LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Dexamfetamine Afortas
(dexamfetamine sulfate)

SE/H/2757/001-003/DC

This module reflects the scientific discussion for the approval of Dexamfetamine Afortas. The procedure was finalised at 2026-02-25. For information on changes after this date please refer to the module 'Steps taken after the finalisation of the initial procedure - Summary'.

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I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have agreed to grant a marketing authorisation for Dexamfetamine Afortas, 5 mg, 10 mg, 20 mg, Tablet.

The active substance is dexamfetamine, dexamfetamine sulfate. A comprehensive description of the indication and posology is given in the SmPC.

II. EXECUTIVE SUMMARY

II.1 About the product

Pharmacotherapeutic group: Psychoanaleptics; psychostimulants, agents used for ADHD and nootropics; centrally acting sympathomimetics

ATC Code: N06BA02

Mechanism of action
Dexamfetamine is a sympathomimetic amine with a central stimulant and anorectic activity.

Pharmacodynamic effects
Peripheral actions include elevations of systolic and diastolic blood pressures and weak bronchodilator and respiratory stimulant action. Neither there is specific evidence that clearly establishes the mechanism whereby amfetamines produce mental and behavioural effects in children, nor conclusive evidence regarding how these effects relate to the condition of the central nervous system.

II.2 General comments on the submitted dossier

The application for Dexamfetamine Afortas, 5 mg, 10 mg, 20 mg, Tablet, is a Generic Art. 10(1) application submitted according to Directive 2001/83/EC. The applicant applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and DK, NO and FI as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Attentin, 5 mg, tablet, authorised in DK since 2014, with Medice Arzneimittel Pütter GmbH & Co. KG as marketing authorisation holder.

II.3 General comments on compliance with GMP, GLP, GCP and agreed ethical principles

The RMS has been assured that acceptable standards of GMP are in place for these product types at all sites responsible for the manufacture and assembly of this product.
For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

GMP active substance
Regarding the statement on GMP for the active substance a statement/declaration is provided from the manufacturer(s) responsible for manufacture of the finished product and batch release situated in the EU.

III. SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 Quality aspects

Drug substance
The structure of the drug substance has been adequately proven, and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described, and satisfactory specifications have been provided for starting materials, reagents and solvents.

The drug substance specification includes relevant tests and the limits for impurities and degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies confirm the retest period.

Drug Product
The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III.2 Non-clinical aspects

Pharmacology/Pharmacokinetics/Toxicology
Pharmacodynamic, pharmacokinetic and toxicological properties of dexamphetamine sulphate are well known. As dexamphetamine sulphate is a widely used, well-known active substance, no further studies are required, nor does the applicant provide any. Overview based on literature review is, thus, appropriate.

Environmental Risk Assessment (ERA)

PHASE I

Posology:
The maximum daily dose of Dexamfetamine for children and adolescents is usually 20 mg, although in rare cases, it may be up to 40 mg.

Risk assessment:
Dexamfetamine is a synthetic substance, and no previous ERA was identified. F_{PEN} was refined using country-specific ADHD prevalence data for Sweden, Norway, Finland, and Denmark. Denmark, representing the worst-case scenario with the highest population-wide ADHD prevalence (3.03%), was used for refinement. The refined PEC_{SW} was calculated based on the maximum daily dose of dexamfetamine.

$$PECsw = \frac{40 \times 0.03}{200 \times 10} = 0.0006 \text{ mg/L} = 0.6\ \mu\text{g/L}$$

The refined PECSW of 0.6 µg/L exceeds the EMA-ERA trigger value (≥ 0.01 µg/L), indicating that a Phase II environmental risk assessment is required.

PBT/vPvB Assessment:
An experimental study was submitted to determine the log Kow of dexamfetamine, incorporating measurements at three environmentally relevant pH values (pH 5, 7, and 9). The study employed a shake-flask method. The resulting mean log Kow values were -2.25 at pH 5, -1.21 at pH 7, and 0.25 at pH 9.

PHASE II

A Phase II environmental risk assessment for dexamphetamine has been submitted, including a justification for the use of racemic amphetamine and methamphetamine as analogues. The dossier comprises literature-based information on these analogues for environmental fate (sorption, biodegradability), aquatic ecotoxicity, sewage treatment plant (STP) effects, and PECs with associated risk quotients for surface water, STP, and groundwater. No experimental data are available for dexamphetamine (or analogues) in sediment; a waiver for sediment testing is proposed based on the high mobility, low adsorption, and low expected sediment exposure inferred from analogue data.

The Phase II part relies entirely on data for amphetamine and methamphetamine; no experimental studies on dexamphetamine itself have been provided.

Assessor's discussion / conclusion

Phase I
Risk: A refined PECSW of 0.6 µg/L was calculated using Denmark's prevalence (3.03%) as a worst case, which is acceptable. As this exceeds the trigger value, the ERA proceeds to Phase II Tier A.

Hazard: Log Kow values at pH 5, 7, and 9 (−2.25, −1.21, 0.25) indicate a strong preference for the aqueous phase and are acceptable for ERA purposes.

Phase II
The current phase II of the ERA is not acceptable at this point. Sediment toxicity data are mandatory and cannot be waived; at least one study on sediment-dwelling organisms is required. Methamphetamine is not an acceptable surrogate, and all related references and ERA conclusions must be removed.

The applicant has provided a signed commitment to submit a new ERA within five years, which is acceptable.

Overall Summary and Conclusion
The present ERA is not acceptable. The applicant has provided a signed commitment to submit a new ERA within five years.

III.3 Clinical aspects

Pharmacokinetics
BCS-based biowaiver

The application is based on a Biopharmaceutical Classification System (BCS) based biowaiver and no bioequivalence study has been submitted. The applicant claims that dexamphetamine is BCS class I substance.

According to the ICH M9 guideline on biopharmaceutics classification system-based biowaivers (EMA/CHMP/ICH/493213/2018), a BCS class I-based biowaiver is applicable for an immediate release, solid orally administered dosage form product, if the drug substance is not considered to have a narrow therapeutic index and has been proven to exhibit high solubility and high permeability (BCS class I). A BCS class III-based biowaiver is applicable for an immediate release product if the drug has been proven to exhibit high solubility but not high permeability (BCS class III).

For BCS class I, *in vitro* dissolution characteristics of the test and the reference product should be either very rapid or similarly rapid and the excipients that might affect bioavailability should be qualitatively the same and quantitatively similar.

For BCS class III, *in-vitro* dissolution characteristics of the test and the reference product should be very rapid and excipients that might affect bioavailability should be qualitatively the same and quantitatively similar and all other excipients should be qualitatively the same and quantitatively similar.

The applicant claims that dexamphetamine is BCS class I substance based on high solubility and literature data supporting high permeability of dexamphetamine.

Discussion and overall conclusion
Substance is not considered to have a narrow therapeutic index.

The data provided cannot be used to conclude that dexamfetamine is a substance with high permeability. High solubility has been demonstrated. As it has not been demonstrated that the extent of absorption is above 85%, dexamfetamine is considered as a BCS class III substance in this application.

None of the excipients included in the drug product are known to influence bioavailability. The difference in excipients is acceptable for a BCS class III-biowaiver.

Acceptable *in vitro* dissolution data has been submitted.

In conclusion, the justification for a BCS (Biopharmaceutics Classification System) based biowaiver can be accepted.

Pharmacodynamics/Clinical efficacy/Clinical safety
No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Provided that bioequivalence with the originator product is demonstrated, additional data is not necessary.

Pharmacovigilance system
Proposed MAH (RMS and CMS DK, FI, NO): 2care4 Generics ApS
The Applicant has submitted a signed Summary of the Applicant's/Proposed Future MAH's Pharmacovigilance System. Provided that the Pharmacovigilance System Master File fully complies with the new legal requirements as set out in the Commission Implementing Regulation and as detailed in the GVP module, the RMS considers the Summary acceptable.

Risk Management Plan

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Dexamfetamine Afortas.

Part II Safety specification

The MAH has submitted the version 0.2 RMP dated 11-Sep-2025 and proposed the following summary safety concerns:

Summary of safety concerns	
Important identified risks	• Drug abuse, misuse, diversion and dependence • Cardiovascular disorders (arterial hypertension, arrhythmias, cardiac ischaemia, and cardiotoxicity) • Psychiatric disorders (including depression, suicidality, aggression and psychosis)

Summary of safety concerns	
	• Growth and development restriction
Important potential risks	None
Missing information	• Long-term safety (cardiovascular, growth, neurological, cognition and psychotic)

The Sumary of safety concerns is endorsed. It is in line with the RMP for recently approved Dexatin, SE/H/02484.

Part III Pharmacovigilance Plan

Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Part V Risk minimisation measures

Routine risk minimisation is suggested and the following additional risk minimisation activities are proposed by the applicant:

Safety concern	Risk minimisation measures	Pharmacovigilance activities
Drug abuse, misuse, diversion and dependence **(Important Identified Risk)**	**Routine risk minimisation measures:** *SmPC sections 4.1, 4.3 and 4.4* *PL section 2 and 3* Restricted medical prescription.	**Routine pharmacovigilance activities beyond adverse reactions and signal detection:** None

Safety concern	Risk minimisation measures	Pharmacovigilance activities
	Additional risk minimisation measures: Educational material (including a guide for health care professionals and carers).	**Additional pharmacovigilance activities:** None.
Cardiovascular disorders (arterial hypertension, arrhythmias, cardiac ischaemia, and cardiotoxicity) **(Important Identified Risk)**	**Routine risk minimisation measures:** *SmPC sections 4.3, 4.4, 4.5 and 4.8* *PL section 2 and 4* Restricted medical prescription. **Additional risk minimisation measures:** Educational material (including a guide for health care professionals and carers).	**Routine pharmacovigilance activities beyond adverse reactions and signal detection:** None **Additional pharmacovigilance activities:** None.
Psychiatric disorders (including depression, suicidality, aggression and psychosis) **(Important Identified Risk)**	**Routine risk minimisation measures:** *SmPC sections 4.3, 4.4 and 4.8* *PL section 2 and 4* Restricted medical prescription. **Additional risk minimisation measures:** Educational material (including a guide for health care professionals and carers).	**Routine pharmacovigilance activities beyond adverse reactions and signal detection:** None **Additional pharmacovigilance activities:** None.

Growth and development restriction **(Important Identified Risk)**	**Routine risk minimisation measures:** *SmPC sections 4.4 and 4.8* *PL section 2 and 4* Restricted medical prescription. **Additional risk minimisation measures:** Educational material (including a guide for health care professionals and carers).	**Routine pharmacovigilance activities beyond adverse reactions and signal detection:** None **Additional pharmacovigilance activities:** None.
Long-term safety (cardiovascular, growth, neurological, cognition and psychotic)	**Routine risk minimisation measures:** *SmPC sections 4.3, 4.4 and 4.8* *PL section 3 and 4* Restricted medical prescription.	**Routine pharmacovigilance activities beyond adverse reactions and signal detection:** None

Safety concern	Risk minimisation measures	Pharmacovigilance activities
(Missing information)	**Additional risk minimisation measures:** None.	**Additional pharmacovigilance activities:** None.

Please see section VII.3 for Key elements of the educational material.

Part VI Summary of the RMP
The Summary of the RMP is endorsed.

Conclusion RMP assessment
The submitted Risk Management Plan, version 0.2 signed 11-Sep-2025 is considered acceptable.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

Periodic Safety Update Report (PSUR)

Active substance is currently listed in the published EURD list

With regard to PSUR submission, the MAH should take the following into account:

- PSURs shall be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal. Marketing authorisation holders shall continuously check the European medicines web-portal for the DLP and frequency of submission of the next PSUR.

- For medicinal products authorized under the legal basis of Article 10(1) or Article 10a of Directive 2001/83/EC, no routine PSURs need to be submitted, unless otherwise specified in the EURD list.

- In case the active substance will be removed in the future from the EURD list because the MAs have been withdrawn in all but one MS, the MAH shall contact that MS and propose DLP and frequency for further PSUR submissions together with a justification.

Common renewal date
The common renewal date will be 5 years after closure of the DCP.

IV. BENEFIT RISK ASSESSMENT

The quality of the generic product, Dexamfetamine Afortas, is found adequate. There are no objections to approval of Dexamfetamine Afortas, from a non-clinical and clinical point of view. The absence of bioequivalence studies is acceptable. The product information is acceptable. The benefit/risk is considered positive, and the application is therefore recommended for approval.

Please refer to section VII.3 for information about the condition regarding educational material, guide for health care professionals and carers.

V. RECOMMENDATIONS AND CONDITIONS FOR MARKETING AUTHORISATION AND PRODUCT INFORMATION

V.1 List of recommendations not falling under Article 21a/22 of Directive 2001/83/EC

Post approval commitments
N/A

V.2 List of conditions pursuant to Article 21a or specific obligations pursuant to Article 22 of Directive 2001/83/EC

- **Additional risk minimisation measures (including educational material)**
  The educational material should contain the following key elements:

  Draft key messages of the additional risk minimisation measures
  Prior to the launch of Dexamfetamine Afortas in each Member State the Marketing Authorisation Holder (MAH) will agree about the content and format of the educational

programme, including communication media, distribution modalities, and any other aspects of the programme, with the National Competent Authority.
The educational programme is aimed to address the importance of and to give tools for continuous monitoring of important identified risks.
The MAH shall ensure that in each Member State where Dexamfetamine Afortas is marketed, all healthcare
professionals and carer who are expected to prescribe, dispense and use Dexamfetamine Afortas have access to/are provided with the following educational package:

• Physician educational material
• Patient information pack

Physician educational material:
• The Summary of Product Characteristics
• Guide for healthcare professionals:
- Relevant information of the safety concern(s) addressed by the aRMM (e.g. seriousness, severity, frequency, time to onset, reversibility of the AE as applicable)
- Details of the population at higher risk for the safety concern addressed by the aRMM (e.g. contraindications, risk factors, increased risk by interactions with certain medicine)
- Details on how to minimise the safety concern addressed by the aRMM through appropriate monitoring and management (e.g. what to do, what not do, and who is most likely to be impacted according to different scenarios, like when to limit or stop prescribing/ingestion, how to administer the medicine, when to increase/decrease the dosage according to laboratory measurements, signs and symptoms)

The patient information pack:
• Patient information leaflet
• Patient/carer guide:
- A description of the correct use of Dexamfetamine Afortas and the risk for drug misuse, abuse, diversion and dependence associated with its use.

- **Obligation to conduct post-authorisation measures in accordance with Article 21a of Directive 2001/83/EC**

N/A

- **Specific obligation to complete post-authorisation measures for the marketing authorisation under Exceptional circumstances in accordance with Article 22 of Directive 2001/83/EC**

N/A

V.3 Summary of Product Characteristics (SmPC)

The approved SmPC is available in the MRI Product Index.

V.4 Package Leaflet (PL)

V.4.1 Package Leaflet

The approved PL is available in the MRI Product Index.

V.4.2 **Assessment of User Testing**

A user consultation with target patient groups on the package information leaflet (PL) has been performed on the basis of a bridging report making reference to

- Amfexa, UK/H/5007/001/DC and UK/H/5007/002-003/DC, regarding content and
- Purimmun, SE/H/1655/001/DC, regarding layout.

The bridging report submitted by the applicant has been found acceptable.

VI. STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected (Yes/No)	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
-	-	-	-	-	-