

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

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

1 NAME OF THE MEDICINAL PRODUCT

Vyndaqel 20 mg soft capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soft capsule contains 20 mg of micronized tafamidis meglumine equivalent to 12.2 mg tafamidis.

Excipients with known effect

Each soft capsule contains no more than 44 mg of sorbitol (E420).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Soft capsule

Yellow, opaque, oblong (approximately 21 mm) capsule imprinted with “VYN 20” in red.

4 CLINICAL PARTICULARS

4.1 Therapeutic indication

Vyndaqel is indicated for the treatment of transthyretin amyloidosis in adult patients with stage 1 symptomatic polyneuropathy to delay peripheral neurologic impairment.

4.2 Posology and method of administration

Treatment should be initiated by and remain under the supervision of a physician knowledgeable in the management of patients with transthyretin amyloid polyneuropathy.

Posology

The recommended dose of tafamidis meglumine is 20 mg orally once daily.

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.

Special populations

Elderly

Data in the elderly patients are very limited.

No dosage adjustment is required for elderly patients (≥ 65 years).

Hepatic and renal impairment

No dosage adjustment is required for patients with renal or mild and moderate hepatic impairment. Tafamidis meglumine has not been studied in patients with severe hepatic impairment and caution is recommended (see section 5.2).

Paediatric population

There is no relevant use of tafamidis in the paediatric population.

Method of administration

Oral use.

The soft capsules should be swallowed whole, not crushed or cut, and taken with or without food.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Women of childbearing potential should use appropriate contraception when taking tafamidis meglumine and continue to use appropriate contraception for 1-month after stopping treatment with tafamidis meglumine (see section 4.6).

Tafamidis meglumine should be added to the standard of care for the treatment of the transthyretin familial amyloid polyneuropathy (TTR-FAP) patient. Physicians should monitor patients and continue to assess the need for other therapy, including the need for liver transplantation, as part of this standard of care. As there are no data available regarding the use of tafamidis meglumine post-liver transplantation, tafamidis meglumine should be discontinued in patients who undergo liver transplantation.

Vyndaqel contains sorbitol (E420). Patients with rare hereditary problems of fructose intolerance should not take this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction

In a clinical study in healthy volunteers, tafamidis meglumine did not induce or inhibit the cytochrome P450 enzyme CYP3A4.

In vitro data also indicated that tafamidis meglumine does not significantly inhibit cytochrome P450 enzymes CYP1A2, CYP3A4, CYP3A5, CYP2B6, CYP2C8, CYP2C9, CYP2C19, and CYP2D6.

In vitro studies with tafamidis meglumine suggest that it is unlikely tafamidis meglumine will cause drug interactions at clinically relevant concentrations with substrates of UDP glucuronosyltransferase (UGT), P-gp transporters, or organic anion-transporting polypeptide transporters (OATP1B1 and 1B3).

However, *in vitro* tafamidis meglumine inhibits the efflux transporter BCRP (breast cancer resistant protein) with $IC_{50}=1.16 \mu M$ and may cause drug-drug interactions at clinically relevant concentrations with substrates of this transporter (e.g. methotrexate, rosuvastatin, imatinib). Likewise, tafamidis meglumine inhibits the uptake transporters OAT1 and OAT3 (organic anion transporters) with $IC_{50}=2.9 \mu M$ and $IC_{50}=2.36 \mu M$, 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).

No interaction studies have been performed evaluating the effect of other medicinal products on tafamidis meglumine.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Contraceptive measures should be used by women of childbearing potential during treatment with tafamidis meglumine, and for one month after stopping treatment, due to the prolonged half life.

Pregnancy

There are no data on the use of tafamidis meglumine in pregnant women. Studies in animals have shown developmental toxicity (see section 5.3). Tafamidis meglumine is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breast-feeding

Available pharmacodynamic/toxicological data in animals have shown excretion of tafamidis in milk. A risk to the newborns/infants cannot be excluded. Tafamidis meglumine should not be used during breast-feeding.

Fertility

No impairment of fertility has been observed in nonclinical studies (see section 5.3).

4.7 Effects on ability to drive and use machines

On the basis of the pharmacodynamic and pharmacokinetic profile, tafamidis meglumine is believed to have no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

Summary of safety profile

The overall clinical data reflect exposure of 127 TTR amyloid polyneuropathy patients to 20 mg of tafamidis meglumine administered daily for an average of 538 days (ranging from 15 to 994 days). The adverse reactions were generally mild or moderate in severity.

Tabulated list of adverse reactions

Adverse reactions are listed below by MedDRA System Organ Class (SOC) and frequency categories using the standard convention: Very common ($\geq 1/10$), Common ($\geq 1/100$ to $< 1/10$), and Uncommon ($\geq 1/1,000$ to $< 1/100$). Within the frequency group, adverse reactions are presented in order of decreasing seriousness. Adverse reactions reported from the clinical programme in the tabular listing below reflect the rates at which they occurred in the Phase 3, double-blind, placebo-controlled study (Fx-005).

System Organ Class	Very Common
Infections and infestations	Urinary tract infection
	Vaginal infection
Gastrointestinal disorders	Diarrhoea
	Upper abdominal pain

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in [Appendix V](#).

4.9 Overdose

Symptoms

No cases of acute overdose have been reported. In clinical trials of healthy volunteers, the highest dose of tafamidis given was 480 mg in a single dose and 60 mg once daily for two weeks. The reported treatment-related adverse events were mild to moderate and included: headache, somnolence, myalgia, insomnia, hordeolum, photosensitivity reaction, and presyncope.

Management

In case of overdose, standard supportive measures should be instituted as required.

5 PHARMACOLOGIC PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other nervous system drugs, ATC code N07XX08

Mechanism of action

Tafamidis meglumine is a specific stabilizer of transthyretin.

Pharmacodynamic effects

TTR amyloid polyneuropathy is a multi-faceted, progressive, axonal degenerative neuropathy characterized by sensory, motor and autonomic impairment. The dissociation of the transthyretin tetramer to monomers is the rate limiting step in the pathogenesis of TTR amyloid polyneuropathy, also known as TTR familial amyloid polyneuropathy (TTR-FAP). The folded monomers undergo partial denaturation to produce alternatively folded monomeric amyloidogenic intermediates. These intermediates then misassemble into soluble oligomers, protofilaments, filaments, and amyloid fibrils. Tafamidis binds non-cooperatively to the two thyroxine binding sites on the native tetrameric form of transthyretin preventing dissociation into monomers. The inhibition of transthyretin tetramer dissociation forms the rationale for the use of tafamidis to slow disease progression.

Clinical efficacy and safety

The pivotal study of tafamidis meglumine was an 18-month, multicenter, randomized, double-blind, placebo-controlled study that evaluated the safety and efficacy of once-daily 20 mg tafamidis meglumine in 128 patients with TTR amyloid polyneuropathy with the V30M mutation and primarily stage 1 disease (do not routinely require assistance with ambulation). The primary outcome measures were the Neuropathy Impairment Score of the Lower Limb (NIS-LL – a physician assessment of the neurologic exam of the lower limbs) and the Norfolk Quality of Life - Diabetic Neuropathy (Norfolk QOL-DN – a patient reported outcome, total quality of life score [TQOL]). Other outcome measures included composite scores of large nerve fiber (nerve conduction, vibration threshold and heart rate response to deep breathing - HRDB) and small nerve fiber function (heat pain and cooling threshold and HRDB) and nutritional assessments utilizing the modified body mass index (mBMI – BMI multiplied by serum albumin in g/L). Eighty-six of the 91 patients completing the 18 month treatment period subsequently enrolled in an open label extension study, where they all received once daily 20 mg tafamidis meglumine for an additional 12 months.

Following 18 months of treatment, more tafamidis meglumine-treated patients were NIS-LL Responders (change of less than 2 points on NIS-LL) Outcomes for the pre-specified analyses of the primary endpoints are provided in the following table:

Vyndaqel versus Placebo: NIS-LL and TQOL at Month 18 (Study Fx-005)		
	Placebo	Vyndaqel
Pre-specified ITT Analysis	N=61	N=64
NIS-LL Responders (% Patients)	29.5%	45.3%
Difference (Vyndaqel minus Placebo)	15.8%	
95% CI of Difference (p-value)	-0.9%, 32.5% (0.068)	
TQOL Change from Baseline LSMean (SE)	7.2 (2.36)	2.0 (2.31)
Difference in LSMeans (SE)	-5.2 (3.31)	
95% CI of Difference (p-value)	-11.8, 1.3 (0.116)	
Pre-specified Efficacy Evaluable Analysis	N=42	N=45
NIS-LL Responders (% Patients)	38.1%	60.0%
Difference (Vyndaqel minus Placebo)	21.9%	
95% CI of Difference (p-value)	1.4%, 42.4% (0.041)	
TQOL Change from Baseline LSMean (SE)	8.9 (3.08)	0.1 (2.98)
Difference in LSMeans (SE)	-8.8 (4.32)	
95% CI of Difference (p-value)	-17.4, -0.2 (0.045)	
In the pre-specified ITT NIS-LL Responder analysis, patients who discontinued prior to the 18-month time point due to liver transplantation were categorized as non-responders. The pre-specified Efficacy Evaluable analysis used observed data for those patients who completed the 18 month treatment per protocol.		

The secondary endpoints demonstrated that tafamidis meglumine treatment resulted in less deterioration of neurologic function and improved nutritional status (mBMI) compared with placebo, as shown in the following table.

Secondary Endpoints Changes from Baseline to Month 18 LSMean (Standard Error) (Intent-to-Treat Population) (Study Fx-005)				
	Placebo N=61	Vyndaqel N=64	P-value	Vyndaqel % change relative to Placebo
NIS-LL change from BL <i>LSMean (SE)</i>	5.8 (0.96)	2.8 (0.95)	0.027	-52%
Large Fiber change from BL <i>LSMean (SE)</i>	3.2 (0.63)	1.5 (0.62)	0.066	-53%
Small Fiber change from BL <i>LSMean (SE)</i>	1.6 (0.32)	0.3 (0.31)	0.005	-81%
mBMI change from BL <i>LSMean (SE)</i>	-33.8 (11.8)	39.3 (11.5)	<0.0001	NA
mBMI was derived as the product of serum albumin and Body Mass Index. NA=Not applicable Based on repeated measures analysis of variance with change from baseline as the dependent variable, an unstructured covariance matrix, treatment, month and treatment-by-month as fixed effects, and subject as a random effect in the model.				

In the open-label extension study, the rate of change in the NIS-LL during the 12 months of treatment was similar to that observed in those patients randomised and treated with tafamidis in the previous double blind 18 month period.

Although data are limited, (one open label study in 21 patients), taking into account the mechanism of action of tafamidis and the results on TTR stabilisation, tafamidis meglumine is expected to be beneficial in patients with stage 1 TTR amyloid polyneuropathy due to mutations other than V30M.

The effects of tafamidis on cardiac disease progression have not yet been adequately characterised.

A supra-therapeutic, single, 400 mg oral dose of tafamidis solution in healthy volunteers demonstrated no prolongation of the QTc interval.

The European Medicines Agency has waived the obligation to submit the results of studies with tafamidis meglumine in all subsets of paediatric population in familial amyloid polyneuropathy (see section 4.2 for information on paediatric use).

This medicinal product has been authorised under 'exceptional circumstances'.

This means that due to the rarity of the disease it has not been possible to obtain complete information on this medicinal product.

The European Medicines Agency will review any new information which may become available every year and this SmPC will be updated as necessary.

5.2 Pharmacokinetic properties

Absorption

After oral administration of the soft capsule, the maximum plasma concentration (C_{max}) is achieved at a median time (t_{max}) of 2 hours after dosing in the fasted state. Concomitant administration of food decreased the rate of absorption, but not the extent of absorption. These results support the administration of tafamidis with or without food.

Distribution

Tafamidis is highly protein bound (99.9%) in plasma. The apparent steady state volume of distribution is 25.7 liters.

Biotransformation and elimination

There is no explicit evidence of biliary excretion of tafamidis in humans. Based on preclinical data, it is suggested that tafamidis is metabolised by glucuronidation and excreted via the bile. This route of biotransformation is plausible in humans, as approximately 59% of the total administered dose is recovered in faeces, and approximately 22% recovered in urine. Following daily administration of a 20 mg dose of tafamidis meglumine for 14 days in healthy subjects, mean steady-state half-life was 59 h and mean total clearance was 0.42 l/h.

Dose and time linearity

Results from once-daily dosing with tafamidis meglumine 15, 30, or 60 mg for 14 days demonstrated dose-dependent increases in C_{max} and AUC between doses of 15 mg and 30 mg and less than dose proportional between 30 and 60 mg, indicating saturation of absorption process beyond 30 mg.

Pharmacokinetic parameters were similar after single and repeated administration of 20 mg dose, indicating a lack of induction or inhibition of tafamidis metabolism.

Results of once-daily dosing with tafamidis meglumine 20 mg for 14 days demonstrated that steady-state was achieved by Day 14. $C_{max(ss)}$ and $C_{min(ss)}$ was 2.7 and 1.6 µg/ml, respectively.

Special populations

Hepatic impairment

Pharmacokinetic data indicated decreased systemic exposure (approximately 40%) and increased total clearance (0.52 l/h vs. 0.31l/h) of tafamidis in patients with moderate hepatic impairment (Child-Pugh Score of 7-9 inclusive) compared to healthy subjects due to a higher unbound fraction of tafamidis. As patients with moderate hepatic impairment have lower TTR levels than healthy subjects, dosage adjustment is not necessary as the stoichiometry of tafamidis with its target protein TTR would be

sufficient for stabilization of the TTR tetramer. The exposure to tafamidis in patients with severe hepatic impairment is unknown.

Renal impairment

Tafamidis has not specifically been evaluated in patients with renal impairment, but a dosage adjustment in patients with renal impairment is considered not necessary.

Elderly

Based on population PK results, subjects older than 60 years old had an average 19% lower estimate of clearance at steady-state compared to subjects less than 60 years old. However, the difference in clearance would not be clinically significant and would not result in clinically relevant different steady-state levels compared to younger subjects.

5.3 Preclinical safety data

Nonclinical data revealed no special hazard for humans based on conventional studies of safety pharmacology, fertility and early embryonic development, genotoxicity and carcinogenic potential. In repeated dose toxicity studies the liver appeared as a target organ for toxicity in the different species tested. Liver effects were seen at doses above (>3) human exposure and have generally been shown to be reversible.

In a developmental toxicity study in rabbits, a slight increase in skeletal malformations and variations, abortions in few females, and reduction in foetal weights were observed at an AUC₀₋₂₄ ratio of 3.2-fold, based on the human AUC at steady state.

In the rat peri- and post-natal development study with tafamidis, decreased pup survival and reduced pup weights were noted following maternal treatment during pregnancy and lactation at doses of 15 and 30 mg/kg. Decreased foetal weights in males were associated with delayed sexual maturation (preputial separation) and impaired performance in a water-maze test for learning and memory. The NOAEL for viability and growth in the F1 generation offspring following maternal treatment during pregnancy and lactation with tafamidis was 5 mg/kg (HED=0.8 mg/kg), a dose approximately 4.6-times the recommended dose.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule shell

Gelatin (E441)
Glycerin (E422)
Yellow iron oxide (E172)
Sorbitan
Sorbitol (E420)
Mannitol (E421)
Titanium dioxide (E171)
Purified water

Capsule contents

Macrogol 400 (E1521)
Sorbitan monooleate (E494)
Polysorbate 80 (E433)

Printing ink (Opacode purple)

Ethyl alcohol

Isopropyl alcohol
Purified water
Macrogol 400 (E1521)
Polyvinyl acetate phthalate
Propylene glycol (E1520)
Carmines (E120)
Brilliant Blue FCF (E133)
Ammonium hydroxide (E527) 28%

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

18 months

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Two polyvinyl chloride/aluminum blisters each containing 15 soft capsules are contained in a wallet.

Pack sizes: 30 or 90 soft capsules

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Pfizer Limited
Ramsgate Road
Sandwich, Kent
CT13 9NJ
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

EU/1/11/717/001
EU/1/11/717/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16 November 2011
Date of latest renewal: 22 July 2016

10 DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency: <http://www.ema.europa.eu>.

ANNEX II

- A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**
- E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE MARKETING AUTHORISATION UNDER EXCEPTIONAL CIRCUMSTANCES**

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Penn Pharmaceutical Services Limited
Units 23-24, Tafarnaubach Industrial Estate
Tafarnaubach
Tredegar
Gwent
NP22 3AA
United Kingdom

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

• Periodic Safety Update Reports

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

• Risk Management Plan (RMP)

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 European Medicines Agency;
- 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.

• Additional risk minimisation measures

The Physician Information Leaflet should contain the following key messages:

- The need to counsel patients on important risks associated with Vyndaqel therapy and appropriate precautions when using the medicine, particularly the avoidance of pregnancy and the need for effective contraception.
- That patients should be advised to contact their doctor about adverse events and that physicians/pharmacists should report suspected adverse reactions to Vyndaqel since there is limited knowledge about the clinical safety due to the rare nature of transthyretin amyloidosis.

- That physicians are encouraged to enter patients in the Transthyretin Amyloidosis Outcome Survey (THAOS) and provided with details how to enroll patients into this international disease registry
- The existence and scope of the Tafamidis Enhanced Surveillance for Pregnancy Outcomes (TESPO) program and the details how to report pregnancies in women who are being treated with Vyndaqel.

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE MARKETING AUTHORISATION UNDER EXCEPTIONAL CIRCUMSTANCES

This being an approval under exceptional circumstances and pursuant to Article 14(8) of Regulation (EC) No 726/2004, the MAH shall complete, within the stated timeframe, the following measure:

Description	Due date
Within the planned post-authorisation sub-study of the THAOS registry the MAH shall evaluate in non-V30M patients the effects of Vyndaqel on disease progression and its long term safety as detailed in a CHMP agreed protocol, and shall provide yearly updates on the collected data within the annual re-assessment.	Annual Reassessment

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1 NAME OF MEDICINAL PRODUCT

Vyndaqel 20 mg soft capsules
tafamidis meglumine

2 STATEMENT OF ACTIVE SUBSTANCES

Each soft capsule contains 20mg tafamidis meglumine equivalent to 12.2 mg tafamidis

3 LIST OF EXCIPIENTS

The capsule contains sorbitol (E420). See leaflet for further information.

4 PHARMACEUTICAL FORM AND CONTENTS

30 soft capsules
90 soft capsules

5 METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use
Lift here

6 SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7 OTHER SPECIAL WARNING(S), IF NECESSARY

8 EXPIRY DATE

EXP

9 SPECIAL STORAGE CONDITIONS

Do not store above 25°C.

10 SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11 NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Pfizer Limited
Ramsgate Road
Sandwich, Kent
CT13 9NJ
United Kingdom

12 MARKETING AUTHORISATION NUMBER(S)

EU/1/11/717/001
EU/1/11/717/002

13 BATCH NUMBER

Lot

14 GENERAL CLASSIFICATION FOR SUPPLY

15 INSTRUCTIONS ON USE

16 INFORMATION IN BRAILLE

Vyndaqel

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC: {number}
SN: {number}
NN: {number}

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Heat sealed blister card of 30 x 20 mg Vyndaqel soft capsules

1 NAME OF MEDICINAL PRODUCT

Vyndaqel 20 mg soft capsules
Tafamidis meglumine

2 NAME OF THE MARKETING AUTHORISATION HOLDER

Pfizer Limited (as MA Holder logo)

3 EXPIRY DATE

EXP

4 BATCH NUMBER

Lot

5 OTHER

To remove capsule push through from this side

Fold and reclose after removing capsule

Pull here

Day 1 to Day 30

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Vyndaqel 20 mg soft capsules

Tafamidis meglumine

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Vyndaqel is and what it is used for
2. What you need to know before you take Vyndaqel
3. How to take Vyndaqel
4. Possible side effects
5. How to store Vyndaqel
6. Contents of the pack and other information

1. What Vyndaqel is and what it is used for

Vyndaqel contains the active substance tafamidis.

Vyndaqel is a medicine which treats a disease called Transthyretin (TTR) amyloid polyneuropathy, also known as TTR familial amyloid polyneuropathy (TTR-FAP). TTR amyloid polyneuropathy is caused by a protein called TTR that does not work properly. TTR is a protein that carries other substances, such as hormones, through the body.

In patients with this disease, TTR breaks up and may form fibres called amyloid. Amyloid can build up around your nerves and in other places in your body, preventing them from working normally. Eventually, the amyloid causes the symptoms of this disease.

Vyndaqel, can prevent TTR from breaking up and forming amyloid deposits. This medicine is used to treat adult patients with this disease whose nerves have been affected (people with symptomatic polyneuropathy) to delay further progression.

2. What you need to know before you take Vyndaqel

Do not take Vyndaqel

If you are allergic to tafamidis meglumine or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor, pharmacist or nurse before taking Vyndaqel.

- Women that can become pregnant should use birth control while taking Vyndaqel and should continue using birth control for one month after stopping treatment with Vyndaqel. There are no data on the use of Vyndaqel in pregnant women.

Children and adolescents

Children and adolescents do not have the symptoms of TTR amyloid polyneuropathy. Vyndaqel is therefore not used for children and adolescents.

Other medicines and Vyndaqel

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

You should inform your doctor or pharmacist if you are taking any of the following:

- non-steroidal anti-inflammatory drugs
- diuretic medicines (e.g. furosemide, bumetanide)
- anti-cancer medicines (e.g. methotrexate, imatinib)
- statins (e.g. rosuvastatin)
- anti-viral medicines (e.g. oseltamivir, tenofovir, ganciclovir, adefovir, cidofovir, lamivudine, zidovudine, zalcitabine)

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

- You should not take Vyndaqel if you are pregnant or breast-feeding.
- If you are able to become pregnant, you must use birth control during treatment and for one month after stopping treatment.

Driving and using machines

Vyndaqel is believed to have no or negligible influence on the ability to drive and use machines.

Vyndaqel contains sorbitol

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take Vyndaqel

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose is one capsule (20 mg Tafamidis meglumine) of Vyndaqel once a day.

If you vomit after taking this medicine and can identify the intact Vyndaqel capsule, then an additional dose of Vyndaqel should be taken in the same day; if you cannot identify the Vyndaqel capsule, then

no additional dose of Vyndaqel is necessary, and you can resume taking Vyndaqel the next day as usual.

Method of administration

Vyndaqel is for oral use.

The soft capsule should be swallowed whole, not crushed or cut.

The capsule may be taken with or without food

If you take more Vyndaqel than you should

You should not take more capsules than your doctor tells you to. If you take more capsules than you have been told to take, contact your doctor.

If you forget to take Vyndaqel

If you forget to take a dose, take your capsules as soon as you remember. If it is within 6 hours before your next dose, skip the missed dose and take the next dose at the usual time. Do not take a double dose to make up for a forgotten dose.

If you stop taking Vyndaqel

Do not stop taking Vyndaqel without first speaking to your doctor. As Vyndaqel works by stabilizing the TTR protein, if you stop taking Vyndaqel, the protein will no longer be stabilized, and your disease may progress.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Very common: may affect more than 1 in 10 people are listed below:

- Diarrhoea
- Urinary tract infection (symptoms may include: pain or a burning sensation when you urinate or a frequent need to urinate)
- Vaginal infection in women
- Stomach ache or abdominal pain

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via [the national reporting system listed in Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Vyndaqel

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the blister card and on the carton. The expiry date refers to the last day of that month.

Do not store above 25°C.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Vyndaqel contains

- The active substance is tafamidis. Each capsule contains 20 mg tafamidis meglumine equivalent to 12.2 mg tafamidis.
- The other ingredients are: gelatin (E441), glycerin (E422), sorbitol (E420), mannitol (E421), sorbitan, yellow iron oxide (E172), titanium dioxide (E171), purified water, macrogol 400 (E1521), sorbitan monooleate (E494), polysorbate 80 (E433), ethyl alcohol, isopropyl alcohol, polyvinyl acetate phthalate, propylene glycol (E1520), carmine (E120), brilliant blue FCF (E133) and ammonium hydroxide (E527).

What Vyndaqel looks like and contents of the pack

Vyndaqel soft capsules are yellow, opaque, oblong (approximately 21 mm) imprinted with “VYN 20” in red. They are supplied on a blister card of 15 soft capsules. There are 2 blister cards in each wallet. A pack of 30 or 90 soft capsules is provided. Not all pack sizes may be marketed.

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This leaflet was last revised in <{MM/YYYY}><{month YYYY}>.

This medicine has been authorised under ‘exceptional circumstances’.
This means that because of the rarity of this disease it has been impossible to get complete information on this medicine.

The European Medicines Agency will review any new information on this medicine every year and this leaflet will be updated as necessary.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: <http://www.ema.europa.eu>. There are also links to other websites about rare diseases and treatments.

If this leaflet is difficult to see or read or you would like it in a different format, please contact the Marketing Authorisation Holder's local office number that is provided in this leaflet.