▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 of the SmPC for how to report adverse reactions."

IMPORTANT INFORMATION ABOUT VYNDAQEL® (TAFAMIDIS)

Key messages to Healthcare Professionals

- Please check that patients meet all clinical criteria for the diagnosis of transthyretin amyloid cardiomyopathy (ATTR-CM) before prescribing Vyndaqel, to avoid administration to non-qualifying patients (see criteria section below).

- Please advise your patients on the important potential risks associated with Vyndaqel therapy - tafamidis is not recommended during pregnancy or during lactation, and strongly encourage patient education around appropriate precautions when using Vyndaqel, particularly to avoid pregnancy by proper use of a highly effective method of contraception.

- Please report to Pfizer all cases of female patients becoming pregnant while receiving Vyndaqel and encourage them to join the Tafamidis Enhanced Surveillance Pregnancy Outcomes (TESPO) programme designed to collect additional data on pregnancy outcome, neonate/infant status at birth and 12-month follow-up on infant milestones reached.

- Please advise your patients to contact you/the treating physician immediately in case of any adverse events while taking Vyndaqel, or to report adverse events directly via the national reporting system listed in the Patient Leaflet.

- Physicians (prescribers) and pharmacists are reminded to report promptly any suspected adverse events related to Vyndaqel via the national reporting system listed in the SmPC or to Pfizer.

- You are encouraged to enroll your patients diagnosed with transthyretin (ATTR) amyloidosis and taking Vyndaqel in the voluntary Transthyretin Amyloidosis Outcomes Survey (THAOS) for the purpose of longitudinal data collection (including but not limited to hepatotoxicity, changes in thyroid function, particularly in pregnant women, patients with severe hepatic impairment, safety and efficacy in patients with ATTR-PN mutations other than Val30Met, safety in patients with hereditary or wild-type ATTR-CM) on the disease and Vyndaqel.

Background Summary

Vyndaqel® (tafamidis meglumine) 20 mg soft capsules was approved under exceptional circumstances on 16 November 2011 by the European Commission "for the treatment of transthyretin amyloidosis in adult patients with stage 1 symptomatic polyneuropathy to delay peripheral neurologic impairment".

On 17 February 2020, the European Commission approved Vyndaqel® (tafamidis) 61 mg soft capsules "for the treatment of transthyretin amyloidosis in adult patients with wild-type or hereditary cardiomyopathy".

The purpose of this HCP Guide is to highlight the importance of strongly advising women to avoid pregnancy or breastfeeding while receiving Vyndaqel, to encourage you to report adverse events and any pregnancies in female patients taking Vyndaqel, to encourage enrolment into THAOS to collect

long term exposure data and confirming the diagnosis of ATTR-CM before prescribing Vyndaqel, to avoid administration to non-qualifying patients.

Avoidance of Pregnancy

Vyndaqel is not recommended for use during pregnancy or in women of childbearing potential who are not using effective methods of contraception. This is because there are limited human pregnancy data and developmental toxicity studies in animals have shown abnormalities. Contraceptive measures should be used by women of childbearing potential during treatment with Vyndaqel and, due to its prolonged half-life, for one month after stopping Vyndaqel.

TESPO - Tafamidis Enhanced Surveillance Pregnancy Outcomes

TESPO is a programme to collect safety data, including major birth defects or other developmental abnormalities in live born infants, in female patients with ATTR amyloidosis who are exposed to Vyndaqel during or within 1 month prior to their pregnancy.

Although patients receiving Vyndaqel are advised to avoid pregnancy and to use highly effective methods of contraception, it is recognised that pregnancies may occur and that the disease can present during the reproductive years in many transthyretin amyloid polyneuropathy (ATTR-PN) female patients and few ATTR-CM female patients.

Healthcare Professionals caring for patients who become pregnant during or within 1 month of exposure to Vyndaqel are asked to report the pregnancy to local Pfizer office (see below for contact information). Basic pregnancy information including due dates and dates of tafamidis exposure will be collected using the Exposure During Pregnancy (EDP) form, follow-up data on the pregnancy outcome will be gathered at the female patient estimated time of delivery and information will be collected on the TESPO 12-Month Infant Follow-up Form (first year survival, age-appropriate milestones, congenital malformations, genetic abnormalities, hospitalisation and major illnesses, vaccinations).

THAOS - Transthyretin Amyloidosis Outcomes Survey

THAOS is a global, multi-center, disease registry for the purpose of longitudinal data collection in patients with inherited or wild-type ATTR amyloidosis and for asymptomatic transthyretin (TTR)-variant carriers. It has been open since 2007 to all patients with ATTR amyloidosis (ATTR-PN and ATTR-CM), regardless of treatment status.

The principal aim of the survey is to better understand and characterize the natural history of the disease and to collect long-term safety information, including but not limited to hepatotoxicity, changes in thyroid function, particularly in pregnant women, patients with severe hepatic impairment, and safety and efficacy in patients with ATTR-PN mutations other than Val30Met, safety in patients with hereditary or wild-type ATTR-CM.

A list of European sites participating in THAOS is provided in **Appendix 1.**

Your participation in THAOS and TESPO is voluntary and will help contribute to the body of safety and effectiveness information on Vyndaqel and medical knowledge on ATTR amyloidosis.

Information gathered from THAOS and TESPO will be used to support pharmacovigilance and risk management activities to support patient safety related to Vyndaqel use in the post-marketing setting.

Clinical criteria for the diagnosis of ATTR-CM

Clinical criteria for the diagnosis of ATTR-CM patients is described in Section 4.2 of the Vyndaqel 61 mg SmPC:
Treatment should be initiated under the supervision of a physician knowledgeable in the management of patients with amyloidosis or cardiomyopathy.
When there is a suspicion in patients presenting with specific medical history or signs of heart failure or cardiomyopathy, etiologic diagnosis must be done by a physician knowledgeable in the management of amyloidosis or cardiomyopathy to confirm ATTR-CM and exclude AL[immunoglobulin light chain] amyloidosis before starting tafamidis, using appropriate assessment tools such as: bone scintigraphy and blood/urine assessment, and/or histological assessment by biopsy, and TTR genotyping to characterise as wild type or hereditary.

CALL FOR REPORTING

Healthcare professionals are reminded to continue to report suspected adverse reactions associated with Vyndaqel ▼ in accordance with the National spontaneous reporting system. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and sent to ADR reporting/Post-Licensing Directorate/Medicines Authority, Sir Temi Zammit Buildings, Malta Life Sciences Park, San Gwann, Malta, or sent by email to: Postlicensing.medicinesauthority@gov.mt

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

OTHER CONTACT INFORMATION

For any suspected adverse reactions you may also report such events promptly to Pfizer at:
Pfizer Hellas S.A., 243 Messoghion Ave. N.Psychiko, Athens GR-15451, Greece.
Pfizer Hellas Pharmacovigilance Department contact details: +30 210 67 85 908 and +30 210 67 85 808 (24hour line), fax: +30 210 81 99 096.

COMPANY CONTACT POINT

Pfizer Medical Information at
https://www.pfizer.com/products/product-contact-information
Also, please contact Pfizer Hellas S.A. Medical Information at +30 210 67 85 800.
Pfizer Hellas Pharmacovigilance Department contact details:

+30 210 6785908 and +30 210 6785808 (24-hour line).
Email: GRC.AEReporting@pfizer.com
Local Representative: Vivian Corporation Ltd.: Tel. +00356 22588600.

Sincerely,
For Pfizer Hellas S.A.,

Damianos Menegas MD, PhD
Medical Director
Greece, Cyprus, Malta

APPENDIX 1 - List of B3461001 (THAOS) European participating sites

Please note that the sites participating in THAOS are subject to change. An up-to-date list of participating sites can be found at www.clinicaltrials.gov.

Country	Contact Name and Organisation Address
Belgium	Dr. Van Cleemput Afdeling Klinische Cardiologie, O&N I Herestraat 49 - bus 7003, Leuven, 3000
Bulgaria	Prof. Tarnev Alexandrovska University Hospital Clinic of Neurology, 1, St. Georgi Sofiiski St, Sofia, 1431
Denmark	Prof. Moelgaard Aarhus University Hospital, Palle Juul-Jensens Boulevard 99, Aarhus, 8200
France	Prof. Lairez CHU de Toulouse - Hopital Rangueil, 1 avenue Jean Poulhes, Toulouse, cedex 09, 31059
France	Prof. Plante-Bordeneuve CHU Henri Mondor, Departement de Neurologie, 51 Avenue du Maréchal de Lattre de Tassigny, Créteil 94000
France	Prof. Adams CHU de Bicetre, Departement de Neurologie, 78 rue de General Leclerc, Le Kremlin-Bicetre, Cedex 94275
France	Dr. Inamo Chu De Fort De France, Departement De Cardiologie, Hopital Pierre Zobda Quitman, Fort de France, Martinique 97261
Germany	Prof. Kristen Medical University of Heidelberg, Im Neuenheimer Feld 410, Heidelberg, D-69120

Germany	Dr. Darstein Johann-Gutenberg-Universität, Langenbeckstr. 1, Mainz, 55131
Germany	Dr. Gess University Hospital of RWTH Aachen, Pauwelsstrasse 30, Aachen, North Rhinewestphali, 52074
Germany	Prof. Schmidt Universitatsklinikum Muenster - Transplant Hepatology, Albert-Schweitzer-Campus 1, Gabaeude A1, Muenster, 48149
Italy	Dr. Luigetti Fondazione Policlinico Gemelli - Universita Cattolica del Sacro Cuore, Largo A.Gemelli 8, Roma, 00168
Italy	Prof. Vita Azienda Ospedaliera Policlinico Universitario “G. Martino” Via Consolare Valeria, 1Messina, 98125
Italy	Dr. Emdin Fondazione Toscana Gabriele Monasterio per la Ricerca Medica e di Sanita’ Pubblica (Ftgm), Via Trieste, 41 Pisa, 56126
Italy	Prof. Merlini Centro per lo Studio e la Cura delle Amiloidosi Sistemiche IRCCS Policlinico S.Matteo, Viale Camillo Golgi, 19Pavia, 27100
Italy	Dr. Cirami Azienda Ospedaliero-Universitaria di Careggi, Largo Brambilla 3, Firenze, 50134
Italy	Prof. Rapezzi Comitato Etico Indipendente di Area Vasta Emilia Centro (CE-AVEC) Azienda Ospedaliero-Universitaria di Bologna, Policlinico S. Orsola-Malpighi,

	Via Albertoni, 15 Bologna, 40138
The Netherlands	Dr. Hans Nienhuis University Medical Center Groningen, Hanzeplein 1, Groningen, 9713 GZ
Portugal	Dr. Coelho Centro Hospitalar do Porto Hospital Santo António, Unidade Corino de Andrade R. D. Manuel II, Pavilhão 2 (Ex-CICAP) 4050 - 345 Porto
Portugal	Dr. Conceicao Centro Hospitalar Universitário Lisboa Norte Hospital Santa Maria, Servico de Neurologia - Piso 7, 1649-035 Lisboa,
Portugal	Dr. Azevedo Hospital Senhora Da Oliveira Guimarães, E.P.E. Rua Dos Cutileiros, Creixomil 4835-004 Guimarães,
Romania	Dr. Sorina Baădelitață Institutul Clinic Fundeni, Șos. Fundeni nr. 258 sector 2, București, 022328
Spain	Dr. Fernandéz Torrón Hospital Universitario Donostia, Instituto de Investigación Biodonostia, Begiristain Doktorea Paseo, Gipuzkoa – San Sebastian, Donostia 20014
Spain	Dr. Gonzalez Costello Hospital Universitari de Bellvitge, Secretaria de Cardiología, Planta 4, C/Feixa Llarga SN, L'Hospitalet de Llobregat, Barcelona, 08907
Spain	Dr. Garcia Pavia Hospital Universitario Puerta de Hierro Majadahonda, Manuel de Falla 1 CP Madrid, 28220
Spain	Dr. Munoz Beamud Hospital Juan Ramon Jimenez, Ronda Norte s/n,

	Servicio de Medicina Interna, secretaria 1ª planta, Huelva 21005
Spain	Dr. Galan Davila Hospital Clinico San Carlos, Madrid, 28040
Spain	Dr. Gonzalez Moreno Hospital Son Llatzer, Carretera de Manacor Km 4, s/n 3a Planta, Palma de Mallorca, Mallorca, 07198
Spain	Dr. Campistol Plana Hospital Clinic i Provincial de Barcelona, Escalera 12 Planta 5, Calle Villarroel 170, Barcelona, 08036
Sweden	Dr. Wixner Umeå University Hospital, Norrlands university hospital, Umeå, 901 85
Sweden	Dr. Press Karolinska University Hospital, Huddinge, Stockholm, 141 86