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Prescribing information for Vyndaqel© ▼ (tafamidis) for Great Britain and Northern Ireland can be found on the last two pages (6-7) of this piece.

Adverse event reporting can be found at the bottom of this page.

TA984

Tafamidis for treating transthyretin amyloidosis with cardiomyopathy

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PP-VYN-GBR-1526. September 2024

Summary of the NICE guidance [TA984] for the use of Vyndaqel (tafamidis) in treating adults with transthyretin amyloidosis with cardiomyopathy

Tafamidis for treating transthyretin amyloidosis with cardiomyopathy [TA984] (Published 19th June 2024)

This summary of National Institute for Health and Care Excellence (NICE) technology appraisal guidance TA984 is a promotional material developed and funded by Pfizer Ltd and is intended for UK healthcare professionals only.

Vyndaqel 61mg is indicated for the treatment of wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy (ATTR-CM).[1] Light chain (AL) amyloidosis must be excluded, using appropriate assessment tools, before starting tafamidis.[1] Treatment should be initiated under the supervision of a physician knowledgeable in the management of patients with amyloidosis or cardiomyopathy.[1]

NICE recommendation for tafamidis[2]

"Tafamidis is recommended, within its marketing authorisation, as an option for treating wild-type or hereditary transthyretin amyloidosis with cardiomyopathy (ATTR-CM) in adults. Tafamidis is only recommended if the company provides it according to the commercial arrangement."

Treatment pathway for ATTR-CM[2]

Since the 2018 pivotal tafamidis trial,[3] the diagnostic pathway for ATTR-CM has changed, with medical imaging now being used to identify the condition at earlier stages, although many remain undiagnosed. Despite this earlier identification, in the absence of disease-modifying treatments, a patient expert highlighted that there is limited value to the diagnosis.

Previously, treatment for ATTR-CM consisted of managing symptoms and provision of supportive care, which did not address underlying disease processes.

Tafamidis is the first licensed medication aiming to address the underlying cause of ATTR-CM.

The importance of treating ATTR-CM[2]

Abnormal hepatic production of transthyretin proteins results in accumulation and deposition in the hearts of patients with ATTR-CM. There are two distinct subtypes of ATTR-CM – the familial cardiomyopathy (or hereditary) type, caused by an inherited genetic mutation in the transthyretin gene, and the wild-type ATTR-CM, which arises more often in men and typically occurs in older patients.

Symptoms of ATTR-CM include chest pain, syncope, fatigue, palpitations, dyspnoea and abnormal heart rhythms. These symptoms are debilitating, life-limiting and progress in severity with time. Loss of mobility as a consequence of the disease can result in reliance on carers to perform activities of daily living and loss of independence. The hereditary variant of ATTR-CM can impact multiple members of the family, leading to parental anxiety about inheritance by children. Progressive heart failure and sudden death are the most common causes of mortality in patients with ATTR-CM.

There is a potential financial burden on patients with ATTR-CM and their carers that results from the requirement to travel long distances to specialist centres for treatment, and also from possibly requiring early retirement.

The burden of hereditary ATTR-CM on patients with African–Caribbean or Hispanic ethnicity was noted by NICE. Patients from such backgrounds are not only genetically predisposed to certain more prevalent mutations that lead to ATTR-CM but are also more likely to receive a diagnosis later in the disease course and have worse outcomes than other patients.

Image for illustrative purposes only – this is not a real patient

NICE determined that prescription of tafamidis may be restricted to specialist centres.

Cost effectiveness analysis of tafamidis for ATTR-CM[2]

The incremental cost-effectiveness ratios for tafamidis compared with best supportive care calculated as part of the base case, which included a commercial arrangement, fell within the range considered to be an acceptable use of NHS resources by NICE. Cost-effectiveness estimates are commercial in confidence.

Implementation[2]

Compliance with NICE guidance recommendations is required by bodies with public health function in England, including NHS England, integrated care boards and local authorities, within 3 months of its publication. In Wales, resources must be provided within 2 months of publication of the final draft guidance.

It is the responsibility of the NHS to ensure access to treatments recommended by NICE “as an option” within the required timeframe. As such, in line with NICE’s recommendations, should a healthcare provider managing a patient with ATTR-CM consider tafamidis the right treatment for their patient, it should be available.

NHS England and integrated care boards

Image for illustrative purposes only – this is not a real patient

committed to earlier implementation of this NICE guidance, within 30 days of publication, to ensure continued access to patients for whom tafamidis had been available through the early access to medicines scheme.

References
1 Vyndaqel 61 mg (tafamidis) Summary of Product Characteristics (SmPC)
2 NICE. Tafamidis for Treating Transthyretin Amyloidosis with Cardiomyopathy. National Institute for Health and Care Excellence; 2024. www.nice.org.uk/guidance/ta984 [last accessed September 2024]
3 Maurer MS, Schwartz JH, Gundapaneni B, et al. Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy. *New England Journal of Medicine*. 2018;379(11):1007-1016. doi:10.1056/NEJMoa1805689

Key points[2]

- Until the availability of tafamidis on the NHS, no disease-modifying treatments for ATTR-CM were available; as such, there is a substantial unmet need for treatment options for patients.
- In patients with ATTR-CM, tafamidis decreases hospitalisations and death compared with placebo.
- When provided according to the commercial arrangement, NICE recommended tafamidis, within its marketing authorisation, as an option for treatment of adult patients with ATTR-CM (wild-type or hereditary).

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Vyndaqel® (tafamidis) 61 mg capsules

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VYNDAQEL® (tafamidis) 61 mg is indicated for the treatment of wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy (ATTR-CM).[1] Treatment should be initiated under the supervision of a physician knowledgeable in the management of patients with amyloidosis or cardiomyopathy. Amyloid light chain (AL) amyloidosis must be excluded before starting treatment with VYNDAQEL.[1]

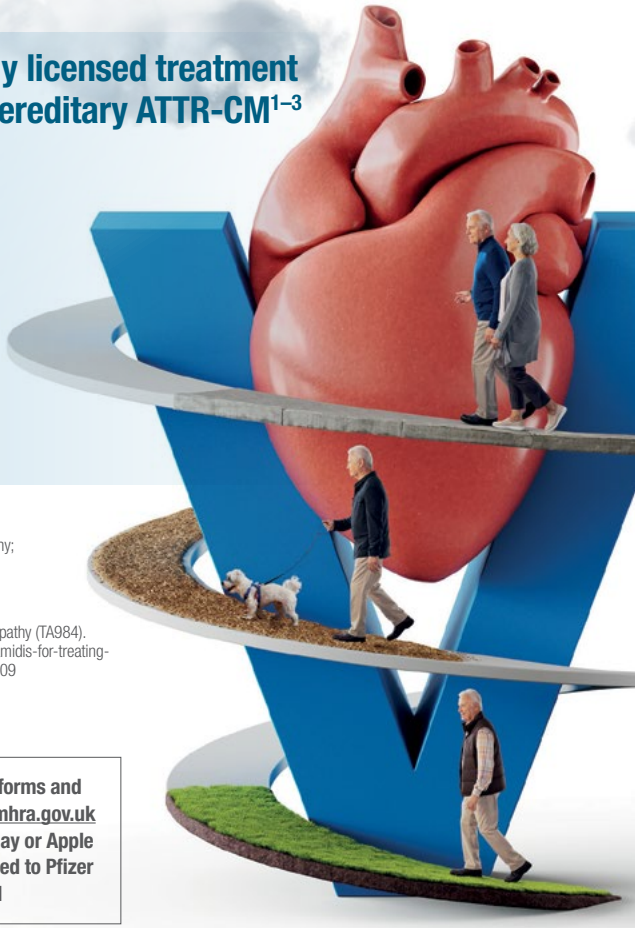
NICE recommends oral VYNDAQEL 61 mg[2]

Tafamidis is recommended, within its marketing authorisation, as an option for treating wild-type or hereditary transthyretin amyloidosis with cardiomyopathy (ATTR-CM) in adults.
Tafamidis is only recommended if the company provides it according to the commercial arrangement.[2]

VYNDAQEL is the first and only licensed treatment for adults with wild-type or hereditary ATTR-CM[1–3]

To discover what this means for your eligible patients, please scan the QR code below:

This QR code will redirect you to a PfizerPro website developed and funded by Pfizer, that contains promotion content for VYNDAQEL



AL=amyloid light chain; ATTR-CM=transthyretin amyloid cardiomyopathy; NICE=National Institute for Health and Care Excellence.

1. VYNDAQEL 61 mg (tafamidis) Summary of Product Characteristics.
2. NICE. Tafamidis for treating transthyretin amyloidosis with cardiomyopathy (TA984). Available at: https://www.nice.org.uk/guidance/ta984/resources/tafamidis-for-treating-transthyretin-amyloidosis-with-cardiomyopathy-pdf-82615910400709 [Last accessed September 2024].
3. Maurer MS, et al. N Engl J Med 2018;379(11):1007–1016.

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PRESCRIBING INFORMATION

▼ 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. Refer to section 4.8 of the SPC for how to report adverse reactions.

Vyndaqel ▼ 61 mg soft capsules (tafamidis)

Great Britain Prescribing Information:

Before prescribing Vyndaqel please refer to the full Summary of Product Characteristics. **Presentation: Vyndaqel 61 mg soft capsules.** Each soft capsule contains 61 mg tafamidis. **Uses:** Vyndaqel is indicated for the treatment of wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy (ATTR-CM). **Dosage:** 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 amyloidosis before starting Vyndaqel, using appropriate assessment tools such as: bone scintigraphy and blood/urine assessment, and/or histological assessment by biopsy, and transthyretin (TTR) genotyping to characterise as wild-type or hereditary. The recommended dose is one capsule of Vyndaqel 61 mg (tafamidis) orally once daily. Vyndaqel 61 mg (tafamidis) corresponds to 80 mg tafamidis meglumine, tafamidis and tafamidis meglumine are not interchangeable on a per mg basis. Vyndaqel should be started as early as possible in the disease course when the clinical benefit on disease progression could be more evident. Conversely, when amyloid-related cardiac damage is more advanced, such as in NYHA Class III, the decision to start or maintain treatment should be taken at the discretion of a physician knowledgeable in the management of patients with amyloidosis or cardiomyopathy. There are limited clinical data in patients with NYHA Class IV. If vomiting occurs after dosing, and the intact Vyndaqel capsule is identified, then an additional dose of Vyndaqel should be administered if possible. If no capsule is identified, then no additional dose is necessary, with resumption of dosing the next day as usual. There are no recommended dosage adjustments for elderly patients or patients with renal or mild and moderate hepatic impairment. Limited data are available in patients with severe renal impairment (creatinine clearance less than or equal to 30 mL/min). Tafamidis has not been studied in patients with severe hepatic impairment and caution is recommended **Contraindications:** Hypersensitivity to the active substance or to any of the excipients as listed in section 6.1 of SPC. **Warnings and Precautions:** Contraceptive measures should be used by women of childbearing potential during treatment with tafamidis and for one month after stopping treatment. Tafamidis should be added to the standard of care for the treatment of patients with transthyretin amyloidosis. Physicians should monitor patients and continue to assess the need for other therapy, including the need for organ transplantation, as part of this standard of care. As there are no data available regarding the use of tafamidis in organ transplantation, tafamidis should be discontinued in patients who undergo organ transplantation. Increase in liver function tests and decrease in thyroxine may occur. This medicinal product contains no more than 44 mg sorbitol in each capsule. Sorbitol is a source of fructose. The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account. The content of sorbitol in medicinal products for oral use may affect the bioavailability of other medicinal products for oral use administered concomitantly. **Pregnancy and Lactation:** Tafamidis is not recommended during pregnancy and in women of childbearing potential not using contraception. Available data in animals have shown excretion of tafamidis in milk. A risk to the newborns/infants cannot be excluded. Vyndaqel should not be used during breastfeeding. **Interactions:** In a clinical study in healthy volunteers, 20 mg tafamidis meglumine did not induce or inhibit the cytochrome P450 enzyme CYP3A4. *In vitro* tafamidis inhibits the efflux transporter BCRP (breast cancer resistant protein) at the 61 mg/day tafamidis dose with IC50=1.16 µM and may cause drug-drug interactions at clinically relevant concentrations with substrates of this transporter (e.g. methotrexate, rosuvastatin, imatinib). In a clinical study in healthy participants, the exposure of the BCRP substrate rosuvastatin increased approximately 2-fold following multiple doses of 61 mg tafamidis daily dosing. Likewise, tafamidis inhibits the uptake transporters OAT1 and OAT3 (organic anion transporters) with IC50=2.9 µM and IC50=2.36 µM, respectively, and may cause drug-drug interactions at clinically relevant concentrations with substrates of these transporters (e.g. non-steroidal anti-inflammatory drugs, bumetanide, furosemide, lamivudine, methotrexate, oseltamivir, tenofovir, ganciclovir, adefovir, cidofovir, zidovudine, zalcitabine). Based on *in vitro* data, the maximal predicted changes in AUC of OAT1 and OAT3 substrates were determined to be less than 1.25 for the tafamidis 61 mg dose, therefore, inhibition of OAT1 or OAT3 transporters by tafamidis is not expected to result in clinically significant interactions. No interaction studies have been performed evaluating the effect of other medicinal products on tafamidis. **Undesirable Effects:** The following adverse events were reported more often in 176 ATTR-CM patients treated with tafamidis meglumine 80 mg compared to placebo: flatulence [8 patients (4.5%) versus 3 patients (1.7%)] and liver function test increased [6 patients (3.4%) versus 2 patients (1.1%)]. A causal relationship has not been established. Safety data for tafamidis 61 mg are available from its open-label long-term extension study. Adverse reactions from cumulative clinical data in ATTR-CM participants: *Common (≥1/100 to < 1/10)* Diarrhoea, rash, pruritus. **Legal category:** POM. **Package Quantities:** Vyndaqel is available in packs containing 30 x 1 soft capsules. **Basic NHS Cost:** £10,685 **Marketing Authorisation number:** PLGB 00057/1695. **Marketing Authorisation Holder:** Pfizer Limited, Ramsgate Road, Sandwich, Kent, CT13 9NJ. For full prescribing information and details of other side effects see Summary of Product Characteristics. Further information is available on request from Medical Information Department at Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS, UK.

Last revised: 02/2023

Ref: VY 61MG GB 5_0

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PRESCRIBING INFORMATION

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Vyndaqel ▼ 61 mg soft capsules (tafamidis)

Northern Ireland Prescribing Information:

Before prescribing Vyndaqel please refer to the full Summary of Product Characteristics. **Presentation: Vyndaqel 61 mg soft capsules.** Each soft capsule contains 61 mg tafamidis. **Uses:** Vyndaqel is indicated for the treatment of wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy (ATTR-CM). **Dosage:** 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 amyloidosis before starting Vyndaqel, using appropriate assessment tools such as: bone scintigraphy and blood/urine assessment, and/or histological assessment by biopsy, and transthyretin (TTR) genotyping to characterise as wild-type or hereditary. The recommended dose is one capsule of Vyndaqel 61 mg (tafamidis) orally once daily. Vyndaqel 61 mg (tafamidis) corresponds to 80 mg tafamidis meglumine, tafamidis and tafamidis meglumine are not interchangeable on a per mg basis. Vyndaqel should be started as early as possible in the disease course when the clinical benefit on disease progression could be more evident. Conversely, when amyloid-related cardiac damage is more advanced, such as in NYHA Class III, the decision to start or maintain treatment should be taken at the discretion of a physician knowledgeable in the management of patients with amyloidosis or cardiomyopathy. There are limited clinical data in patients with NYHA Class IV. If vomiting occurs after dosing, and the intact Vyndaqel capsule is identified, then an additional dose of Vyndaqel should be administered if possible. If no capsule is identified, then no additional dose is necessary, with resumption of dosing the next day as usual. There are no recommended dosage adjustments for elderly patients or patients with renal or mild and moderate hepatic impairment. Limited data are available in patients with severe renal impairment (creatinine clearance less than or equal to 30 mL/min). Tafamidis has not been studied in patients with severe hepatic impairment and caution is recommended **Contraindications:** Hypersensitivity to the active substance or to any of the excipients as listed in section 6.1 of SPC. **Warnings and Precautions:** Contraceptive measures should be used by women of childbearing potential during treatment with tafamidis and for one month after stopping treatment. Tafamidis should be added to the standard of care for the treatment of patients with transthyretin amyloidosis. Physicians should monitor patients and continue to assess the need for other therapy, including the need for organ transplantation, as part of this standard of care. As there are no data available regarding the use of tafamidis in organ transplantation, tafamidis should be discontinued in patients who undergo organ transplantation. Increase in liver function tests and decrease in thyroxine may occur. This medicinal product contains no more than 44 mg sorbitol in each capsule. Sorbitol is a source of fructose. The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account. The content of sorbitol in medicinal products for oral use may affect the bioavailability of other medicinal products for oral use administered concomitantly. **Pregnancy and Lactation:** Tafamidis is not recommended during pregnancy and in women of childbearing potential not using contraception. Available data in animals have shown excretion of tafamidis in milk. A risk to the newborns/infants cannot be excluded. Vyndaqel should not be used during breastfeeding.

Interactions: In a clinical study in healthy volunteers, 20 mg tafamidis meglumine did not induce or inhibit the cytochrome P450 enzyme CYP3A4. *In vitro* tafamidis inhibits the efflux transporter BCRP (breast cancer resistant protein) at the 61 mg/day tafamidis dose with IC50=1.16 µM and may cause drug-drug interactions at clinically relevant concentrations with substrates of this transporter (e.g. methotrexate, rosuvastatin, imatinib). In a clinical study in healthy participants, the exposure of the BCRP substrate rosuvastatin increased approximately 2-fold following multiple doses of 61 mg tafamidis daily dosing. Likewise, tafamidis inhibits the uptake transporters OAT1 and OAT3 (organic anion transporters) with IC50=2.9 µM and IC50=2.36 µM, respectively, and may cause drug-drug interactions at clinically relevant concentrations with substrates of these transporters (e.g. non-steroidal anti-inflammatory drugs, bumetanide, furosemide, lamivudine, methotrexate, oseltamivir, tenofovir, ganciclovir, adefovir, cidofovir, zidovudine, zalcitabine). Based on *in vitro* data, the maximal predicted changes in AUC of OAT1 and OAT3 substrates were determined to be less than 1.25 for the tafamidis 61 mg dose, therefore, inhibition of OAT1 or OAT3 transporters by tafamidis is not expected to result in clinically significant interactions. No interaction studies have been performed evaluating the effect of other medicinal products on tafamidis. **Undesirable Effects:** The following adverse events were reported more often in 176 ATTR-CM patients treated with tafamidis meglumine 80 mg compared to placebo: flatulence [8 patients (4.5%) versus 3 patients (1.7%)] and liver function test increased [6 patients (3.4%) versus 2 patients (1.1%)]. A causal relationship has not been established. Safety data for tafamidis 61 mg are available from its open-label long-term extension study. Adverse reactions from cumulative clinical data in ATTR-CM participants: *Common (≥1/100 to < 1/10)* Diarrhoea, rash, pruritus. **Legal category:** POM. **Package Quantities:** Vyndaqel is available in packs containing 30 x 1 soft capsules. **Basic NHS Cost:** £10,685

European Marketing Authorisation number: EU/1/11/717/003. **Marketing Authorisation Holder:** Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 Bruxelles, Belgium. For full prescribing information and details of other side effects see Summary of Product Characteristics. Further information is available on request from Medical Information Department at Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS, UK.

Last revised: 02/2023

Ref: VY 61MG NI 5_0

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