COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Atorvastatine SUN 10 mg, 20 mg, 40 mg and 80 mg, film-coated tablets (atorvastatin calcium trihydrate)

NL/H/6395/001-004/DC

Date: 27 August 2025

This module reflects the scientific discussion for the approval of Atorvastatine SUN 10 mg, 20 mg, 40 mg and 80 mg, film-coated tablets. The procedure was finalised at 15 September 2011 in Malta (MT/H/0126/001-004/DC). After a transfer on 11 March 2025, the current RMS is the Netherlands. For information on changes after this date please refer to the 'steps taken after finalisation' at the end of this PAR.

List of abbreviations

ASMF	Active Substance Master File
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
CHMP	Committee for Medicinal Products for Human Use
CMD(h)	Coordination group for Mutual recognition and Decentralised procedure for human medicinal products
CMS	Concerned Member State
EDMF	European Drug Master File
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
Ph.Eur.	European Pharmacopoeia
PL	Package Leaflet
RH	Relative Humidity
RMP	Risk Management Plan
RMS	Reference Member State
SmPC	Summary of Product Characteristics
TSE	Transmissible Spongiform Encephalopathy

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted a marketing authorisation for Atorvastatine SUN 10 mg, 20 mg, 40 mg and 80 mg, film-coated tablets from Sun Pharmaceutical Industries Europe B.V.

The product is indicated for:

Hypercholesterolaemia:
Atorvastatin is indicated as an adjunct to diet for reduction of elevated total cholesterol (total-C), LDL-cholesterol (LDL-C), apolipoprotein B, and triglycerides in adults, adolescents and children aged 10 years or older with primary hypercholesterolaemia including familial hypercholesterolaemia (heterozygous variant) or combined (mixed) hyperlipidaemia (Corresponding to Types IIa and IIb of the Fredrickson classification) when response to diet and other nonpharmacological measures is inadequate.
Atorvastatin is also indicated to reduce total-C and LDL-C in adults with homozygous familial hypercholesterolaemia as an adjunct to other lipid-lowering treatments (e.g. LDL apheresis) or if such treatments are unavailable.

Prevention of cardiovascular disease:
Prevention of cardiovascular events in adult patients estimated to have a high risk for a first cardiovascular event, as an adjunct to correction of other risk factors.

A comprehensive description of the indications and posology is given in the current SmPC.

The marketing authorisation has been granted pursuant to Article of Directive 2001/83/EC based on Article 10(1) of Directive 2001/83/EC, so called 'generic' application.

The reference medicinal products which have been authorised for not less than 6/10 years in the EEA are LIPITOR® 10mg/20mg/40mg Tablets, Pfizer Ireland Pharmaceuticals, UK (authorisation date: 08.09.1997) and LIPITOR® 80mg Tablets, Pfizer Ireland Pharmaceuticals, UK (authorisation date: 15.08.2000).

Prescription-only medicine which may be renewed.

II. QUALITY ASPECTS

II.1 Introduction

Pharmaceutical form
Film coated tablets

Formulation,
Core:
Calcium carbonate (E170)
Microcrystalline cellulose (E460)
PAR Scientific discussion 3/13
Lactose monohydrate
Croscarmellose sodium (E468)
Polysorbate 80 (E433)
Hydroxypropyl cellulose (E463)
Magnesium stearate (E470b)

Film-coat:
Opadry YS-1-7040 White
Hypromellose (E464),
Macrogol 8000,
Titanium dioxide (E171)
Talc (E553b)
Simeticone Emulsion
Candelila wax (for the10mg, 20mg and 40mg tablets only) (E 902)

Container system
Desiccant embedded cold form blister pack**:** Oriented polyamine/Aluminium foil/ PE + desiccant with HDPE coating, with aluminium foil laminate lidding.

II.2 Drug Substance

The applicant refers to the Pharmeuropa monograph of the active substance (namely, Pharmeuropa monograph from Pharmeuropa 21.3 – July 2009 for Atorvastatin Calcium trihydrate). The active substance (atorvastatin calcium trihydrate) is described in the current Ph. Eur. (monograph 04/2011:2191). At the time of submission, the active substance was not yet described in the Ph. Eur. The DS specifications (criteria and limits) being proposed by the DS manufacturer are the same as those by the DP manufacturer, with the additional limits set for particle size by the DP manufacturer.

The specifications listed in the drug substance specifications match those listed in the Ph.Eur. monograph of atorvastatin calcium trihydrate. In the drug substance specifications adopted by the drug substance manufacturer reference is made to in-house analytical methods, while

in the drug substance specifications adopted by the drug product manufacturer reference is made to in-house analytical methods as well as additional reference made to current Ph.Eur. methods for some tests.

INN
The active substance is Atorvastatin calcium (crystalline)

Chemical features like chemical class

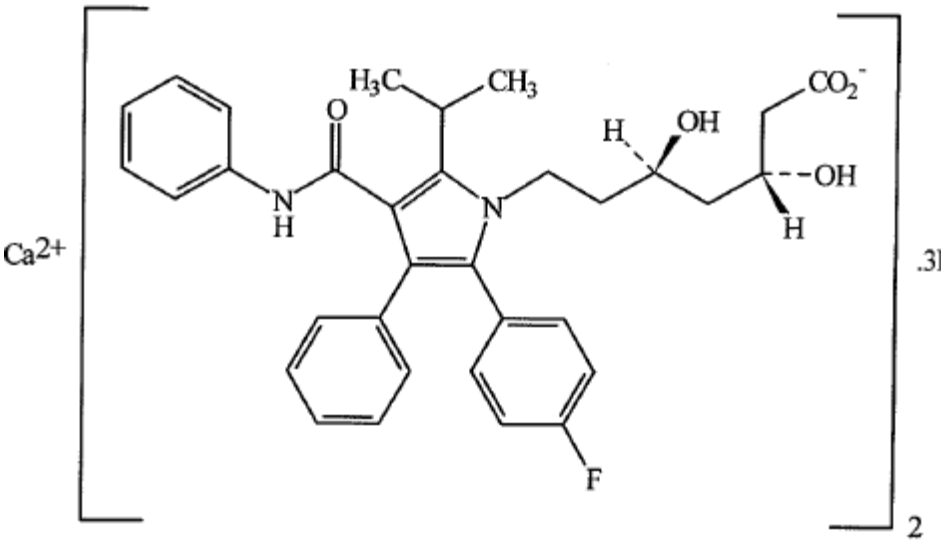
Pharmacotherapeutic group: Lipid modifying agents, HMG-CoA-reductase inhibitors, ATC code: C10AA05

Atorvastatin Calcium (crystalline)

Recommended INN (BANM, USAN): Atorvastatin Calcium

Chemical Name:
Calcium (3*R*,5*R*)-7-[2-(4-fluorophenyl)-5-(1-methylethyl)-3-phenyl-4-(phenylcarbamoyl)-1*H*pyrrol-1-yl]-3,5-dihydroxyheptanoate trihydrate.

Structure
Physical Form: White to off-white powder
Structural Formula:



Molecular Formula: C66H68CaF2N4O10.3H2O
Molecular Weight: 1209

Chirality
Atorvastatin calcium has two chiral centres. The two stereoisomeric impurities observed in Atorvastatin calcium (crystalline) are Impurity E (ent. Atorvastatin/enantiomeric impurity) and Impurity B (3-epi-atorvastatin/Diastereomer of atorvastatin) and these are already controlled in Atorvastatin calcium (crystalline) specifications.

Manufacturing process
The manufacturing process of the active substance has been described in the restricted part of the ASMF.

Stability of drug substance
Stability studies according to the relevant EU/ICH stability guidelines have been submitted and no significant changes in any parameters were observed.

II.3 Medicinal Product

Pharmaceutical development
The development of the product has been described, the choice of excipients is justified and their functions explained; excipients common to pharmaceutical manufacture have been selected. The size of the bio batch was the same formulation and specification as that proposed for marketing.

Quality control of drug product
The required comparative dissolution profiles have been submitted. Validations of the analytical methods have been presented. Batch analysis has been performed on two batches of each strength (including the bio batch).

Stability of drug product
Stability studies according to the relevant EU/ICH stability guidelines have been submitted and no significant changes in any parameters were observed. Based on stability results submitted, the proposed shelf life of 24 months for the product in the proposed commercial pack (desiccant embedded cold form pack) and 12 months in the bulk pack, with no special storage conditions, can be granted.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Not applicable.

III. NON-CLINICAL ASPECTS

III.1 Introduction

Pharmacotherapeutic group: Lipid modifying agents, HMG-CoA-reductase inhibitors, ATC code: C10AA05

Pharmacodynamic, pharmacokinetic and toxicological properties of atorvastatin are well known. As atorvastatin is a widely used, well-known active substance, the applicant has not provided additional studies and further studies are not required. Overview based on literature review is, thus, appropriate.

The expert report on the non-clinical pharmacology, pharmacokinetics and toxicology provides an adequate overview of preclinical investigations on the mechanistic activity and toxicity of atorvastatin. The report supports the non-clinical texts within the originator's SmPC and the texts as recently established following the conclusion of referral procedures:

- EMEA/H/A-30/1154 (EC decision: 13.12.2010) intended to harmonise the prescribing information for Lipitor within the European Union, AND
- EMEA/H/A-29/PAD/1253-1255 (EC decision: 01.07.2010) intended to extend the indication to include treatment of hypercholesterolemia in paediatric patients aged 10 years or older and to update the product information to provide information for use of atorvastatin in the paediatric population.

III.2 Pharmacokinetics

Absorption

Atorvastatin is rapidly absorbed after oral administration; maximum plasma concentrations (Cmax) occur within 1 to 2 hours. Extent of absorption increases in proportion to atorvastatin dose. After oral administration, atorvastatin film-coated tablets are 95% to 99% bioavailable compared to the oral solution. The absolute bioavailability of atorvastatin is approximately 12% and the systemic availability of HMG-CoA reductase inhibitory activity is approximately 30%. The low systemic availability is attributed to presystemic clearance in gastrointestinal mucosa and/or hepatic first-pass metabolism.

Distribution

Mean volume of distribution of atorvastatin is approximately 381 l. Atorvastatin is ≥ 98% bound to plasma proteins.

Biotransformation

Atorvastatin is metabolized by cytochrome P450 3A4 to ortho- and parahydroxylated derivatives and various beta-oxidation products. Apart from other pathways these products are further metabolized via glucuronidation. In vitro, inhibition of HMG-CoA reductase by ortho- and parahydroxylated metabolites is equivalent to that of atorvastatin. Approximately 70% of circulating inhibitory activity for HMG-CoA reductase is attributed to active metabolites.

Excretion

Atorvastatin is eliminated primarily in bile following hepatic and/or extrahepatic metabolism. However, atorvastatin does not appear to undergo significant enterohepatic recirculation. Mean plasma elimination half-life of atorvastatin in humans is approximately 14 hours. The half-life of inhibitory activity for HMG-CoA reductase is approximately 20 to 30 hours due to the contribution of active metabolites.

Special populations

Elderly: Plasma concentrations of atorvastatin and its active metabolites are higher in healthy elderly subjects than in young adults while the lipid effects were comparable to those seen in younger patient populations.

Paediatric: In an open-label, 8-week study, Tanner Stage 1 (N=15) and Tanner Stage 2 (N=24) paediatric patients (ages 6-17 years) with heterozygous familial hypercholesterolemia and baseline LDL-C 4 mmol/L were treated with 5 or 10 mg of chewable or 10 or 20 mg of film-coated atorvastatin tablets once daily, respectively. Body weight was the only significant covariate in atorvastatin population PK model. Apparent oral clearance of atorvastatin in paediatric subjects appeared similar to adults when scaled allometrically by body weight. Consistent decreases in LDL-C and TC were observed over the range of atorvastatin and o-hydroxyatorvastatin exposures.

Gender: Concentrations of atorvastatin and its active metabolites in women differ from those in men (Women: approx. 20% higher for Cmax and approx. 10% lower for AUC). These differences were of no clinical significance, resulting in no clinically significant differences in lipid effects among men and women.

Renal insufficiency: Renal disease has no influence on the plasma concentrations or lipid effects of atorvastatin and its active metabolites.

Hepatic insufficiency: Plasma concentrations of atorvastatin and its active metabolites are markedly increased (approx. 16-fold in Cmax and approx. 11-fold in AUC) in patients with chronic alcoholic liver disease (Child-Pugh B).

SLOC1B1 polymorphism: Hepatic uptake of all HMG-CoA reductase inhibitors including atorvastatin, involves the OATP1B1 transporter. In patients with SLCO1B1 polymorphism there is a risk of increased exposure of atorvastatin, which may lead to an increased risk of rhabdomyolysis. Polymorphism in the gene encoding OATP1B1 (SLCO1B1 c.521CC) is associated with a 2.4-fold higher atorvastatin exposure (AUC) than in individuals without this genotype variant (c.521TT). A genetically impaired hepatic uptake of atorvastatin is also possible in these patients. Possible consequences for the efficacy are unknown.

III.3 Toxicology

Specific treatment is not available for atorvastatin over dosage. Should an overdose occur, the patient should be treated symptomatically and supportive measures instituted, as required. Liver function tests and serum CK levels should be monitored. Due to extensive atorvastatin binding to plasma proteins, haemodialysis is not expected to significantly enhance atorvastatin clearance.

III.4 Ecotoxicity/environmental risk assessment (ERA)

Since Atorvastatine SUN 10 mg, 20 mg, 40 mg and 80 m, film-coated tablets is intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

Module 1.6 justifies the absence of an ERA based on the fact that atorvastatin calcium is not a new active substance. The current applications concern 4 generic products which are meant to substitute a percentage of total prescriptions for the innovator products and are therefore

not expected to increase the amount of active substance that is released into the environment.

III.5 Discussion on the non-clinical aspects

The application is made under reference to article 10(1) of Directive 2001/83/EC as amended. Abridged applications avoid the need for repetitive tests on animals and humans.

IV. CLINICAL ASPECTS

IV.1 Introduction

This procedure concerns a generic application claiming essential similarity to 4 products already established on the market in a number of EU member states. The efficacy and safety parameters are thus well established for the active ingredient as formulated within the respective finished product presentations.

IV.2 Pharmacokinetics

Bioequivalence studies and biowaiver

To support these applications, the applicant has submitted one open label, balanced, randomised, two period, two treatment, crossover, single dose, comparative evaluation of relative bioavailability of Atorvastatin 80mg Tablets (as atorvastatin calcium equivalent to 80mg atorvastatin) (Test Product) against LIPITOR® 80mg Tablets (as atorvastatin calcium equivalent to 80mg atorvastatin) of Pfizer S.A., Belgium (Reference Product) in 80 healthy adult human subjects under fasting conditions.

The performance of a single bioequivalence study under fasting conditions was considered appropriate from a pharmacokinetic perspective and the investigation is adequate for purposes of upholding a waiver from conducting *in vivo* bioequivalence studies on the lower dose products namely: Atorvastatine SUN 10mg, 20mg and 40mg, film-coated tablets.

In accordance with the requirements of the 'Guideline on the Investigation of Bioequivalence' (CPMP/QWP/EWP/1401/98 Rev.1), comparative dissolution profile analyses were performed among both the test and reference products' strengths' series using 4 different buffers and the official release dissolution media. The data generated adequately supported similarity in the products' release characteristics and served to uphold the waiver from conducting *in vivo* bioequivalence studies for the 10mg, 20mg and 40mg tablet formulations.

The choice of reference product selected for purposes of bioequivalence analyses was appropriate and the applicant confirmed that Atorvastatin 80mg Tablets (the test product) has an identical formulation and method of manufacture as that proposed in respect of Atorvastatine SUN 10 mg, 20 mg, 40 mg and 80 mg, film-coated tablets.

Results:

Statistical comparison of the pharmacokinetic parameters of the two formulations was made to assess bioequivalence. The 90% confidence intervals were determined for the ratios of the means of Ln-transformed pharmacokinetic parameters Cmax, AUCt and AUC∞ of atorvastatin for the test and reference formulations. Bioequivalence was to be established if the 90% confidence intervals for the geometric mean ratios of the ln-transformed parameters for atorvastatin fell within the 80%-125% limit.

Analysis of variance (ANOVA) was performed on ln-transformed Cmax, AUCt and AUC∞ for atorvastatin, 2-hydroxy atorvastatin and 4-hydroxy atorvastatin. The ANOVA model assessed the significance of sequence, period, formulation and subject-within-sequence effects as potential sources of variation.

The appropriate variables were measured and both statistical methodology and the prospectively defined acceptance criteria for bioequivalence are acceptable.

The sampling schedule provided adequate estimation of Cmax and graphical representation of the plasma concentration time curve indicated that it was sufficient to provide an estimate of the extent of absorption.

AUCt was >80% AUC∞ following administration of both test and reference formulations.

The terminal log-linear phase was sufficient to allow for reliable estimation of the terminal rate constant with subsequent evaluation of AUC∞.

Ratios of LSM for log transformed pharmacokinetic parameters for Atorvastatin
(90% Confidence Interval)
(Including treatment* group interaction effect)

Parameter	Atorvastatin Test (T) vs Reference (R)
ln C_{max}	109.70% (98.66% – 121.97%)
ln AUC_{0-t}	103.36% (97.45% – 109.63%)
ln $AUC_{0-\infty}$	103.26% (97.48% – 109.39%)

Ratios of LSM for log transformed pharmacokinetic parameters for Atorvastatin
(90% Confidence Interval)
(Excluding treatment* group interaction effect)

Parameter	Atorvastatin Test (T) vs Reference (R)
ln C_{max}	109.70% (98.66% – 121.97%)
ln AUC_{0-t}	103.36% (97.49% – 109.58%)
ln $AUC_{0-\infty}$	103.26% (97.53% – 109.34%)

Ratios of LSM for log transformed pharmacokinetic parameters for 2-Hydroxy Atorvastatin (Including treatment* group interaction effect)

Parameter	2-Hydroxy Atorvastatin Test (T) vs Reference (R)
ln C_{max}	110.85%
ln AUC_{0-t}	103.15%
ln $AUC_{0-\infty}$	103.29%

Ratios of LSM for log transformed pharmacokinetic parameters for 2-Hydroxy Atorvastatin (Excluding treatment* group interaction effect)

Parameter	2-Hydroxy Atorvastatin Test (T) vs Reference (R)
ln C_{max}	110.85%
ln AUC_{0-t}	103.15%
ln $AUC_{0-\infty}$	103.29%

Ratios of LSM for log transformed pharmacokinetic parameters for 4-Hydroxy Atorvastatin (Including treatment* group interaction effect)

Parameter	4-Hydroxy Atorvastatin Test (T) vs Reference (R)
ln C_{max}	104.93%
ln AUC_{0-t}	103.81%
ln $AUC_{0-\infty}$	94.77%

Ratios of LSM for log transformed pharmacokinetic parameters for 4-Hydroxy Atorvastatin (Excluding treatment* group interaction effect)

Parameter	4-Hydroxy Atorvastatin Test (T) vs Reference (R)
ln C_{max}	104.88%
ln AUC_{0-t}	103.73%
ln $AUC_{0-\infty}$	94.71%

<u>Conclusion on bioequivalence studies:</u>

Based on the submitted bioequivalence study for Atorvastatin 80mg Tablets (as atorvastatin calcium equivalent to 80mg atorvastatin) (Test Product) is considered bioequivalent with LIPITOR® 80mg Tablets (as atorvastatin calcium equivalent to 80mg atorvastatin) of Pfizer S.A., Belgium (Reference Product).

The results of study **119_ATORV_10** with 80mg formulation can be extrapolated to other strengths 10mg, 20mg and 40mg according to conditions in Guideline on the Investigation of Bioequivalence CPMP/EWP/QWP/1401/98 Rev. 1/Corr*, section 4.1.6.

The justification for BCS (Biopharmaceutics Classification System) - based biowaiver can be accepted.

IV.3 Pharmacodynamics

Pharmacotherapeutic group:
Lipid modifying agents, HMG-CoA-reductase inhibitors, ATC code: C10AA05.

Atorvastatin is a selective, competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme responsible for the conversion of 3-hydroxy-3-methyl-glutaryl-coenzyme A to mevalonate, a precursor of sterols, including cholesterol. Triglycerides and cholesterol in the liver are incorporated into very low-density lipoproteins (VLDL) and released into the plasma for delivery to peripheral tissues. Low-density lipoprotein (LDL) is formed from VLDL and is catabolized primarily through the receptor with high affinity to LDL (LDL receptor).

Atorvastatin lowers plasma cholesterol and lipoprotein serum concentrations by inhibiting HMG-CoA reductase and subsequently cholesterol biosynthesis in the liver and increases the number of hepatic LDL receptors on the cell surface for enhanced uptake and catabolism of LDL.

Atorvastatin reduces LDL production and the number of LDL particles. Atorvastatin produces a profound and sustained increase in LDL receptor activity coupled with a beneficial change in the quality of circulating LDL particles. Atorvastatin is effective in reducing LDL-C in patients with homozygous familial hypercholesterolaemia, a population that has not usually responded to lipid-lowering medicinal products.

Atorvastatin has been shown to reduce concentrations of total-C (30% - 46%), LDL-C (41% - 61%), apolipoprotein B (34% - 50%), and triglycerides (14% - 33%) while producing variable increases in HDL-C and apolipoprotein A1 in a dose response study. These results are consistent in patients with heterozygous familial hypercholesterolaemia, nonfamilial forms of hypercholesterolaemia, and mixed hyperlipidaemia, including patients with noninsulin-dependent diabetes mellitus.

Reductions in total-C, LDL-C, and apolipoprotein B have been proven to reduce risk for cardiovascular events and cardiovascular mortality.

A comprehensive description of the Pharmacodynamic properties is given in the SmPC.

No PD studies have been submitted and none are required.

IV.4 Clinical efficacy

No new studies have been performed and none is required for this type of application.

IV.5 Clinical safety

The bioequivalence study has raised no new or unexpected safety concerns.

IV.6 Discussion on the clinical aspects

These procedures concern generic applications claiming essential similarity to 4 products already established on the market in a number of EU member states. The efficacy and safety parameters are thus well established for the active ingredient as formulated within the respective finished product presentations. Since they are abridged applications, the need for repetitive tests on animals and humans is not required.

The reference medicinal products which have been authorised for not less that 6/10 years in the EEA are LIPITOR® 10mg/20mg/40mg Tablets, Pfizer Ireland Pharmaceuticals, UK (authorisation date: 08.09.1997) and LIPITOR® 80mg Tablets, Pfizer Ireland Pharmaceuticals, UK (authorisation date: 15.08.2000).

To support these applications, the applicant has submitted one open label, balanced, randomised, two period, two treatment, crossover, single dose, comparative evaluation of relative bioavailability of Atorvastatin 80mg Tablets (as atorvastatin calcium equivalent to 80mg atorvastatin) (Test Product) against LIPITOR® 80mg Tablets (as atorvastatin calcium equivalent to 80mg atorvastatin) of Pfizer S.A., Belgium (Reference Product) in 80 healthy adult human subjects under fasting conditions.

The performance of a single bioequivalence study under fasting conditions was considered appropriate from a pharmacokinetic perspective and the investigation was adequate for purposes of upholding a waiver from conducting *in vivo* bioequivalence studies on the lower dose products namely: Atorvastatine SUN 10 mg, 20 mg and 40 mg, film-coated tablets.

V. USER CONSULTATION

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) of Directive 2001/83/EC as amended by Directive 2004/27/DC. The language used for the purpose of user testing the PIL was conducted in English, on members of the British population.

The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The clinical efficacy, safety and quality of atorvastatin are well-documented.

The application is approvable. The applicant has committed to perform a number of post authorisation follow-up measures and specific obligations to be reported back to the Member States within predefined timeframes. A list of such follow-up measures and specific obligations are in section VI of this report.

List of commitments from the applicant.

1. The applicant commits to perform comparative dissolution profile testing on the first three production batches against the dissolution profile of the bioequivalence study test batch [Atorvastatin 80mg Tablets]. If the dissolution profiles do not show similar in vitro dissolution profiles when employing dissolution test conditions as per finished product standard testing procedure, the results shall be reported to the agency giving proposal for further course/s of action.

2. The applicant commits to perform process validation studies on the first three production-scale batches of each strength of Atorvastatin tablets manufactured with proposed additional commercial batch sizes. CoAs will be provided for the first three production scale batches manufactured which will be used to perform process validation. The applicant commits to conduct process validation on the first three commercial batches as per the submitted process validation protocols in Module 3.2.R

3. The applicant commits to present additional data on a third batch on commercialisation. The applicant commits that the CoAs will be provided for the first three production scale batches manufactured which will be used to perform process validation.

4. The applicant commits that stability data on additional third batch data shall be presented on commercialisation for each strength and pack.

5. The finished product manufacturer, commits to perform stability studies at long term stability conditions (i.e. 25 ± 2°C / 60 ± 5% RH) and accelerated stability conditions (i.e. 40 ± 2°C / 75 ± 5% RH), on one batch of exhibit batch size of each strength.The finished product manufacturer, also commits to perform stability studies at long term stability conditions (i.e. 25 ± 2°C / 60 ± 5% RH) and accelerated stability conditions (i.e. 40 ± 2°C / 75 ± 5% RH), on the first three production batches of batch size other than the exhibit batch size for each strength. The applicant also commits to notify the competent authorities of any OOS results obtained during the stability studies.

Specific obligations

1. In compliance with CPMP/EWP/QWP/1401/98 Rev 01, January 2010, the

applicant commits to perform comparisons of the dissolution profiles obtained for the first three production scale batches of Atorvastatine SUN 10 mg, 20 mg, 40 mg and 80 mg, film-coated tablets against the dissolution profile for Atorvastatin 80mg Tablets and to report to the RMS, if the results are not similar giving proposals for further course/s of action.

List of commitments from the ASMF holder.
Commitment from ASMF in restricted part of the ASMF.

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
NL/H/6395/003 /IA/047	Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size 40 mg tablets only	No	14-07-2025	Approved	N.A.