İFU-MODÜL XI PAZARLAMA SONRASI YARAR RISK DEĞERLENDIRMESI 3. REVIZYON 20.01.23_EN

REPUBLICOFTURKEYMINISTRYOFHEALTH TURKISHMEDICINESAND MEDICALDEVICESAGENCY GOODPHARMACOVIGILANCEPRACTICES (GVP)GUIDELINEMODULEXI-POST-MARKETINGBENEFIT/RISKASSESSMENT FVK-KLVZ-11 EffectiveDateoftheFirstVersion 20.06.2022 EffectiveDateof1stRevision 15.11.2022 EffectiveDateof2ndRevision 30.11.2022 EffectiveDateof3rdRevision 20.01.2023 SöğütözüMahallesi,2176.SokakNo:506520 Çankaya/ANKARA Phone:(0312)2183000FaxNo:(0312)2183599 E-mail:tufam@titck.gov.trWebsite: https://www.titck.gov.tr

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DocumentNo. IssuedFirstOn RevisionDate RevisionNo. Page FVK-KLVZ-11 20/06/2022 20/01/2023 3 1/11 CHAPTERI IntroductionandScope 1.1.Introduction 1.1.1.Objective Theobjectiveofbenefit/riskevaluationistoidentifywhethersufficientevidenceis availabletodemonstratethatthebenefitsofaproductarecontinuingtooutweighitsrisks. Thisguidelineisintendedforguidingmarketingauthorizationholdersforensuringconsistent andtransparentpost-marketingbenefit/riskevaluationofmedicinesandfacilitatingdecision makingprocess.Forthefulfillmentoftherequirementsofthisguideline,thecommentsand examplesunderthebenefit/riskassessmenttemplateofModuleX-Pre-Marketing

sion published by the Turkish Medicines and Medical Devices Agency (TİTCK), imported from the AIFD Legislation Portal archive. In the event of any discrepancy, the Turkish original text (mevzuat.g

Benefit/RiskAssessmentGuidelinecanbeused.
Informationgiveninthisdocumentcontains,butisdifferentfrom,sectionswhichcan beusedinPeriodicSafetyUpdateReport(PSUR)andPeriodicBenefit/RiskEvaluation Report(PBRER)(seeAppendix1). CHAPTERII StructuresandProcesses 2.1Post-MarketingBenefit/RiskEvaluation
Thisguidelineoutlineshowtheinformationrequestedbytheagencyingeneralwillbe organizedaspartofabenefit/riskevaluation.TheAgencymaymakeadditionalrequestsas thecasemaybe.Themarketingauthorizationholdertowhomtherequestisaddressedis responsibleforcollectingevidencethatwillsupportbenefit/riskevaluationofitsown medicineonly.IftheAgency,forexample,isevaluatingthebenefit/riskofawidergroupof medicinesthathavethesameactivesubstances,eachmarketingauthorizationholdershallbe subjecttothesamerequirementsforitsownmedicines.Thefollowinginformation summarizestheinformationadvisedforeachsectionofevaluation. 2.1.1BackgroundInformation
Thissectionexplainsthebackgroundinformationonthemedicineincludingitsuse, previoussafetyinterventions,ifany,andthediseases/conditionsforwhichthemedicineis indicated.Itdescribesotherpotentialalternativesfromthesametreatmentgroupthatare comparedordiscussedinbenefit/riskevaluationandtheirplaceintreatmentofpatientor referstothem. 2.1.1.1Objective Thissectionprovidesabriefoverviewofmainissuesthatleadtoarequestfor benefit/riskevaluation. 2.1.1.2ProductInformation
Thissectionexplainsthemedicinethatisbeingevaluated.Thisinformationmayinclude indicationsapprovedinourcountry,classinformation,formulationand/orlabeling informationregardingthesafetyriskunderexamination(Contraindications,Adversereactions etc.).Otherindicationspermittedbycompetentauthoritiesofothercountriesmustalsobe includedinthissection.

 2.1.1.3LegislationHistory
Thissectionexplainstheregistrationdates(internationalandinTurkey)andlegal regulationhistoryoftheproductincludingtheapplicablelegalregulatoryandmarketing statusoftheproductbeforeregulatoryauthoritiesinourcountryandalsoinothercountries wheretheproductisregistered. 2.1.1.4CurrentRiskMinimizationStrategies
Thissectionprovidesinformationoncurrentandpreviousriskminimizationstrategies thatwereinplaceuntilbenefit/riskevaluation.Thesemayincludebutarenotlimitedtothe labelinginthelatestProductMonographofTurkey,allavailabletrainingmaterialsandany riskreportingwhichmighthavebeenpublished.
Whereapplicable,keydifferencesbetweenthelabelingofTurkeyandothermembersof InternationalCouncilforHarmonization(ICH)mustbehighlighted.Safety-relatedissues addressedthroughpastregulatoryinterventionsinTurkeyandothercountriesmustbelisted. 2.1.1.5ExposureEstimates Thissectionincludesexposureinformation:
Forinternationaldataandthedataspecifictoturkey,anexplanationmustbemade regardinghowexposureiscalculated,includingthefollowing: oDataused oHowthedatawereused oStartingandendingdatesusedforcalculation
Acomparisonmustbemadebetweenexposureinturkeyandinternationalexposure soastodrawattentiontoanyrelevantconfoundingand/orbiaswhichmighthave affectedexposurerates. 2.1.1.6InformationonDiseasesorConditions
Thissectionexplainstheunderlyingdiseases/conditionsforwhichthemedicineisused andmustincludeinformationspecifictoTurkey.Thissection,forexample,mayincludethe following: Findingsandsymptoms Targetpopulationfortheindication Pathophysiology Epidemiology(includingriskfactorsaswellasinternationalincidenceand prevalenceratesandtheratesinTurkey)
Thissectionmustalsoincludeabriefdescriptionofhowthedisease/conditionis managedincludingtreatmentoptionsforindividualpatients/populationsaswellas

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uncertaintiesofthediseaseanditstreatments. 2.1.1.7OtherTreatmentAlternatives Thissectionprovidesbackgroundinformationaboutotherrelevantmedicaltreatments includingthebenefitsandrisksofthemedicinelistedinbriefproductinformation.This informationisforcomparisonpurposeswithinthescopeofbenefit/riskevaluation.Other issues,ifany,thatmaybeincludedaretheimpedimentstopatientpreferenceorsafeand effectiveuse.Thisinformationmustbeincludedforrelevantmedicaltreatmentsuseofwhich arepermittedinTurkey.Inordertoprovideadditionalcontextalloff-labeltreatmentsusedto treattheconditionmustbediscussed.

DocumentNo. IssuedFirstOn RevisionDate RevisionNo. Page FVK-KLVZ-11 20/06/2022 20/01/2023 3 1/11 2.2EvaluationofBenefits 2.2.1CharacterizationofBenefits Thissectiondescribesthefollowing: Intendedbenefitsoftheproductforapprovedindication oForexample,treatinganacutecondition,minimizingorstabilizingachronic disorderinordertopreventadisease,reducetheriskofaseriousoutcome. Possibleeffectsontherelevant,subsequentormoreseriousconditions Informationonefficacyobtainedfromthepre-orpost-marketingevidence; oThismustincludeinformationrelatingtothepowerofefficacyevidence,for example,dataobtainedfromclinicalstudies,systematicreviewsandmeta-analyses(fromclinicaltrialsorobservationalstudies)and/ordataobtained fromtherapeuticefficacystudies.ReferencessuchasCochranecanbeused whendiscussingthequalityorpowerofevidence. Informationonreal-worldefficacyfrompost-marketingevidence. Addthefollowingtothissectionwhichisnotlistedinaspecificorder: Targetpopulationfortheindication Known/relevantpharmacologicalcharacteristicsofmedicineanditsmetabolites Identificationofthecourses,patternsand/orcorrelationsofthebenefitsevaluated Consistencyofdata Identificationofbiasandconfoundingfactors Comparisonsbetweenefficacyduringclinicaltrialsandpost-marketing(real-world) effectiveness Theroleofmedicineinprovidingabenefitwithinthecontextofmedicalpracticesinour country Primaryandsecondaryefficacy,therapeuticoutcomes(endpoints) Expectedorpotentialbenefits Developmentsinpatient-reportedoutcomes Developmentsinconsistency,persistencyand/oreaseofuse 2.2.2DiscussionofComparativeBenefits Ifdataareavailable,thissectionmaybeusefulinprovidingcontextualinformationin relationtoabenefit/riskevaluationasitcomparesefficacyinclinicaltrials/real-worldefficacy ofmedicine(ormedicineclass,ifany)withthefollowing: Nointervention Otherconventionaltreatmentsofinterventions Adescriptionofpre-orpost-marketingevidenceofcomparativeefficacy/real-world efficacybenefitsforapprovedindication(s)mustbeincluded.InadditiontoPhaseI-III clinicaltrials,thedescriptionmayincludethefollowing: PhaseIVclinicaltrials(whereapplicable) Systematicreviewsandmeta-analysesofobservationalstudies Comparativetherapeuticefficacyobservationalstudies Dataselectionprocess Evidencequality Studiesontheproductsthatarenotincludedintheanalysismustbeclearlydefinedandreasons forexclusionmustbeexplicitlysubmitted.

DocumentNo. IssuedFirstOn RevisionDate RevisionNo. Page FVK-KLVZ-11 20/06/2022 20/01/2023 3 1/11 Ifany,inthecaseofpresenceofaknownbenefitaccordingtocomparativeproductsor otheravailabletreatments,provideinformationontheuniquenessoftheproductoron comparativeefficacywhichmustincludeevidenceforalimitedpopulation,e.g. Studydesignandmethodologies Statisticalandclinicalsignificanceofresults Adequacyofstatisticalmethodsandanalyses Consistenciesandinconsistenciesbetweenefficacyandreal-worldefficacydatain pre-marketingapplications Relationshipbetweenshort-andlong-termbenefits Real-worldefficacyversusefficacyinclinicaltrials Exposure-responserelations Methodologiesforsynthesizingtrialevidence

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Compliancewithbestpractices(e.g.,Cochrane)formanagingsystematicreviewsof observationalstudies
Adequacyofmethodologiesforintegratingdataobtainedfromdifferentobservational designs
Methodologiesforintegratingrandomizedclinicaltrialdataandobservationaldata
Otherfactorsthatneedtobeconsideredintheanalysisofcomparativebenefitsareasfollows:
Adversedrugreactions/verifiedsignals Significantidentifiedrisks
Significantpotentialrisks/pharmacologicalclasseffects
Decreaseinpatient-reportedpositiveoutcomes Decreaseincompliance,persistencyand/oreaseofuse
Lackofefficacy 2.3EvaluationofRisk 2.3.1CharacterizationofIdentifiedRisk
Thissectiondescribestheissuestobediscussedfocusingontheissuethattriggered benefit/riskevaluation.Regardingtheissue(identifiedrisk),provideashortmedicalbrief whichincludesappropriateinformationonepidemiology,clinicalcharacteristics,medical severity,associatedoutcome(recoverability,morbidity,mortality),duration,preventability, predictability,measurability,capacitytofollow-uptheissue,uncertaintiesinbenefit/risk evaluationandifnotpreviouslysubmitted,knownriskfactors.Importantpotential risks/missinginformationshouldbeidentified.
Onlyaddressthepotentialriskthatleadtoundesirableclinicaloutcomesandfor whichthereisscientificevidencetosuspectthepossibilityofacausalrelationshipwiththe medicinalproduct,butwherethereiscurrentlyinsufficientevidencetoconcludethatthis associationiscausal. Theimportantpotentialrisksarethoseimportantpotentialrisksthat,whenfurther characterizedandifconfirmed,wouldhaveanimpactontherisk/benefitbalanceofthe medicinalproduct.Wherethereisascientificrationalethatanadverseclinicaloutcomemight beassociatedwithoff-labeluse,useinpopulationsnotstudied,orresultingfromthelong-termuseoftheproduct,theadversereactionshouldbeconsideredapotentialrisk,andif deemedimportant,shouldbeincludedinthelistofsafetyconcernsasanimportantpotential risk.Importantpotentialriskswouldusuallyrequirefurtherevaluationaspartofthe pharmacovigilanceplan.

DocumentNo. IssuedFirstOn RevisionDate RevisionNo. Page FVK-KLVZ-11 20/06/2022 20/01/2023 3 1/11 Missinginformationrelevanttotheriskmanagementplanningreferstogapsin knowledgeaboutthesafetyofamedicinalproductforcertainanticipatedutilization(e.g., long-termuse)orforuseinparticularpatientpopulations,forwhichthereisinsufficient knowledgetodeterminewhetherthesafetyprofilediffersfromthatcharacterizedsofar.The absenceofdataitself(e.g.exclusionofapopulationfromclinicalstudies)doesnot automaticallyconstituteasafetyconcern.Instead,theriskmanagementplanningshouldfocus onsituationsthatmightdifferfromtheknownsafetyprofile.
Evidencerelatedtotheissue(identifiedrisk)mustbedefinedstartingfromthemost appropriateevidenceandanalyzedcritically.Thetypeofevidencemaybesubjecttothe nature,incidenceand/orseverityoftheadverseevent.Incaseofpresenceofmultipletypesof evidence,itisrecommendedtosubmithighqualityevidencefirstandthenproceedtolower evidencelevels.Discussthevalidityofevidencewhichmayincludethefollowing:
Meta-analysesandsystematicreviews:
oSourceandtypeofdata(brieflydescribestrategies/termsusedforliterature search)
oStudydesignandmethodologiesincludingdatasource,selectioncriteria, weighting,riskdifferencesorratiodifferences(ifany)etc.
oStatisticalandclinicalsignificanceofresults(ifpossibleandsignificant)
oLimitationsofstudydesign,implementationorinterpretation
Clinicaltrialdata,inparticularPhaseIVstudies:
oSourceandtypeofdata(brieflydescribestrategies/termsusedforliterature search)
oStudydesignandmethodologiesincludingqualityofstudyalongwiththe informationsuchasendpointsused,treatmentandfollow-upperiodand withdrawalrates
oIncidence/prevalenceofsafetyissueinclinicaltrialscomparedtoplaceboor othertreatments

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oStatisticalandclinicalsignificanceofresults oConsistencybetweenstudies oStudyselectionprocess oLimitationsofclinicaltrialdata(e.g.,samplesizes,excludedpopulations, follow-upperiod) Observationalstudies: oSourceandtypeofdata(brieflydescribestrategies/termsusedforliterature search) oStudydesignandmethodologiesincludingqualityofstudyalongwiththe informationsuchasendpointsused,treatmentperiodandfollow-up oFrequency/prevalenceofsafetyissue oClinical/scientificsignificanceofmeasurementofriskamount oClinical/scientificvalidityofstudy/studiesincludingmethodsforcorrecting confoundingfactorssuchaspotentialbiasandmissingdata

 AdverseDrugReactionReports: oDatasourceandtype:Spontaneouspost-marketingADR(AdverseDrug Reaction)reportsgroupedaccordingtoSOC(SystemOrganClasses)or classificationschemainMedDRA(MedicalDictionaryforRegulatory Activities) oReportingperiod,searchstrategiesand/orSMQ(StandardisedMedDRA Queries)terms oThenumber,natureandoutcomeof(relevant)seriouscases oThecourses,modelsand/orcorrelationsofADRsintherelevantsubgroups (e.g.age,gender,dose,predisposingfactor,latency,treatmentperiod, demography,concomitantdrugs,underlyingdiseases,overdoseand/orfoodor druginteractionsandincidence/prevalencevaluesinnon-exposedpopulation) oSummaryofimportantcasereports oCausalityevaluationofselectedcases oWherepossible,quantitativeanalysesoftherelation(e.g.,reportingspeed, ratioofproportionalreporting,reportingprobabilityratio,information coefficient(IC)andIC025etc.) oLimitationsofADRreportsandquantitativeanalyses(e.g.qualityofreports, reportingspeed,missinginformation,dataminingassumptions,validity).

2.3.2IssuesRegardingtheSubjectMatter(IdentifiedRisk)

Thissectionsummarizestheevidenceregardingsafetyissues.Discussionsmayincludethefollowing: Relevantpharmacologicalcharacteristicsofmedicineanditsmetabolites(e.g., known/advisedmechanism(s)ofaction,potentialclasseffect); Overdoseofmedicine Susceptible/sensitivepopulationsincludingpharmacogenomics Relevantexposure/usedata Approvedusevs.off-labeluse Administrationortreatmentproblemsregardingmedicine Quantitativepoweroftherelationshipbetweentheuseofdruganddefinedsafetyissue; Evaluatethepowerandqualityofevidence.ReferencessuchasCochraneorGRADE canbeusedasappropriate. 2.3.3DiscussionofComparativeRisks

Thissectionmaybeusefulinprovidingcontextualinformationonbenefit/risk evaluationasitcomparesthedrawback(s)(identifiedrisk)ofmedicine(ormedicineclass,if any)withtheriskissuesassociatedwiththefollowing: Otherconventionaltreatments Surgicaltreatments/otherinterventions Nointervention Miscellaneousissues

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2.4EvaluationofBenefit/RiskProfile

2.4.1SummaryandAnalysisofBenefit/RiskProfileforIdentifiedRisk

Thissectionprovidesthecontextandrationalefortheoveralldecisiononbenefit/risk profileoftheproduct.Itmustincludeasummaryofbasicbenefitsandkeyrisksofthe medicinelistedaccordingtopriorityorderandwhererelevant,supportingexplanation.This sectionmustalsocomparethebenefitsandrisksofproductwhenusedunderapproved indicationsforeachissuefromsourceslikethefollowing: Meta-analysesandsystematicreviews Clinicaltrialdata,includingPhaseIVstudies ObservationalStudies AdverseDrugReactionreports(atfirstinternationalsourcesandthensourcesfrom Turkey) Qualityofevidencemustbeaddressedinthissection(forexample,ifawell-designed PhaseIVstudyiscomparedwithapoorlydesignedmeta-analysis).Discussionmustinclude thedistinctionbetweenthedatausedforinterpretingthedegreeofbenefitversusthedegree ofharmandvaluejudgments,andalsotheeffectofuncertaintyonevaluation.Referencescan

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beusedasappropriate,e.g.,Cochrane.
2.4.2SummaryandAnalysisofBenefit/RiskProfileforPotentialRisk
Ifthereareimportantpotentialrisksrelatedtotheproduct,youshouldconsiderwhetherthe benefit/riskprofileisimpactedornottakingintoaccountthese risks.
2.4.3QuantitativeBenefit/RiskAnalysis
Currently,specificquantitativeorsemiquantitativemethodologiesarenotnecessaryfor benefit/riskevaluations;however,theycanbeincludedinpresentationstosupportbenefit/risk evaluation.Adetaileddescriptionofmethodologies,software,referencesandanalyzeddata mustbeadded.Discusstheresultsobtainedfromanyquantitativeorsemiquantitative methodologyusedforabenefit/riskevaluationonthemedicine.Addabriefjustification explainingwhyeachmethodologyisused. 2.4.4Benefit/RiskAnalysisContext
Thissection,whencomparedwithnewriskdataoravailableinformationsuchas comparisonwithnewermedicines,mustexplainthedevelopmentofknownbenefitsandrisks oftheproductduringregistration.Wherepossible,similarparametersandoutcomemeasures mustbeused.Factorsthatneedtobeconsideredmayincludethefollowing:
Benefitsandriskswithinthecontextofcurrentmedicalpractice
Changeintheknownaboutthebenefitsandrisksofproduct
Limitationsofbenefit/riskevaluation(e.g.,significantuncertaintiesortheunknown).
2.5ConclusionsandRiskMinimizationOptions 2.5.1Conclusions
Summarizetheconclusiondevelopedthroughbenefit/riskanalysisofthemedicinewitha justificationindicatingwhethergeneralbenefit/riskprofileofthemedicinehaschangedandif so,howithasbecome.

2.5.2RiskMinimizationOptions
Ifavailable,describepossibleriskminimizationoptionsifthegeneralbenefit/riskprofile haschanged.Thesemeasuresmayincluderoutineand/oradditionalriskminimization measures.
Routineriskminimizationactivities
Routineriskminimizationactivitiesarethosewhichapplytoeverymedicinalproduct.These relateto: Thesummaryofproductcharacteristics(SmPC) Thelabellingoninnerandouterpackaging, Thepackageleaflet(PL), Thepacksize, Thelegalstatusoftheproduct. Eventheformulationitselfmayplayanimportantroleinminimizingtheriskoftheproduct. SmPCandPL
TheSmPCandPLareimportanttoolsforriskminimizationastheyconstitutea controlledandstandardizedformatforinforminghealthcareprofessionalsandpatientsabout themedicinalproduct.
Bothmaterialsprovideroutineriskminimizationrecommendations;however,thereare twotypesofmessagestheSmPCandPLcanprovide:
Routineriskcommunicationmessages:usuallyfoundinsection4.8oftheSmPCor section4ofthePL;thesemessagescommunicatetohealthcareprofessionalsand patientstheundesirableeffectsofthemedicinalproduct,sothataninformeddecision onthetreatmentcanbemade.
Routineriskminimizationactivitiesrecommendingspecificclinicalmeasuresto addresstherisk:usuallyfoundinsections4.2and4.4oftheSmPCbutcanalsobe foundinsections4.1,4.3,4.5,4.6,4.7and4.9,andsections2and3ofthePL;
examplestothewarningandprecautionmessagesandrecommendationsintheSmPC willinclude: Performingatestbeforethestartoftreatment, Monitoringoflaboratoryparametersduringtreatment, Monitoringforspecificsignsandsymptoms,
Adjustingthedoseorstoppingthetreatmentwhenadverseeventsareobserved orlaboratoryparameterschange, Performingawash-outprocedureaftertreatmentinterruption, Providingcontraceptionrecommendations,
Prohibitingtheuseofothermedicineswhiletakingtheproduct,
Treatingorpreventingtheriskfactorsthatmayleadtoanadverseevent,

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Recommendinglong-termclinicalfollow-uptoidentifythedelayedadverse eventsinearlystages.
Packsize Sinceeverypacksizeisspecificallyauthorizedforamedicinalproduct,planningthe numberofdosageunitswithineachpackandtherangeofpacksizesavailablecanbe consideredaformofroutineriskmanagementactivity.Intheory,controllingthenumberof dosageunitsshouldmeanthatpatientswillneedtoseeahealthcareprofessionalatdefined

intervals,thusincreasingtheopportunityfortestingandreducingthelengthoftimeapatient iswithoutexamination.
Asmallpacksizecanalsobeuseful,especiallyifoverdoseordiversionarethoughtto bemajorrisks.
Legalstatus Controllingtheconditionsunderwhichamedicinalproductmaybemadeavailablecan reducetherisksassociatedwithitsuseormisuse.
Themarketingauthorizationmustincludedetailsofanyconditionsorrestrictions imposedonthesupplyortheuseofthemedicinalproduct,includingtheconditionsunder whichamedicinalproductmaybemadeavailabletopatients.Thisiscommonlyreferredtoas the“legalstatus”ofamedicinalproduct.Typicallyitincludesinformationonwhetherornot themedicinalproductissubjecttomedicalprescription.Itmayalsorestrictwherethe medicinalproductcanbeadministered(e.g.inahospital)orbywhomitmaybeprescribed (e.g.specialist).
Medicinalproductsonlyavailableonprescriptionmaybeclassifiedintothosesubjectto specialprescriptionsandthosesubjecttorestrictedmedicalprescriptionforusespecific specialareas.
Restrictedmedicalprescription
Thismaybeusedtocontrolwhichspecialistmayinitiatetreatment,whomayprescribe themaintenanceprescriptionsandthesettinginwhichthemedicinalproductcanbegivenor used.Thefollowingfactorsshallbetakenintoaccountwhenconsideringclassificationofa medicinalproductassubjecttorestrictedmedicalprescription:
Themedicinalproduct,becauseofitspharmaceuticalcharacteristicsornoveltyorin theinterestsofpublichealth,maybereservedfortreatmentswhichcanonlybe followedinahospitalenvironment.
Themedicinalproductmaybeusedinthetreatmentofconditionswhichmustbe diagnosedinahospitalenvironmentorininstitutionswithadequatediagnostic facilities,althoughadministrationandfollow-upmaybecarriedoutelsewhere.
Themedicinalproductisintendedforoutpatientsbutitsusemayproduceveryserious adversereactions,therebyitrequiresaprescriptiondrawnupasrequiredbya specialistandspecialsupervisionthroughoutthetreatment. Specialmedicalprescription
Thefollowingfactorsshallbetakenintoaccountforclassificationassubjecttospecialmedical prescription: Themedicinalproductcontainsasubstanceclassifiedasanarcotic,psychotropicor precursorsubstancewithinthemeaningoftheinternationalconventionsinforce,such astheUnitedNationsConventionsof1961,1971,and1988.
Themedicinalproductislikely,ifincorrectlyused,topresentasubstantialriskof medicinalabuse,toleadtoaddictionorbemisusedforillegalpurposes.
Themedicinalproductcontainsasubstancewhich,byreasonofitsnoveltyor properties,couldbeconsideredasbelongingtothegroupenvisagedintheprevious paragraphasaprecautionarymeasure.

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Additionalriskminimizationactivities
Additionalriskminimizationactivitiesshouldonlybesuggestedforthesafeand effectiveuseofthemedicinalproduct.Ifadditionalriskminimizationactivitiesareproposed, theneedfortheseshouldbedetailedandjustified.Theneedforcontinuingwithsuch measuresshouldbeperiodicallyreviewed(SeeGoodPharmacovigilancePractices(GVP) GuidelineModuleIX–RiskMinimizationMeasures:SelectionofToolsandEffectiveness Indicators-ChapterII). 2.5.3Post-MarketingRoutineBenefit/RiskEvaluation

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Oneofthefundamentaltoolstobeusedforthepost-marketingbenefits/risksassessmentof themedicinesarePBRERs.Practicesandrequirementsregardingthepreparationand presentationofthePBRERareexplainedundertheGoodPharmacovigilancePractices(GVP) GuidelineModuleIII-PeriodicBenefitRiskEvaluationReport.

2.6.OperationsToBePerformedbytheInstitution

Afterthebenefit/riskassessmentmadebythemarketingauthorizationholder,iftheInstitution deemsitnecessary,itinitiatesthefollowingproceduresandnotifiesthemarketing authorizationholder: Conductingpost-authorizationsafetystudy. Implementationofmeasurestominimizerisk. Suspension,cancellation,orrefusaltoextendthevalidityperiodofthemarketing authorization. Prohibitionofdrugsupply.

Changesindruginformation,suchasaddinganewcontraindication,reducingthe recommendeddoseandlimitingtheindication.

Appendix1:SectionsforwhichPSURorPBRERcanbeutilizedorwhichcanbereused

Benefit/riskevaluation PeriodicSafety UpdateReport (PSUR) PeriodicBenefit/Risk EvaluationReport (PBRER) 1 BackgroundInformation:Productinformation,usage, exposureestimates,previoussafetyinterventions, disease(s)/condition(s)andothertreatmentoptions Sections:1,3,4,5 Sections:1,3,4,5 *Characterizationofsafetyissue:Evidenceandanalysis ofsafetyissueincludingmedicalhistory Notincluded Notincluded CharacterizationandEvaluationofBenefits: Comparisonwithalternativetreatmentssupportedby evidenceofefficacyandreal-worldefficacy,relevant pharmacologicalcharacteristicsofproductand metabolites,dataobtainedfromclinicalstudiesand observationalstudies Notincluded Section17(advanced analysisisrequired) *CharacterizationandEvaluationofRisks: Relevantrisksidentifiedpre-andpost-marketing Notincluded Sections:13,15,16 EvaluationoftheBenefit/RiskProfileensures verificationandcontextoftheoveralldecisionon benefit/riskprofileoftheproduct,quantitativeor semiquantitativeanalysisisrequired. Notincluded Section18(advanced analysisisrequired) FinalConclusionsandRiskMinimizationOptions: Follow-uptechniquesincludingeffectanalysis Notincluded Section19(advanced analysisisrequired) *InformationisavailableinRiskManagementPlan(RMP)forProduct.

References:

1.Formatandcontentforpost-marketdrugbenefit-riskassessmentinCanadaGuidance document,HealthCanadaFebruary2019.https://www.canada.ca/content/dam/hc-sc/documents/services/publications/drugs-health-products/content-drug-benefit-risk-assessment/content-drug-benefit-risk-assessment-eng.pdf

REVISIONHISTORY

RevisionNo.	RevisionDate	JustificationandExplanations
1	15.11.2022	Formatupdated.
2	30.11.2022	Thepotentialriskwasdefinedandthesummaryof thebenefit/riskprofileforthepotentialriskwas explained. Routineriskminimizationactivitieswere explainedindetail.
3	20.01.2023	2.6.Operationstobeperformedbytheinstitution sectionwasadded Thereferencesusedinpreparationoftheguideline wereadded.

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