochemotherapy.
Toprotectagainstdelayedorprolongedemesisafterthefirst24hours,oralorrectaltreatmentwithondansetronhydrochlorideshouldbecontinuedforuptofivedaysafteracourseoftreatment.
PaediatricPopulation
CINVin childrenaged≥6monthsandadolescents.Weight-baseddosingresultsinhighertotaldailydoses compared to BSA-baseddosing.
DosingbyBSA
Ondansetronhydrochlorideshouldbeadministeredimmediatelybeforechemotherapyasasingleintravenous doseof5mg/m2.Theintravenous dosemustnotexceed8mg.
Oraldosingcancommencetwelvehours laterandmay becontinuedforupto5days(Table1).Thetotaldailydosemustnotexceedadultdoseof32mg.
Table 1:BSA-baseddosingforChemotherapy-Childrenaged≥6months andadolescents

BSA	**Day 1[(a,b)]**	**Days 2-6[(b)]**
<0.6m^2	5mg/m^2i.v.plus 2mgsyrupafter12hrs	2mgsyrupevery12hrs
≥0.6m^2	5mg/m^2i.v.plus4mgsyruportabletafter12 hrs	4mgsyruportabletevery12hrs

aTheintravenous dosemustnotexceed8mg.
bThe totaldailydosemustnotexceedadultdoseof32mg

Dosingbybodyweight
Weight-baseddosingresultsinhighertotaldailydoses comparedtoBSA-baseddosing.Ondansetronhydrochlorideshouldbeadministeredimmediatelybeforechemotherapyasasingleintravenous doseof0.15mg/kg.Theintravenous dosemustnotexceed8mg.
Twofurtherintravenousdosesmaybegivenin4-hourlyintervals.Thetotaldailydose mustnotexceedadultdoseof32mg.

Oraldosingcancommencetwelvehours laterandmay becontinuedforupto5days(Table2).Table2:Weight-baseddosingforChemotherapy-Childrenaged≥6monthsandadolescents

Weight	**Day1**[a,b]	**Days 2-6**[b]
≤ 10Kg	Upto3dosesof0.15mg/kgevery4hrs	2mgsyrupevery12hrs
>10Kg	Upto3dosesof0.15mg/kgevery4hrs	4mgsyrup ortabletevery12hrs

aTheintravenous dosemustnotexceed8mg.
bThe totaldailydosemustnotexceedadultdoseof32mg.

Elderly: Ondansetronhydrochlorideis welltoleratedbypatientsover 65yearsand noalterationofdosage,dosingfrequencyorrouteofadministrationarerequired.
PatientswithRenalImpairment:Noalterationofdailydosageorfrequencyofdosing,orrouteofadministrationarerequired.
PatientswithhepaticImpairment:ClearanceofOndansetronhydrochlorideissignificantlyreducedandserum half-lifesignificantlyprolongedinsubjectswithmoderateorseverеimpairmentofhepaticfunction.Insuchpatientsatotaldailydoseof8mgshouldnotbeexceeded.
Post-operativenauseaandvomiting(PONV):

Adults:ForthepreventionofPONVondansetronhydrochloridecanbeadministeredorally orbyintravenousor intramuscularinjection.

Ondansetronhydrochloridemaybeadministeredasasingledoseof4mggivenbyintramuscularorslowintravenousinjectionatinductionofanaesthesia.

FortreatmentofestablishedPONVasingledoseof4mggivenbyintramuscularorslowintravenousinjectionisrecommended.

Paediatricpopulation

PONVin childrenaged≥1monthandadolescents

Oral formulation:

Nostudieshavebeenconductedontheuseoforallyadministeredondansetroninthepreventionortreatmentofpost-operativenauseaandvomiting;slowi.v.injection isrecommendedforthispurpose.

ForpreventionofPONVinpaediatricpatientshavingsurgery performedundergeneralanaesthesia,asingledoseofondansetronmaybeadministeredbyslowintravenousinjection(notlessthan30seconds)atadoseof 0.1mg/kguptoamaximum of4mgeitherpriorto,at orafterinductionofanaesthesia.

Forthetreatment ofPONVafter surgery in paediatricpatientshavingsurgeryperformedundergeneralanaesthesia,asingledoseofondansetronhydrochloridemaybeadministeredbyslowintravenousinjection(notlessthan30seconds)atadoseof0.1mg/kguptoamaximumof4mg.Thereareno dataontheuseofondansetronhydrochlorideinthetreatmentofPONVinchildrenbelow2yearsofage.

Elderly:Thereislimitedexperienceintheuseofondansetronhydrochlorideinthepreventionandtreatment of

PONVintheelderly,howeverondansetronhydrochlorideiswelltoleratedinpatientsover65yearsreceivingchemotherapy.

Patientswithrenalimpairment:Noalterationofdailydosageorfrequencyofdosing,orrouteofadministrationarerequired.

Patientswithhepaticimpairment:Clearanceofondansetronhydrochlorideissignificantlyreducedandserum half-lifesignificantlyprolongedinsubjectswithmoderateorsevereimpairmentofhepaticfunction.Insuchpatientsatotaldailydoseof8mgshouldnotbeexceeded.

Patientswithpoor sparteine/debrisoquinemetabolism:Theeliminationhalf-lifeofondansetronhydrochlorideisnotalteredinsubjectsclassifiedaspoormetabolisersofsparteineanddebrisoquine.Consequentlyinsuchpatientsrepeatdosingwillgivedrugexposurelevelsnodifferentfromthoseofthegeneralpopulation.Noalterationofdailydosageorfrequencyofdosingarerequired.

4.3 Contraindications

Hypersensitivityto anycomponentofthepreparation.

4.4 Specialwarnings andprecautionsforuse

Hypersensitivityreactionshavebeenreportedinpatientswhohaveexhibitedhypersensitivitytootherselective5HTsreceptorantagonists.Respiratoryeventsshouldbetreatedsymptomaticallyandcliniciansshouldpayparticularattentiontothemasprecursorsofhypersensitivityreactions.

Rarely,transient ECGchangesincludingQTintervalprolongationhavebeenreportedinpatientsreceivingondansetron.Inaddition,post-marketingcasesofTorsadedePointeshavebeenreportedinpatientsusingondansetron.Ondansetronshouldbeadministeredwithcautiontopatientswhohaveormaydevelopprolongationof QTc.Theseconditionsincludepatientswithelectrolyteabnormalities,withcongenitallongQTsyndrome,orpatientstakingothermedicinalproductsthatleadtoQTprolongation.Therefore,cautionshouldbeexercisedinpatientswithcardiacrhythmor conductiondisturbances,inpatientstreatedwithantiarrhythmicagentsorbeta-adrenergicblockingagentsandinpatientswithsignificantelectrolytedisturbances.

Asondansetronisknowntoincreaselargebowel transittime,patientswithsignsofsubacuteintestinalobstructionshouldbemonitoredfollowingadministration.

Inpatientswithadenotonsillarsurgerypreventionofnauseaandvomitingwithondansetronmaymaskoccultbleeding.Therefore,suchpatientsshouldbefollowedcarefullyafterondansetron.

Patientswithrarehereditaryproblemsofgalactoseintolerance,theLapplactasedeficiency orglucose-galactosemalabsorptionshouldnottakethismedicine.

PaediatricPopulation

Paediatricpatientsreceivingondansetronwithhepatotoxicchemotherapeuticagentsshouldbemonitoredcloselyforimpairedhepaticfunction.

CINV

Whencalculating thedoseonanmg/kgbasisandadministering threedosesat4-hourlyintervals,thetotaldailydosewillbehigherthanifonesingledoseof 5mg/m2followedbyanoraldoseisgiven.Thecomparativeefficacyofthesetwodifferent dosingregimenshasnotbeeninvestigatedinclinicaltrials.Cross-trialcomparisonindicatessimilarefficacyforbothregimens.

4.5 Interactionwithothermedicinalproducts andotherforms of interaction

Thereisnoevidencethatondansetroneitherinducesorinhibitsthemetabolism ofotherdrugscommonlyco-administeredwithit.Specificstudieshaveshownthattherearenopharmacokineticinteractionswhenondan

setronisadministeredwithalcohol,temazepam,furosemide,alfentanil,tramadol,morphine,lidocaine,thiopentalorpropofol.

Ondansetronismetabolisedbymultiplehepaticcytochrome P-450enzymes:CYP3A4,CYP2D6andCYP1A2.Duetothemultiplicityof metabolicenzymescapableofmetabolisingondansetron,enzymeinhibitionorreducedactivityofoneenzymee.g.CYP2D6geneticdeficiency)isnormally compensatedbyotherenzymesandshouldresultinlittleornosignificantchangein overallondansetronclearanceordoserequirement.

Phenytoin,CarbamazepineandRifampicin:Inpatientstreatedwithpotent inducersofCYP3A4(i.e.phenytoin,carbamazepine,andrifampicin),theoralclearanceofondansetronwasincreasedandondansetronbloodconcentrationsweredecreased.

Tramadol: Datafromsmallstudiesindicatethatondansetron mayreducetheanalgesiceffect oftramadol.

UseofondansetronwithQTprolongingdrugsmayresultinadditionalQTprolongation.Concomitantuseofondansetronwithcardiotoxicdrugs(e.g.anthracyclines)mayincreasetherisk ofarrhythmias.

4.6 Pregnancyandlactation

Pregnancy

Thesafetyofondansetronforusein humanpregnancyhasnotbeenestablished.

Evaluationofexperimentalanimalstudiesdoesnotindicatedirectorindirectharmfuleffectswithrespecttothedevelopmentoftheembryo,orfoetus,thecourseofgestationandpre-andpost-natal development.Howeverasanimalstudiesarenotalwayspredictiveofhumanresponsetheuseofondansetron in pregnancy isnotrecommended.

Lactation

Testshaveshownthatondansetronpassesintothemilkoflactatinganimals.Itisthereforerecommendedthatmothersreceivingondansetronshouldnotbreast-feedtheirbabies.

4.7 Effects onabilitytodriveandusemachines

Notknown

4.8 Undesirableeffects

Adverseeventsarelistedbelowbysystemorganclassandfrequency.Frequenciesaredefinedas:verycommon(≥1/10),common(≥1/100to<1/10),uncommon(≥1/1000to<1/100),rare(≥1/10,000to<1/1000)andveryrare(<1/10,000).Verycommon,commonanduncommoneventsweregenerallydeterminedfromclinicaltrialdata.Theincidenceinplacebowastakenintoaccount.Rareandveryrareeventsweregenerallydeterminedfrompost-marketingspontaneousdata.

Thefollowingfrequenciesareestimatedatthestandardrecommendeddosesofondansetronaccordingtoin

dicationandformulation.

Immunesystem disorders	
Rare:	Immediatehypersensitivityreactions,sometimessevereincludingana phylaxis.
Nervoussystem disorders	
Verycommon:	Headache.
Uncommon:	Seizures,movementdisorders(includingextrapyramidalreactionssuchasd ystonicreactions,oculogyriccrisisanddyskinesia),observedwithoutdefini tiveevidenceofpersistentclinical sequelae.
Rare:	Dizzinessduringrapidintravenousadministration.
Eyedisorders	
Rare:	Transientvisualdisturbances (e.g.blurredvision),predominantlyduringintravenousadministratio
Veryrare:	Transientblindness,predominantlyduringintravenousadministration.Th emajorityoftheblindnesscases reportedresolvedwithin20minutes.Mostpatientshadreceivedchemothera peuticagents,whichincludedcisplatin.Somecasesoftransientblindnesswe rereportedascorticalinorigin.
Cardiacdisorders	
Uncommon:	Arrhythmias,chestpainwithorwithoutSTsegmentdepression,brady cardia.
Veryrare:	TransientECGchangesincludingQTintervalprolongation,predo minantlywithintravenousadministrationof ondansetron.
Vasculardisorders	
Common:	Sensationofwarmthorflushing.
Uncommon:	Hypotension.
Respiratory,thoracicandmediastinaldisorders	

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 via EFDA yellow Card Scheme, online at https://primaryreporting.who-umc.org/ET or toll free call 8482 to Ethiopian food and drug authority (EFDA).

4.9 Overdose

SymptomsandSigns

Thereislimitedexperienceofondansetronoverdose.Inthemajorityofcases,symptomsweresimilartothosealreadyreportedin patients receivingrecommendeddoses.Manifestationsthathavebeenreportedincludevisualdisturbances,severeconstipation,hypotensionandavasovagalepisodewithtransientseconddegreeAVblock.

Treatment

Thereisnospecificantidoteforondansetron,thereforeinallcasesofsuspectedoverdose,symptomaticandsupportivetherapyshouldbegivenasappropriate.

Theuseofipecacuanhatotreatoverdosewithondansetron isnotrecommended,aspatients areunlikelyto respondduetotheanti-emeticactionofondansetronitself.

5. Pharmacologicalproperties

5.1 Pharmacodynamicproperties

Pharmacotherapeutic group: selective 5-HT3 receptor antagonist

ATC code:- A04AA01

Mode of action

Ondansetronisapotent,highlyselective5HTsreceptor-antagonist.Itsprecisemodeofactionin thecontrolofnauseaandvomitingisnotknown.Chemotherapeuticagents andradiotherapymaycausereleaseof5HTin thesmallintestineinitiatingavomotingreflexbyactivatingvagalafferentsvia5HTsreceptors.Ondansetronblockstheinitiationofthisreflex.Activationofvagalafferentsmayalsocauseareleaseof5HTintheareapostrema,locatedonthefloorofthefourthventricle,andthismayalsopromoteemesisthroughacentralmechanism.Thus,theeffectofondansetroninthemanagementofthenauseaandvomitinginducedbycytotoxicchemotherapyandradiotherapyisprobablyduetoantagonismof5HT3receptorsonneuronslocatedbothintheperipheralandcentralnervoussystem.Themechanismsofactioninpost-operativenauseaandvomitingarenotknownbut theremaybecommonpathwayswithcytotoxicinducednauseaandvomiting.

5.2 PharmacokineticProperties

Followingoraladministration,ondansetronispassivelyandcompletelyabsorbedfromthegastrointestinaltractandundergoesfirstpassmetabolism.Peakplasmaconcentrationsofabout30ng/mlareattainedapproximately1.5hoursafteran8mgdose.Fordosesabove8mgtheincreaseinondansetronsystemicexposurewithdoseisgreaterthanproportional;thismayreflectsomereductioninfirstpassmetabolismathigheroraldoses.Bioavailability,followingoraladministration,isslightlyenhancedbythepresenceoffoodbutunaffectedbyantacids.Studiesin healthyelderlyvolunteershaveshownslight,butclinicallyinsignificant,age-relatedincreasesinbothoralbioavailability(65%)andhalf-life(fivehours)ofondansetron.Genderdifferenceswereshowninthedispositionofondansetron,withfemaleshavingagreaterrateandextentofabsorptionfollowinganoraldose andreducedsystemicclearanceandvolumeofdistribution(adjustedfor weight).Thedispositionofondansetronfollowingoral,intramuscular(IM)andintravenous(IV)dosingissimilarwithaterminalhalflifeofaboutthreehoursandsteadystatevolumeofdistributionofabout140L.EquivalentsystemicexposureisachievedafterIM andIVadministrationofondansetron. Ondansetronisnothighlyproteinbound(70-76%).Ondansetronisclearedfromthesystemiccirculationpredominantlybyhepaticmetabolismthroughmultipleenzymaticpathways.Lessthan5%oftheabsorbeddoseisexcretedunchangedintheurine. Theabsenceof theenzymeCYP2D6(thedebrisoquinepolymorphism)hasnoeffectonondansetron'spharmacokinetics.Thepharmacokineticpropertiesofondansetronareunchanged onrepeatdosing.

SpecialPatientPopulations

ChildrenandAdolescents(aged1monthto17years)

Inpaediatricpatientsaged1to 4months(n=19)undergoingsurgery,weightnormalisedclearancewasapproximately30%slowerthaninpatientsaged5to24months(n=22)butcomparabletothepatientsaged3to12years.Thehalf-lifeinthepatientpopulationaged1to4monthwasreportedtoaverage6.7hourscomparedto2.9hoursforpatientsinthe5to24monthand3to12yearagerange.Thedifferencesinpharmacokineticparametersinthe1to4monthpatientpopulationcanbeexplainedinpartbythehigherpercentageoftotalbodywaterinneonatesandinfantsandahighervolumeofdistributionforwatersolubledrugslikeondansetron.

Inpaediatricpatientsaged3to12yearsundergoingelectivesurgerywithgeneralanaesthesia,theabsolutevaluesforboththeclearanceandvolumeofdistributionofondansetronwerereducedincomparisontovalueswithadultpatients.Bothparametersincreasedinalinearfashionwithweightandby12yearsofage,thevalueswereapproachingthoseofyoung adults.

5.3 Preclinical safetydata

Therearenopre-clinicaldata ofrelevance

6. Pharmaceuticalparticulars

6.1 Listofexcipients:

Magna Sweet (Mono Ammonium Glycyrrhizinate)
Sucralose
Crospovidone
Mannitol DC (Perlitol SD 160)
Avicel 200(Microcrystalline Cellulose 200)
Magnesium Stearate
Colour Sunset yellow Lake
Aerosil 200(Colloidal anhydrous Silica)
Flavour Orange Powder (Trusil Bush Boake)
Flavour Peppermint DC-117

6.2 Incompatibilities

NotApplicable

6.3 Shelflife

36months

6.4 Specialprecautions forstorage

Storein
adryplace,below25°C.Protectfromlight.Keepoutofreacho
fChildren.

6.5 Natureandcontents of container

10tabletspackedinAluAluStripandsuch1Strippackedinaprintedmonocartonwithpackinsert.

6.6 Specialprecautions fordisposalandotherhandling

NotApplicable

7 MarketingauthorizationholderCach etPharmaceuticalsPvt.Ltd.

415,ShahNaharIndustrialEstate,
Dr. E.MosesRoad,Worli,
Mumbai-400018,Maharashtra,India.

NameandAddress of Manufacturer

CachetPharmaceuticalsPvt.Ltd

Village-Thana,Baddi,Dist-Solan,HimachalPradesh–
173205

8. MarketingAuthorizationNumbers

CAC/IND/030

9. DateofFirstAuthorization/RenewaloftheAuthorization

Date of first authorisation: 11/02/2019

10. DateofRevisionoftheText

05/07/2023