SUMMARY OF THE RISK MANAGEMENT PLAN FOR TYBOST (COBICISTAT)

This is a summary of the risk management plan (RMP) for Tybost. The RMP details important risks of Tybost, how these risks can be minimised, and how more information will be obtained about Tybost's risks and uncertainties (missing information).

Tybost's summary of product characteristics (SmPC) and package leaflet (PL) give essential information to healthcare professionals and patients on how Tybost should be used.

This summary of the RMP for Tybost should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of Tybost's RMP.

1. The Medicine and What is it Used for

Tybost is authorized as a pharmacokinetic enhancer of the human immunodeficiency virus (HIV)-1 protease inhibitors atazanavir (ATV) or darunavir (DRV) in adults and adolescents aged 12 years and older, weighing at least 35 kg co-administered with ATV or weighing at least 40 kg co-administered with DRV (see SmPC for the full indication). It contains cobicistat (COBI) as the active substance and it is given orally.

Further information about the evaluation of Tybost's benefits can be found in Tybost's EPAR, including its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine's webpage:
http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/002572/WC500153017.pdf

2. Risks Associated with the Medicine and Activities to Minimise or Further Characterize the Risks

Important risks, together with measures to minimise such risks and the proposed studies for learning more about the risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific Information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;

- Important advice on the medicine's packaging;

- The authorized pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;

- The medicine's legal status — the way a medicine is supplied to the public (e.g. with or without prescription) can help to minimises its risks.

Together, these measures constitute routine risk minimization measures.

Information about adverse reactions is collected continuously and regularly analyzed including periodic safety update report (PSUR) assessment so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of Tybost is not yet available, it is listed under 'missing information' below.

2A. List of important risks and missing information

Important risks are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Tybost. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

Table 1. List of Important Risks and Missing Information

Important Identified Risks	None
Important Potential Risks	Concurrent use of drugs whose coadministration with COBI is contraindicated
Missing Information	Safety in pregnancy and lactation
	Safety in patients with cardiac conduction disorders

2B. Summary of Important Risks

Table 2. Summary of Important Risk(s) and Missing Information

Important Potential Risk	**Concurrent use of drugs whose coadministration with COBI is contraindicated**
Evidence for linking the risk to medicine	A small number of postmarketing cases of concurrent use of COBI with a contraindicated drug have been reported.
Risk factors and risk groups	Not known
Risk minimization measure(s)	Routine risk communication: SmPC section 4.3, 4.4 and 4.5 PL Section 2
Missing Information	**Safety in pregnancy and lactation**
Risk Minimization Measure(s)	Routine risk communication: SmPC Section 4.6 PL Section 2
Additional Pharmacovigilance activities	Antiretroviral Pregnancy Registry See section 0 of this summary for an overview of the post-authorization development plan.
Missing Information	**Safety in Patients with Cardiac Conduction Disorders**
Risk Minimization Measure(s)	No routine risk minimization measures are considered necessary for this population at this time.
Additional Pharmacovigilance activities	None

2C. Post-authorization Development Plan

2C.1 Studies which are Conditions of the Marketing Authorization

There are no studies which are conditions of the marketing authorization or specific obligation of Tybost.

2C.2 Other Studies in Post-Authorization Development Plan

Table 3. Other Studies in Post-Authorization Development Plan

Short Study Name	**Purpose of the Study**
Antiretroviral Pregnancy Registry	To collect information on the risk of birth defects in patients exposed to COBI during pregnancy