

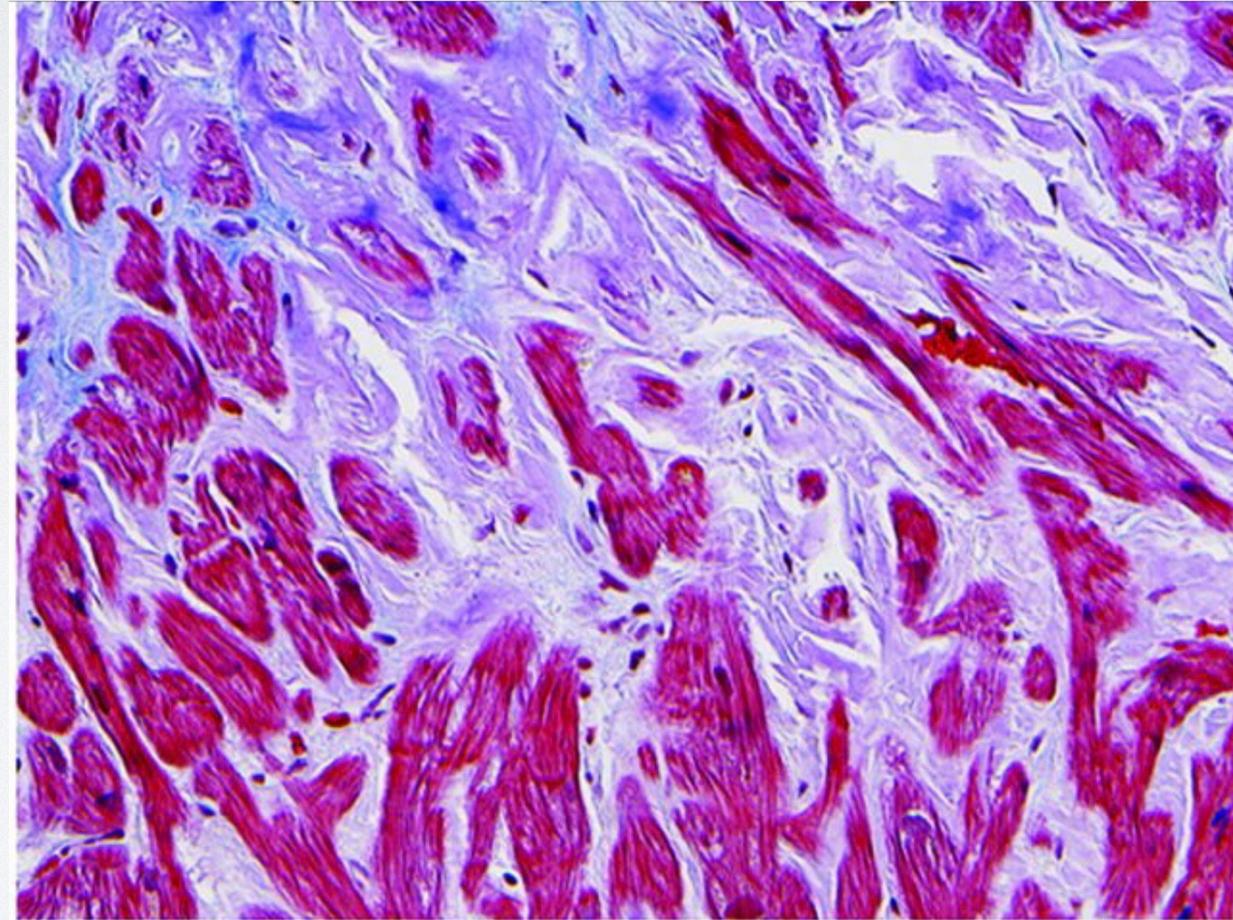
# COST-EFFECTIVENESS OF THERAPY FOR AMYLOID CARDIOMYOPATHY

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Right Care Initiative  
October 12, 2020

Disclosures: Pfizer

# THERAPY FOR AMYLOIDOSIS

- Chemotherapy and Stem Cell transplant: AL amyloidosis
- Anti-inflammatory: AA amyloidosis
- Organ transplantation: ATTR cardiac
- Diflunisal: wtTTR cardiac and neuropathy
- Tafamidis: wtTTR cardiac
- Patisiran: hTTR neuropathy
- Inotersen: hTTR neuropathy
- AG10: cardiac; PRX-004: neuropathy trials

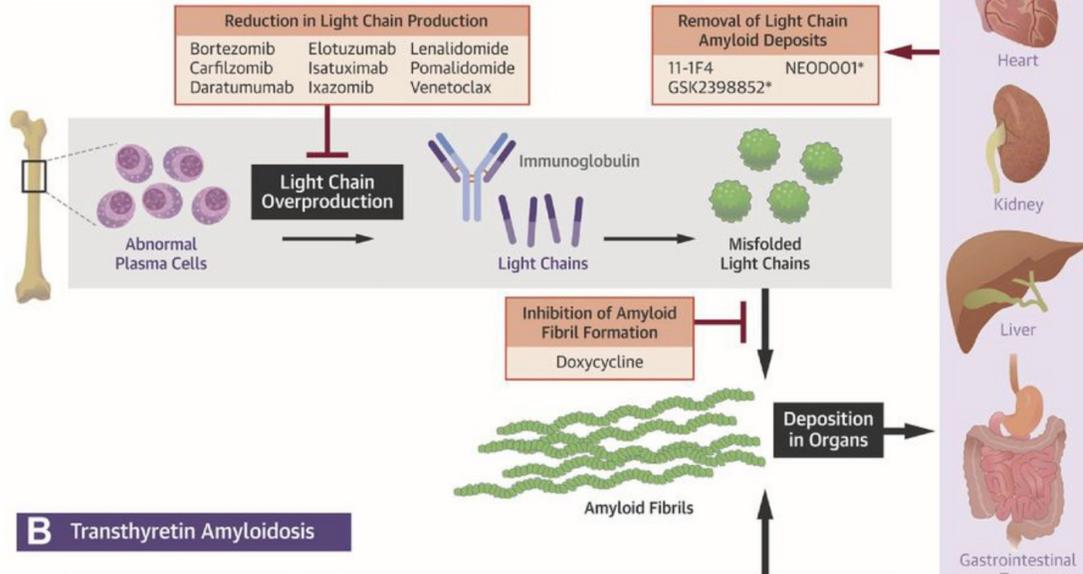


# CENTRAL ILLUSTRATION: Pathophysiology of Light Chain and Transthyretin Amyloidosis and Mechanism of Action of Novel Therapeutics

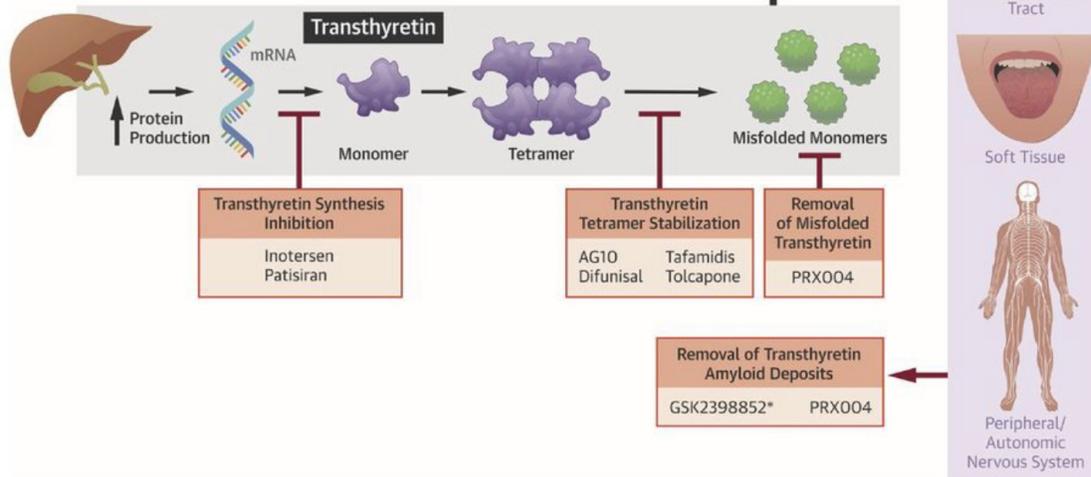
Ask your doctor about



## A Light Chain Amyloidosis



## B Transthyretin Amyloidosis



**Doxycycline Monohydrate Tablets**

**100mg**

\$1.05/tablet

Give as directed

\*\*Keep out of reach of children

**\$1.05/tablet**

**\$116/tablet**

# THERAPIES FOR AMYLOIDOSIS

755,98

© 2005 GS

Prescription Settings

**Diflunisal**

DIFLUNISAL is

generic

**GoodRx** Discount Drug Coupon

Your prescription

**Vyndamax 10 capsules of 61mg**

3 dose packs

Discounted price with this coupon

**\$18503.40** at Raley's

This is your estimated price. The pharmacy will provide exact pricing.

Customer questions call: 1-855-426-4465

**\$32/month**

# DIFLUNISAL

140, No. Suppl\_1 > Abstract 13123: Diflunisal is Associated With Improved Mortality in Pati...

HEART FAILURE AND CARDIOMYOPATHIES

SESSION TITLE: PROGNOSIS IN HEART FAILURE/CARDIOMYOPATHY

## Abstract 13123: Diflunisal is Associated With Improved Mortality in Patients With Wild-Type ATTR Cardiac Amyloidosis: The BU Amyloidosis Center Experience

Yuliya Y Mints, John L Berk, Lawreen Connors, Gheorghe Doros, Deepa M Gopal, Shivangi Kataria, Graham Lohrmann, Alexandra R Pipilas, Frederick L Ruberg, Omar K Siddiqi

Originally published 11 Nov 2019 | Circulation. 2019;140:A13123

**Results:** There were 105 patients evaluated (97% male, 81% white), with 35 receiving diflunisal and 70 in the control group. Patients in the diflunisal group were younger (76.7 years vs 79.3 years,  $p = 0.07$ ), with lower BNP levels ( $340.9 \pm 365.0$  vs  $520.9 \pm 297.4$  pg/mL,  $p = 0.008$ ), and troponin I levels ( $0.098 \pm 0.1$  vs  $0.19 \pm 0.34$  ng/mL,  $p = 0.03$ ). There was a trend towards worse renal function in the control group (eGFR  $53.35 \pm 19.45$  vs  $61.53 \pm 24.29$  mL/min,  $p = 0.14$ ). Diflunisal administration was associated with improved survival in unadjusted survival analysis (HR 0.20, 95% CI 0.08 - 0.49,  $p = 0.0001$ ), which persisted after adjustment for BNP, creatinine, troponin I, interventricular septal thickness, and LVEF (HR 0.23, 95% CI 0.09 - 0.60,  $p = 0.003$ ). Diflunisal use was also associated with non-significant improvement in BNP, stability in troponin I and echocardiographic parameters, and a non-significant increase in serum creatinine as compared to controls.

**Conclusion:** Diflunisal use in ATTRwt cardiac amyloidosis was well tolerated in selected patients and was associated with improved survival, as well as stability in echocardiographic and biochemical markers of disease.

**Diflunisal** Generic Dolobid

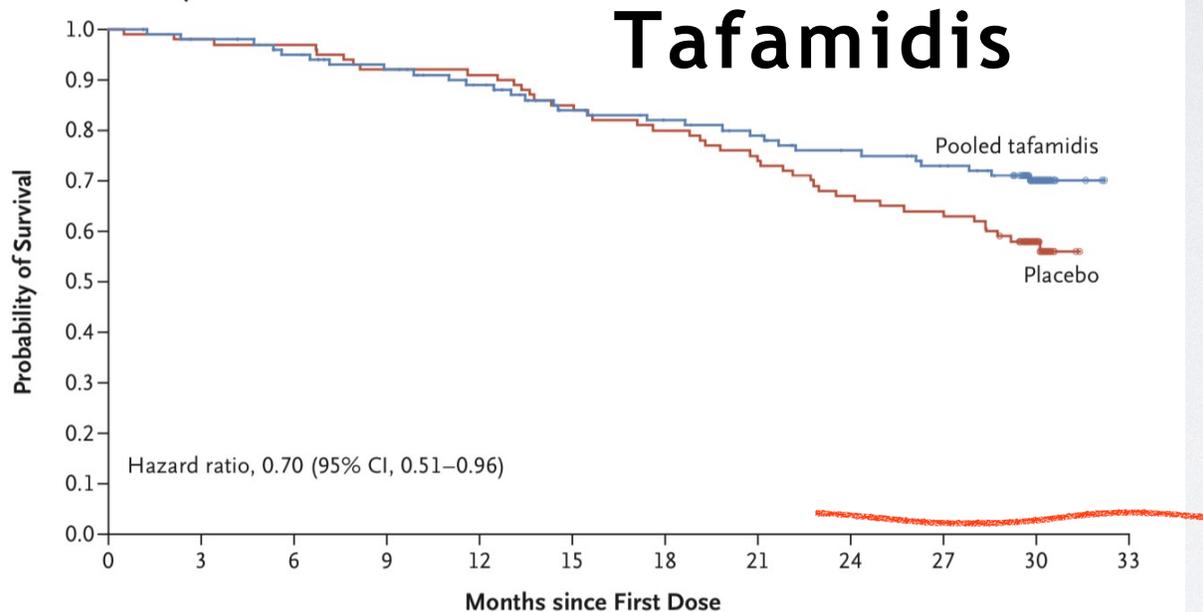
DIFLUNISAL is used to treat osteoarthritis, rheumatoid arthritis, or mild to moderate pain. The lowest GoodRx price for the most common version of diflunisal is around **\$32.45**, 69% off the average retail price of \$106.90.



**A Primary Analysis, with Finkelstein–Schoenfeld Method**

|                  | No. of Patients | P Value from Finkelstein–Schoenfeld Method | Win Ratio (95% CI) | Patients Alive at Mo 30<br>no. (%) | Average Cardiovascular-Related Hospitalizations during 30 Mo among Those Alive at Mo 30<br>per patient per yr |
|------------------|-----------------|--|--------------------|------------------------------------|---|
| Pooled Tafamidis | 264             | <0.001                                     | 1.70 (1.26–2.29)   | 186 (70.5)                         | 0.30  |
| Placebo          | 177             |  |                    | 101 (57.1)                         | 0.46  |

**B Analysis of All-Cause Mortality**



**No. at Risk (cumulative no. of events)**

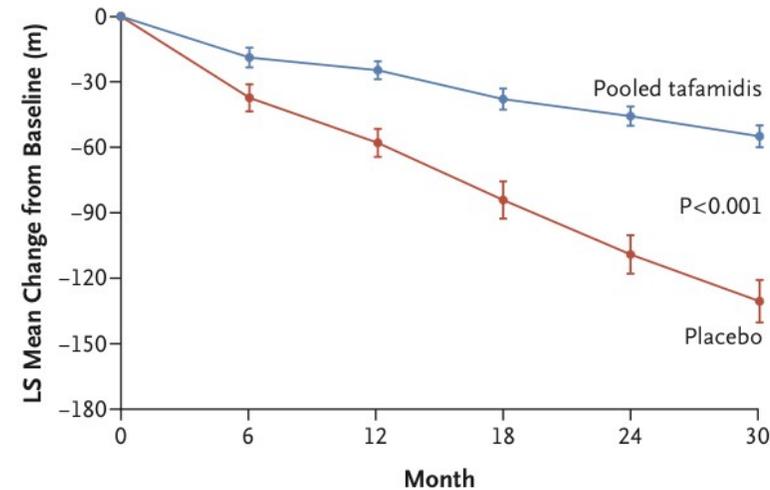
|                  | 0       | 3       | 6        | 9        | 12       | 15       | 18       | 21       | 24       | 27       | 30      | 33     |
|------------------|---------|---------|----------|----------|----------|----------|----------|----------|----------|----------|---------|--------|
| Pooled tafamidis | 264 (0) | 259 (5) | 252 (12) | 244 (20) | 235 (29) | 222 (42) | 216 (48) | 209 (55) | 200 (64) | 193 (71) | 99 (78) | 0 (78) |
| Placebo          | 177 (0) | 173 (4) | 171 (6)  | 163 (14) | 161 (16) | 150 (27) | 141 (36) | 131 (46) | 118 (59) | 113 (64) | 51 (75) | 0 (76) |

**C Frequency of Cardiovascular-Related Hospitalizations**

|                  | No. of Patients | No. of Patients with Cardiovascular-Related Hospitalizations<br>total no. (%) | Cardiovascular-Related Hospitalizations<br>no. per yr | Pooled Tafamidis vs. Placebo Treatment Difference<br>relative risk ratio (95% CI) |
|------------------|-----------------|---|---|---|
| Pooled Tafamidis | 264             | 138 (52.3)  | 0.48  | 0.68 (0.56–0.81)  |
| Placebo          | 177             | 107 (60.5)  | 0.70  |   |

Figure 2 Primary Analysis and Components

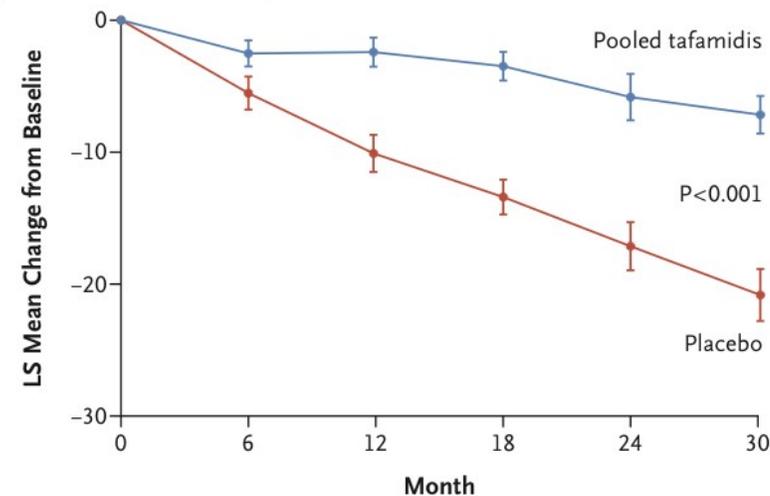
**A Change from Baseline in 6-Minute Walk Test**



**No. of Patients**

|           | 0   | 6   | 12  | 18  | 24  | 30  |
|-----------|-----|-----|-----|-----|-----|-----|
| Tafamidis | 264 | 233 | 216 | 193 | 163 | 155 |
| Placebo   | 177 | 147 | 136 | 111 | 85  | 70  |

**B Change from Baseline in KCCQ-OS**



**No. of Patients**

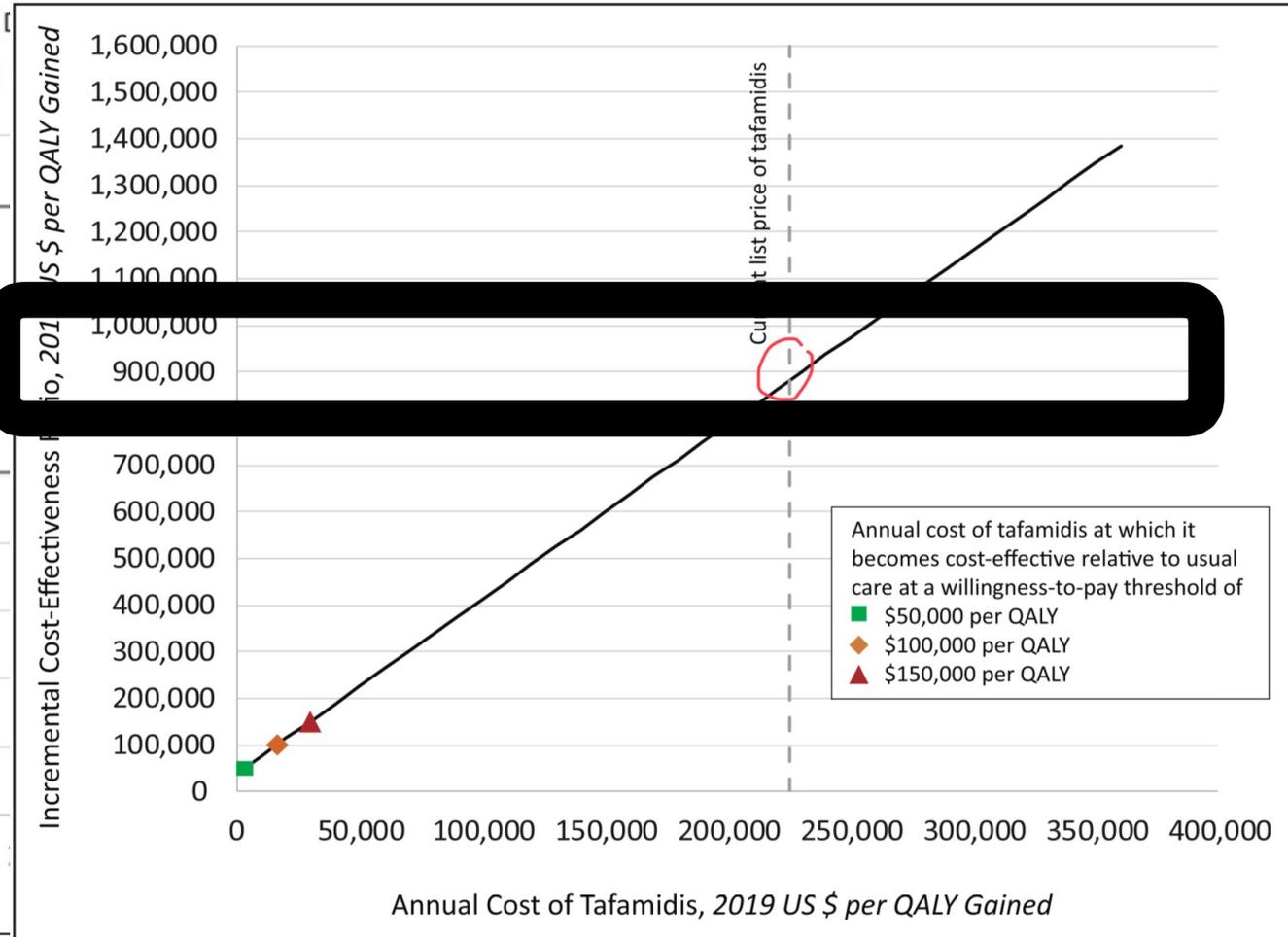
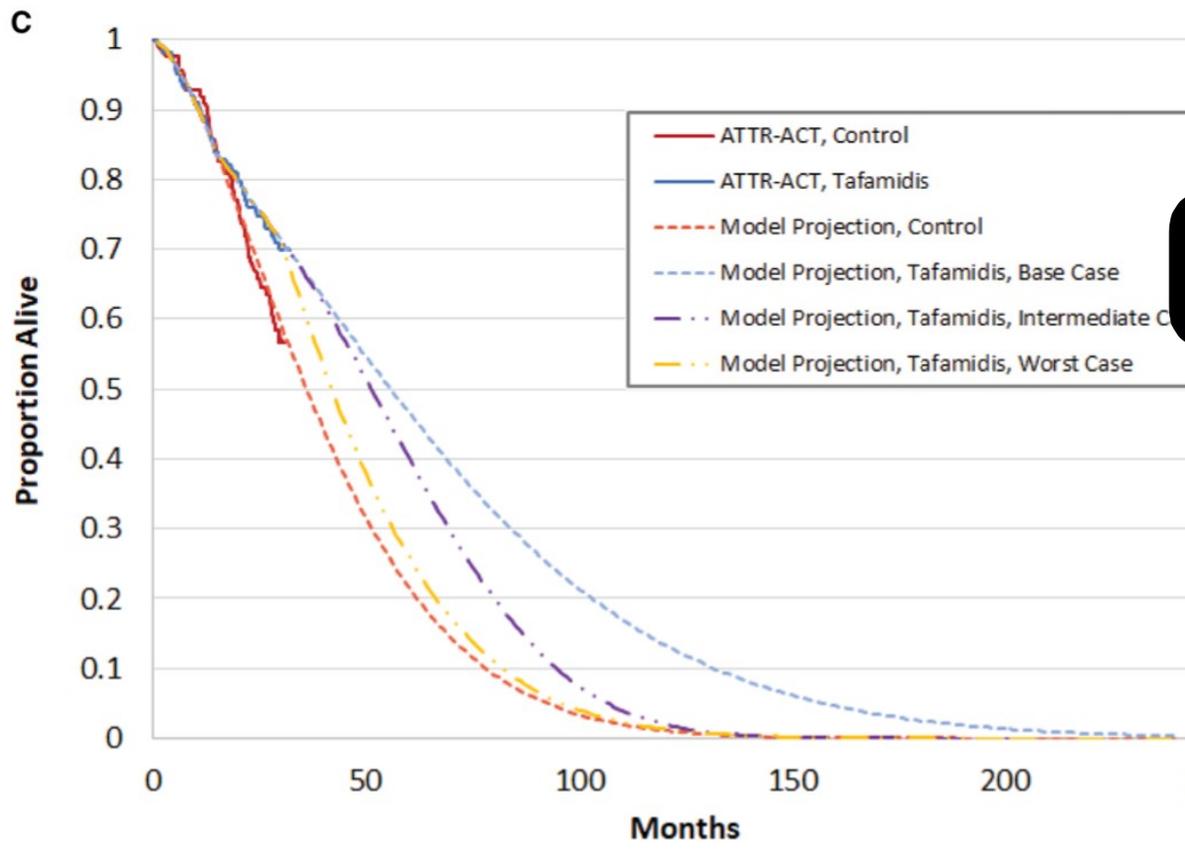
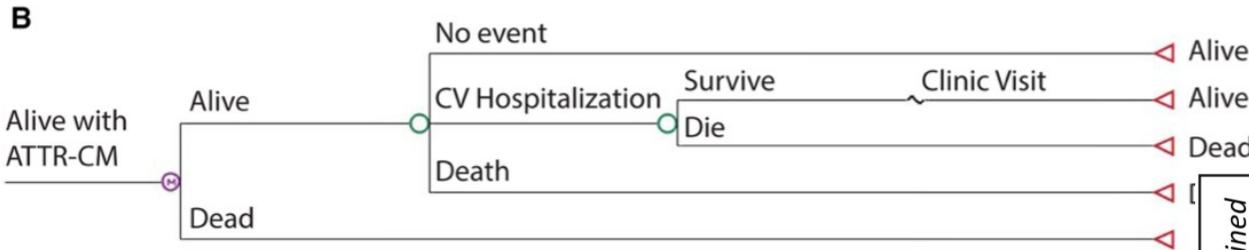
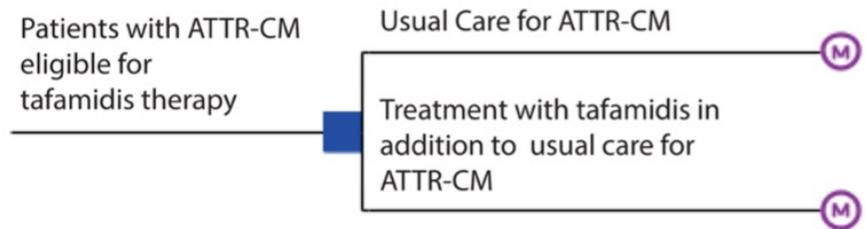
|           | 0   | 6   | 12  | 18  | 24  | 30  |
|-----------|-----|-----|-----|-----|-----|-----|
| Tafamidis | 264 | 241 | 221 | 201 | 181 | 170 |
| Placebo   | 177 | 159 | 145 | 123 | 96  | 84  |

Figure 4. Key Secondary End Points.

# TAFAMIDIS VS SACUBITRIL QALY

1.29 QALYs, a relatively large health gain compared with other contemporary cardiovascular therapies, justifying its designation as a breakthrough therapy that addresses an important unmet clinical need.<sup>26,27</sup> For comparison, the use of sacubitril-valsartan in heart failure with reduced ejection fraction is projected to yield 0.62 QALYs over a patient's lifetime.<sup>26</sup>

# TAFAMIDIS COST



# TAFAMIDIS COST-EFFECTIVENESS

life expectancy by an average of 1.29 QALYs, but the ICER of \$880,000 per QALY gained would be substantially higher than conventional cost-effectiveness thresholds. A 92.6% reduction in the annual price of tafamidis, from \$225,000 to \$16,563, would be needed for the drug to be cost-effective at a commonly accepted threshold of \$100,000 per QALY gained. Savings

The problem here is that ATTR cardiomyopathy not only isn't rare, it's actually downright common if you are looking at older populations with HF with preserved ejection fraction. Plus, we now have an easy/inexpensive screening test available to make the diagnosis, by sending off a couple of simple laboratory tests and ordering an inexpensive/noninvasive nuclear scan, so the sky is the limit for the number of people who will be eligible to take the drug.

On an individual patient level, because most patients eligible for tafamidis are older and insured through Medicare, they have the "donut hole" and the 5% drug copay, so their out-of-pocket costs approach \$15,000 a year. While there are assistance programs available for some patients with the lowest incomes, for patients who have a moderate income but who are by no means wealthy, they are caught in a really bad situation

Ronald M. Witteles, MD, Director, Stanford Amyloid Center

**Table ES13. Value-Based Benchmark Prices for Inotersen and Patisiran**

|                  | List Price | Net Price  | Price to Achieve \$100,000 per QALY | Price to Achieve \$150,000 per QALY | Discount from List Price to Reach Threshold Prices |
|------------------|------------|------------|-------------------------------------|-------------------------------------|--|
| <b>Inotersen</b> | \$450,000* | \$345,000* | \$15,275                            | \$25,379                            | 94% to 97%   |
| <b>Patisiran</b> | \$450,000  | \$345,000  | \$24,700                            | \$46,488                            | 90% to 95%   |

QALY: quality-adjusted life year

\*Assumed placeholder price for inotersen

The approval was notable not only for the promise that it offers patients, but also for the strategy by which Anylam hopes to sell the drug: In order to help payers cope with the \$450,000 annual list price of patisiran, Anylam is working with commercial insurance plans to offer value-based contracts for the therapy.

After a confidential price cut, Akcea has persuaded NICE to change its position on regaden, paving the way for the first-ever treatment for hATTR to be made available to patients with the ultra-rare, progressive condition, which causes the liver to produce abnormal transthyretin protein.

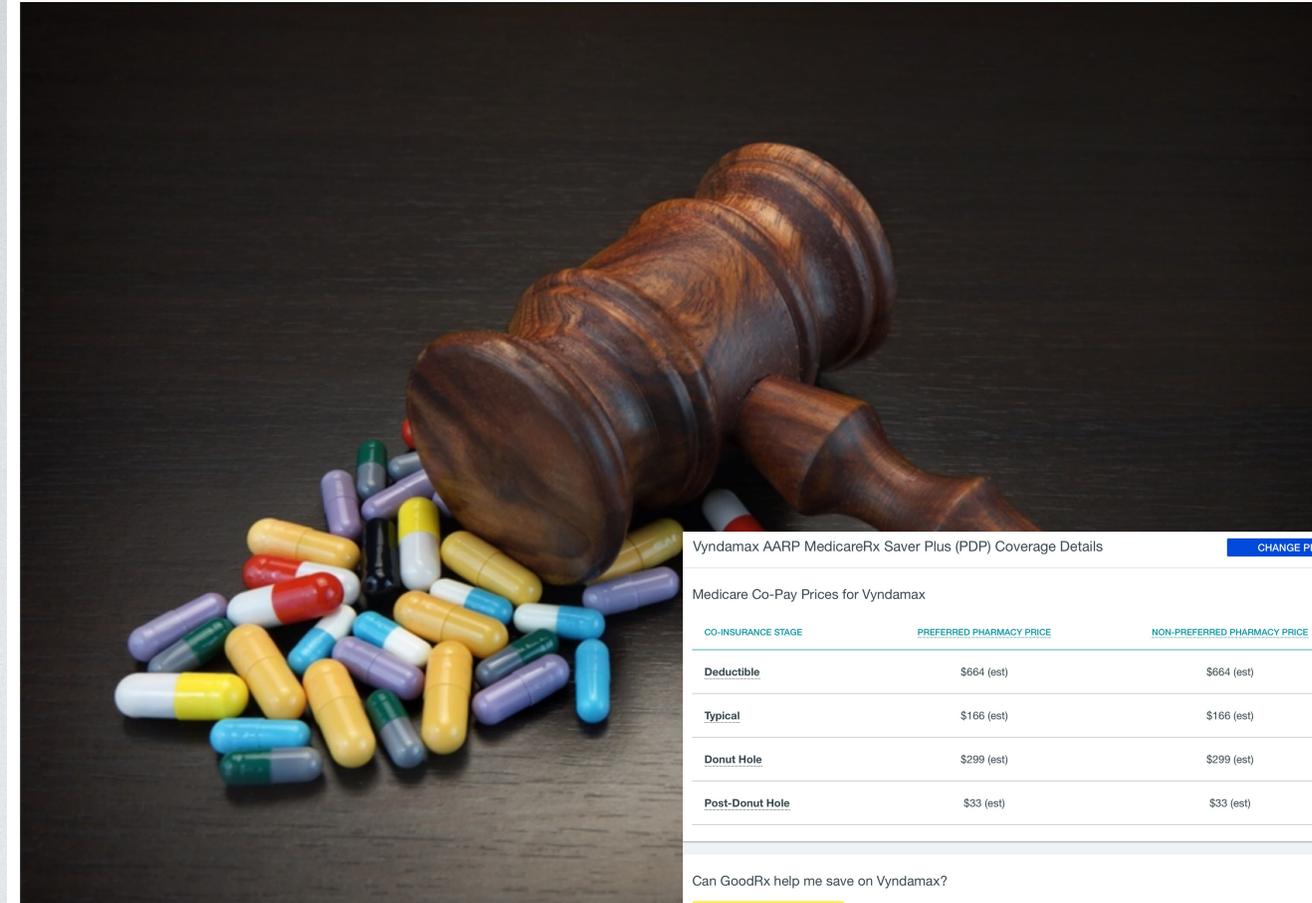
# THERAPY FOR MEDICARE

Medicare Part D beneficiaries—who, given the natural history of the disease, are likely to represent the majority of US patients eligible for this novel therapy—

because their copayments are calculated from the list price of the drug before the application of any rebates or discounts. As a result, Medicare Part D beneficiaries without secondary insurance may be responsible for tens of thousands of dollars per year in out-of-pocket costs. This would put the drug out of reach for many fixed-income seniors.

# Pfizer sues to cut Vyndaqel copays, calling Medicare ban unconstitutional

by Angus Liu | Jun 29, 2020 12:34pm



Vyndamax AARP MedicareRx Saver Plus (PDP) Coverage Details CHANGE PLA

Medicare Co-Pay Prices for Vyndamax

| CO-INSURANCE STAGE | PREFERRED PHARMACY PRICE | NON-PREFERRED PHARMACY PRICE |
|--------------------|--------------------------|------------------------------|
| Deductible         | \$664 (est)              | \$664 (est)                  |
| Typical            | \$166 (est)              | \$166 (est)                  |
| Donut Hole         | \$299 (est)              | \$299 (est)                  |
| Post-Donut Hole    | \$33 (est)               | \$33 (est)                   |

Can GoodRx help me save on Vyndamax?

|                                       |  |
|---------------------------------------|--|
| <b>LOWEST GOODRX PRICE</b>            | No. While GoodRx discounts can often cost less than your Medicare co-insurance, in this case plan's prices are the lowest. |
| <b>\$18503.40</b><br>WITH FREE COUPON |  |

Pfizer is suing the U.S. government over anti-kickback practices to get M Images/AVNphotolab)

Pfizer's rare heart disease med Vyndaqel, at \$225,000 a year, is too pricey for many patients. To help Medicare participants afford the expensive drug—and maintain its hefty sticker price—the Big Pharma is going as far as to argue the U.S. government's anti-kickback policy is unconstitutional.

According to Pfizer, under Medicare Part D, a patient would normally have to pay \$13,000 a year out of pocket to get Vyndaqel (tafamidis) or its sister formulation Vyndamax. That means the drug is only affordable to the wealthy and to those with incomes so low that Medicare waives almost all their out-of-pocket costs. And Medicare covers most of Vyndaqel patients, because the condition it treats, called transthyretin amyloid cardiomyopathy (ATTR-CM), mostly affects people 65 years and older.

Slashing the drugs' prices directly wouldn't work, the lawsuit claims, because even at half the cost, Medicare Part D would still require patients to shell out \$8,000 per year. Instead, Pfizer would like to offer programs that cap copays at \$35 per month for eligible patients, the lawsuit says.

## RELATED: Pfizer's blockbuster-to-be Vyndaqel is too costly for heart patients, study suggests

The pharma giant argues that its Medicare assistance programs would not constitute an illegal kickback, that they present “no risk of inappropriately steering ATTR-CM patients toward tafamidis or improperly inducing prescriptions for tafamidis,” given that the med is the only medicine approved in the U.S. to treat the condition.

In Pfizer's view, strict enforcement practices by HHS' Office of Inspector General and the DOJ have basically ruled all financial support to middle-income Medicare patients as kickbacks, Pfizer states.

One way out of the dilemma is to get a special ruling from the OIG so that it wouldn't have to fear legal actions. However, the agency has over the past year declined to acknowledge that Pfizer's proposed programs are legal or to propose modifications, the company says in its complaint.

## A much bigger argument

But Pfizer doesn't just stop at making a case from the standpoint of its own tafamidis offerings, it's trying to overthrow OIG's entire interpretation of the anti-kickback laws by invoking the **1st** Constitution.

The company argues that, by restricting drugmakers'—but not other industries'—communications and donations to charities that provide for Medicare patients, the OIG violates the First

Plus, as the interpretation effectively deprives only middle-income Medicare enrollees of benefits “based solely on their economic status,” it would violate “the equal protection principles enshrined in the Fifth Amendment, Pfizer says. **5th**

# COST-EFFECTIVENESS OF THERAPY FOR AMYLOID CARDIOMYOPATHY



You got to know when to  
hold 'em, know when to  
fold 'em,  
Know when to walk away  
and know when to run.  
You never count your  
money when you're sittin'  
at the table.  
There'll be time enough for  
countin' when the dealin's  
done.