Vyndaqel® (tafamidis meglumine) | NEW Vyndamax™ (tafamidis)

The first and only* medication indicated to reduce CV mortality and CV-related hospitalization in adult patients with wild-type or hereditary ATTR-CM

Tafamidis is recommended by the CCS/CHFS for patients with ATTR-CM and NYHA class I-III symptoms[1†]

VYNDAQEL and VYNDAMAX are indicated for the treatment of adult patients with cardiomyopathy due to transthyretin-mediated amyloidosis (ATTR-CM), wild-type or hereditary, to reduce cardiovascular (CV) mortality and CV-related hospitalization.[2]

CCS/CHFS = Canadian Cardiovascular Society/Canadian Heart Failure Society
* Comparative clinical significance unknown.
† Please consult the CCS/CHFS Joint Position Statement for complete recommendations.

Pfizer

Pooled VYNDAQEL demonstrated a significant reduction in all-cause mortality* and CV-related hospitalizations vs. placebo at 30 months[2†]

The pivotal study was conducted with VYNDAQEL (tafamidis meglumine). Tafamidis 61 mg (VYNDAMAX) was not administered in the pivotal study.

The primary analysis used a hierarchical combination applying the Finkelstein-Schoenfeld (FS) method, which compared each patient to every other patient within each stratum in a pair-wise manner that proceeded in a hierarchical fashion using all-cause mortality* followed by frequency of cardiovascular-related hospitalizations when patients cannot be differentiated based on mortality.

	Pooled tafadamis meglumine (VYNDAQEL) (n=264)	Placebo (n=177)
Primary analysis†		
Number (%) of subjects alive‡ at Month 30	186 (70.5%)	101 (57.1%)
Average CV-related hospitalizations per patient per year during 30 months among those alive at Month 30	0.297	0.455
P-value	p=0.0006	
NNT for all-cause mortality[3]	7.5	
CV-related hospitalization frequency		
Total number (%) of subjects with CV-related hospitalizations§	138 (52.3%)	107 (60.5%)
CV-related hospitalizations per year	0.48	0.70
Relative risk ratio	0.68	
P-value	p<0.0001	
NNT for CV-related hospitalizations[3]	4.4	

Adapted from Product Monograph[2]

The difference in mortality events between groups was attributable to CV-related events. Overall, 20.8% of the pooled tafadamis meglumine and 33.3% of the placebo groups had CV-related deaths. Non-CV-related deaths were reported in 5.3% of the pooled tafadamis meglumine and 4.7% of the placebo group.

- Pooled tafadamis meglumine significantly reduced the risk of all-cause mortality* and frequency of CV-related hospitalizations vs. placebo[2]
  - All-cause mortality: RRR 30%, HR 0.70, 95% CI 0.51-0.96, p=0.026
  - CV-related hospitalization frequency during 30 months: 0.48/year for tafadamis meglumine vs. 0.70 for placebo, RRR 32%, relative risk ratio§ 0.68, p<0.0001; NNT = 4.4[3]

Key secondary endpoints

- A significant treatment effect favouring tafadamis meglumine was first observed at Month 6 and remained significant through Month 30 for both functional capacity (measured by the 6MWT) and health status (measured by the KCCQ-OS)[2]

NNT = number needed to treat; RRR = relative risk reduction; 6MWT = 6-Minute Walk Test;
KCCQ-OS = Kansas City Cardiomyopathy Questionnaire-Overall Summary

* VYNDAQEL is only indicated in the reduction of CV mortality and CV-related hospitalization.

† Data from the Transthyretin Amyloidosis Cardiomyopathy Clinical Trial (ATTR-ACT), a double-blind, placebo-controlled study in which 441 ATTR-CM patients were randomized to tafadamis meglumine 80 mg/day + standard of care (e.g., diuretics, n=176), tafadamis meglumine 20 mg/day + standard of care (n=88) or placebo + standard of care (n=177) for 30 months.

‡ Heart transplantation and cardiac mechanical assist device implantation are considered indicators of approaching end stage. As such, these subjects are treated in the analysis as equivalent to death. Therefore, such subjects are not included in the count of "number of subjects alive at Month 30" even if such subjects are alive based on 30-month vital status follow-up assessment.

§ This analysis was based on a Poisson regression model with treatment, transthyretin (TTR) genotype (variant and wild-type), New York Heart Association (NYHA). Baseline classification (NYHA Classes I and II combined and NYHA Class III), treatment-by-TTR genotype interaction, and treatment-by-NYHA baseline classification interaction terms as factors.

Adverse events

- The data across clinical trials reflect exposure of 377 ATTR-CM patients to either tafadamis meglumine 20 mg or 80 mg daily for an average of 24.5 months (ranging from 1 day to 111 months)

- The frequency of adverse events (AEs) in patients treated with tafadamis meglumine 20 mg or 80 mg was comparable to placebo[2]

	Tafadamis meglumine (VYNDAQEL) 80 mg (n=176)	Tafadamis meglumine (VYNDAQEL) 20 mg (n=88)	Placebo (n=177)
Most frequently reported treatment-emergent serious AEs			
Condition aggravated	22.7%	23.9%	32.8%
Cardiac failure	19.3%	18.2%	22.6%
Cardiac failure congestive	11.9%	15.9%	17.5%
Cardiac failure acute	13.1%	4.5%	9.6%
Fall	5.1%	5.7%	2.8%
Syncope	3.4%	0%	5.6%
Treatment-emergent AEs with a higher incidence in the tafadamis meglumine groups than placebo (≥2x placebo and reported by ≥4 patients)			
Cystitis	3.4%	2.3%	0%
Sinusitis	5.7%	5.7%	0.6%
Asthenia	10.2%	12.5%	6.2%
Balance disorder	8.5%	2.3%	1.1%
Cataract	5.1%	3.4%	1.1%
Most commonly reported treatment-emergent AEs (≥10%) in the tafadamis meglumine groups that occurred at rates higher than placebo			
Atrial fibrillation	19.9%	18.2%	18.6%
Cardiac failure	26.1%	34.1%	33.9%
Cardiac failure acute	13.6%	4.5%	9.6%
Cardiac failure congestive	12.5%	19.3%	18.6%
Asthenia	10.2%	12.5%	6.2%
Edema peripheral	17.0%	19.3%	17.5%
Bronchitis	11.9%	10.2%	10.7%
Pneumonia	13.1%	11.4%	9.6%
Fall	24.4%	30.7%	23.2%
Muscle spasms	8.5%	11.4%	7.9%
Pain in extremity	15.3%	6.8%	11.3%
Insomnia	11.4%	13.6%	12.4%
Hematuria	5.7%	11.4%	9.6%
Cough	11.9%	18.2%	16.9%
Hypotension	10.8%	13.6%	10.7%

Adapted from Product Monograph[2]

NEW Vyndamax™

a single-capsule, once-daily treatment for patients with ATTR-CM[4]

1 dose = one 61 mg capsule

The dose 61 mg may be reduced to one 20 mg capsule of VYNDAQEL if not tolerated.

To avoid dosing errors, it is important that prescriptions of tafamidis/tafamidis meglumine specify the salt form and the prescribed dose

OR

Vyndaqel®

a once-daily treatment for patients with ATTR-CM

1 dose = 4 x 20 mg capsules

For the recommended dose of 80 mg per day, patients should take four 20 mg capsules orally once daily[2]

Can be taken with or without food

Capsules should be swallowed whole and not crushed or cut

Bioavailability information

VYNDAMAX and VYNDAQEL are different formulations with the active moiety tafamidis and are not interchangeable on a per mg basis.

The relative bioavailability of VYNDAMAX (tafamidis) capsules was compared to that of VYNDAQEL (tafamidis meglumine) capsules in a multiple dose 2-way crossover comparative bioavailability study in 30 healthy adult male subjects.

Please consult the Product Monographs for complete dosing and administration information.

Supporting patient access for VYNDAQEL/VYNDAMAX

Enroll your patients in the Patient Support Program

In 4 easy steps:

1. Your patient fills out the PATIENT INFORMATION section and signs the CONSENT
2. You fill out the PHYSICAN INFORMATION section or stamp the area with your information
3. You fill out the PRESCRIPTION information section, sign the prescription and sign the CONSENT
4. You EMAIL the completed enrolment form to VYNDAQEL@INNOMAR-STRATEGIES.COM or FAX it to: 1-833-375-1413

Our patient support offerings

TREATMENT ACCESS SERVICES

Reimbursement navigation and assessment

Coordination of insurance benefits

Financial assistance

PHARMACY SERVICES

Access to specialty pharmacies

Medication home delivery

PATIENT EDUCATION

Educational call by trained nurse on ATTR-CM and VYNDAQEL/VYNDAMAX

Access to a patient education brochure

Clinical use:

Pediatrics: Not indicated.

Geriatrics: Safety and efficacy demonstrated in this population.

Relevant warnings and precautions:

- Not recommended in organ transplant patients.
- Should not be used during pregnancy; women of childbearing potential should use appropriate contraception when taking VYNDAQEL and VYNDAMAX and continue to use contraception for 1 month after stopping treatment; studies in animals have shown developmental toxicity; potential risk for humans unknown
- Should not be used by nursing women; studies in animals suggest potential for serious adverse reactions in breastfed infants.
- Not recommended in patients with severe hepatic impairment
- Data limited in patients with severe renal impairment

For more information:

Please consult the Product Monographs at http://pfizer.ca/pm/en/vyndaqel.pdf and http://pfizer.ca/pm/en/vyndamax.pdf for important information relating to adverse reactions, drug interactions, and dosing information which have not been discussed in this piece. The Product Monograph is also available by calling 1-800-463-6001.

References:

1. Fine NM *et al.* Canadian Cardiovascular Society/Canadian Heart Failure Society joint position statement on the evaluation and management of patients with cardiac amyloidosis. *Can J Cardiol* 2020;36:322-34.
2. VYNDAQEL Product Monograph. Pfizer Canada ULC, January 20, 2020.
3. Pfizer Canada ULC. Data on file. Medical letter dated May 5, 2020.
4. VYNDAMAX Product Monograph. Pfizer Canada ULC, July 9, 2021.

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INNOVATIVE MEDICINES CANADA

REVIEWED BY PAAB