



Early Access to Medicines Scientific Opinion - Public Assessment Report	
<b>Product</b>	<b>Vyndaqel (tafamidis)</b>
<b>Condition</b>	<b>Transthyretin amyloidosis (ATTR) is caused by abnormal transthyretin (TTR) proteins being produced by the liver and accumulating as deposits in the tissues of the body (amyloidosis) Transthyretin amyloid cardiomyopathy (ATTR-CM) is a type of transthyretin amyloidosis in which most deposits accumulate in the heart, causing the heart tissue to thicken and stiffen.</b>
<b>Full indication</b>	<b>Treatment of transthyretin amyloidosis in adult patients with wild type or hereditary cardiomyopathy to reduce all-cause mortality and cardiovascular-related hospitalisation</b>
<b>Company</b>	<b>Pfizer Limited</b>
<b>EAMS number</b>	<b>00057/0004</b>

## Introduction

The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines to UK patients that have a high unmet clinical need. The MHRA scientific opinion provides benefit and risk information to doctors who may wish to prescribe the unlicensed medicine under their own responsibility. More information about the scheme can be found here:

<http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm>

The scientific opinion is based on the information supplied to the MHRA on the benefits and risks of a promising new medicine. As such this is a scientific opinion and should not be regarded as a medicine licensed by the MHRA or a future commitment by the MHRA to license such a medicine. The General Medical Council's guidance on prescribing unlicensed medicines can be found here:

<https://www.gmc-uk.org/ethical-guidance/ethical-hub/trans-healthcare#prescribing>

## What is Vyndaqel (tafamidis)?

Tafamidis is the active substance of an oral medicine (Vyndaqel) used to prevent the breakdown of a protein called transthyretin (TTR), that can deposit in the heart when it does not function properly.

## What is Vyndaqel (tafamidis) used to treat?

Transthyretin amyloidosis occurs when TTR does not function properly. TTR is produced in the liver and carries other substances, such as hormones, through the body.

In patients with transthyretin amyloidosis, TTR breaks up and may form fibrils called amyloid. Amyloid can build up between the cells in the heart (known as transthyretin amyloid cardiomyopathy or ATTR-CM) and in other places in the body. When this build-up of amyloid occurs in the heart, it prevents the

heart from working normally and can lead to heart failure. There are two forms of the disease: (1) wildtype ATTR-CM that is more common and not inherited from relatives, and (2) hereditary ATTR-CM, which is inherited as an autosomal dominant trait.

Vyndaqel (tafamidis) can prevent TTR from disassembling and forming amyloid. It is used to treat adult patients whose heart has been affected by either wild-type or hereditary transthyretin amyloidosis.

### **How is Vyndaqel (tafamidis) used?**

Treatment with Vyndaqel (tafamidis) should be started and supervised by a specialist doctor knowledgeable in the management of patients with transthyretin amyloid cardiomyopathy.

The recommended dose for ATTR-CM is one tafamidis 61mg capsule taken orally once daily.

### **How does Vyndaqel (tafamidis) work?**

Vyndaqel (tafamidis) binds to TTR and stabilises it, preventing breakdown of TTR into harmful fibrils called amyloid. By interfering with this essential step in the disease, Vyndaqel (tafamidis) can prevent harmful amyloid fibrils from forming and depositing on the heart. By preventing the breakdown of TTR, Vyndaqel (tafamidis) can slow the progression of ATTR-CM.

### **How has Vyndaqel (tafamidis) been studied?**

The effects of Vyndaqel (tafamidis) were studied in a placebo-controlled clinical trial (ATTR-ACT) that evaluated its effectiveness and safety in 441 patients with heart failure due to ATTR-CM. A total of 264 patients received Vyndaqel (tafamidis) and 177 patients received placebo. The main measure of effectiveness (how well the medicine worked) was a combination of death from any cause and the frequency of hospitalisations (admissions to hospital) related to cardiovascular causes with Vyndaqel (tafamidis) compared to placebo.

### **What benefits and risks has Vyndaqel (tafamidis) shown during these studies?**

#### *Benefits*

The ATTR-ACT trial found that in patients with heart failure due to ATTR-CM, treatment with Vyndaqel (tafamidis) significantly reduced the combination of deaths from any cause and cardiovascular-related hospitalisations compared to placebo. The proportion of patients alive after 30 months (the end of the study) was 70.5% in group of patients treated with Vyndaqel (tafamidis) and 57.1% in those treated with placebo. The rate of cardiovascular-related hospitalisations was 33% lower in the group that received Vyndaqel (tafamidis) when compared to patients that received placebo.

#### *Risks*

Like all medicines, Vyndaqel (tafamidis) may cause side effects, although not everybody gets them. In the ATTR-ACT study, the rate of side effects in patients treated with Vyndaqel (tafamidis) was similar to the rate seen in patients receiving placebo. No side effects were identified as adverse reactions linked to the administration of Vyndaqel (tafamidis) in the ATTR-ACT study.

### **Why has Vyndaqel (tafamidis) been given a positive Early Access to Medicine Scientific opinion?**

ATTR-CM is a progressive and life-threatening disease with no available treatment options. Patients with ATTR-CM have a poor prognosis, admissions to hospital are common and their quality of life is significantly impaired. There is a significant unmet need for an effective and safe treatment option to

slow the progression of disease in patients with ATTR-CM.

Vyndaqel (tafamidis) has been shown to reduce both mortality from any cause and hospital admissions due to cardiovascular causes. Patients treated with Vyndaqel (tafamidis) have also shown significant favourable differences in measures of quality of life and functional capacity when compared to those treated with placebo. Furthermore Vyndaqel (tafamidis) is a well-tolerated oral medicine, and the ATTR-ACT study showed the safety profile was similar across Vyndaqel (tafamidis) and placebo groups. In summary, the efficacy and safety data for Vyndaqel (tafamidis) demonstrate a favourable benefit-risk profile in the treatment of ATTR-CM.

### **What are the uncertainties?**

The ATTR-ACT study included patients with ATTR-CM and heart failure, with a New York Heart Association (NYHA) class I-III. Whether patients with more severe heart failure (NYHA class IV) or those with evidence of transthyretin cardiac amyloid without a history of symptoms will benefit from treatment is not established.

### **Are there on-going clinical studies?**

A long-term extension study to the ATTR-ACT study is ongoing.

### **What measures are in place to monitor and manage risks?**

A risk management plan has been developed to ensure that Vyndaqel (tafamidis) is used as safely as possible. Based on this plan, the Company that makes Vyndaqel (tafamidis) must ensure that all healthcare professionals expected to use the medicine, as well as patients, are provided with information on the medicine including possible side effects and recommendations for preventing or minimising the impact of side effects.

Information will be collected about patients before they enter the scheme. Healthcare professionals will be asked by the Company to report side effects experienced by patients receiving Vyndaqel (tafamidis) through the scheme. These safety data will be reviewed and reported to the MHRA on a regular basis by the Company.

**Other information about Vyndaqel (tafamidis) – see EAMS Treatment Protocol**