MINI-REVIEW

Navigating the Complex Web of Prescribing Amyloidosis Therapeutics: A Primer

Hongya Chen, PharmD; Pranav Chandrashekar, MD; Katherine Fischer, RN, MSN; Dayna Carlson, BS; Urja Narayan, PharmD; Jack Chen, CPhT; Ahmad Masri, MD, MS

ABSTRACT: Advancement in the diagnosis and treatment of transthyretin amyloid cardiomyopathy has made great strides in recent years. Novel therapeutics for transthyretin amyloidosis such as tafamidis, patisiran, and inotersen have shown significant benefits in a not-so-rare disease but come with high listing price tags ranging from a quarter to more than a half million dollars per year. These costs create significant financial barriers for the majority of patients, especially those with existing Medicare insurance plans. Of 72 patients reviewed, 67% were Medicare beneficiaries. Financial assistance was explored for the majority, and 37 (51%) patients with Medicare Part D received financial assistance that reduced their copayments to $0. Only one-third of our patients were able to afford these medications without any forms of financial assistance. Of these patients, 4 (6%) had the highest copayments ranging from $13,000 to $15,000 per year. To navigate the complexities of prescribing and affordability in amyloidosis, a multidisciplinary team including a dedicated clinical pharmacist is crucial in guaranteeing patients’ success to secure these novel therapeutics. In this article, we discuss our experiences with prescribing, acquiring insurance authorizations, and financing these life-saving medications based on patient-specific insurance plans and socioeconomic status.

Key Words: amyloidosis ■ inotersen ■ insurance benefits ■ patisiran ■ prealbumin ■ tafamidis ■ transthyretine

Transthyretin amyloid cardiomyopathy (ATTR-CM) was thought to be a rare disease, difficult to diagnose, and without proven effective treatments. In recent years, tremendous progress has been made in noninvasive diagnostic approaches as well as targeted treatments. These advances uncovered a significant population of patients living with ATTR-CM. For example, ATTR-CM was found to coexist in up to 16% of the patients with aortic stenosis and 13% to 17% of the patients with heart failure with preserved ejection fraction.1,2 Heart failure with preserved ejection fraction is a heterogenous clinical syndrome that affects >3 million adults in the United States, and ATTR-CM is a one cause of heart failure where traditional guideline-directed medical therapies do not improve outcomes.3,4 In fact, guideline-directed medical therapies for heart failure such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or β-blockers generally are poorly tolerated in patients with ATTR-CM.5 Currently, there are 3 available transthyretin-specific treatments approved by the US Food and Drug Administration for transthyretin amyloidosis (ATTR). Inotersen and patisiran were approved for the treatment of polyneuropathy attributed to hereditary ATTR, whereas tafamidis was approved for the treatment of ATTR-CM, both hereditary and wild type. It is worth noting that tafamidis is currently the only medication that is associated with 30% relative risk reduction of all-cause mortality and 32% relative risk reduction in cardiovascular-related hospitalizations in patients with ATTR-CM.6 Inotersen and patisiran are specifically approved to improve clinical symptoms of polyneuropathy in patients with hereditary ATTR.7,8 All 3 novel therapies have high listing prices9 and require special handling (Table 1). Navigating this complex web of prescribing, authorizing, and financing is challenging for patients, physicians, pharmacists, and other health care providers. Despite many of the challenges, our
multidisciplinary team, which includes a dedicated pharmacist, has been successful in securing these medications for patients, and our early experience with tafamidis is just one example.\textsuperscript{10} Despite the emergence of tremendous advances in the rare disease domain, the cost of medications remains a difficult barrier limiting patient access. Aside from the high listing prices, types of insurance and the extent of prescription coverage play a significant part in determining patients’ accessibility to these medications. For example, of 72 patients with an active prescription for inotersen, patisiran, and/or tafamidis in our program in 2021, the majority were insured with Medicare plans (67%) followed by commercial plans (15%) and Tricare/Veterans Affairs (VA) plans (14%), and the remaining patients were uninsured (4%). Based on the type of insurance and level of household income, patients may qualify for different financial assistance programs offered by either drug manufacturers or charitable foundations to overcome the barrier of high out-of-pocket (OOP) costs. In this review, we untangle this complex web and focus on the challenges faced by patients in accessing novel therapies for ATTR. We recognize that few clinicians and programs will have access to a dedicated pharmacist to navigate this process, but we hope this review will provide the framework and some guidance of this process to clinicians, which in turn can result in higher success rates of securing these vital therapies for patients diagnosed with ATTR.

INSURANCE PLANS AND PRESCRIPTION COPAYMENTS

Medicare

In 2021, Medicare drug plans, either as stand-alone prescription drug plans or Medicare Advantage drug plans, require up to a $445 deductible before entering into the initial coverage phase where enrollees are responsible up to 25% for nonpreferred drugs (eg, tafamidis) until the $4130 minimum is spent. Next phase is the coverage gap (commonly known as the donut hole), where enrollees are responsible for up to 25% of the cost of all prescription drugs until true OOP spending reaches $6550. Enrollees will then enter the catastrophic phase where plans are responsible for 95% of the cost of prescription drugs. Figure 1 provides a hypothetical example to simplify these concepts.

Using our cohort as an example, in the year of 2021, patients who were enrolled in standard Medicare drug plans and were prescribed tafamidis had a mean initial copayment of $3405 (SD, $396) and a median of $3240 (range, $2833–$4041) for a 30-day supply of tafamidis. The high cost of tafamidis pushes the benefit phase directly into the catastrophic phase after the initial fill, making patients responsible for a hefty copayment to satisfy the deductible, initial payment, and gap coverage phases in the beginning of each year. For the rest of the year, a patient is typically responsible for 5% of the contracted wholesale price, which equates to $900 to $1000 every month. In totality, a patient with Part D will be responsible for $12,900 to $16,000 of OOP costs annually for tafamidis alone. In a similar fashion, based on real-life examples of patients with Medicare plans, the inotersen initial copayment would be as high as $3000 to $4000, with subsequent monthly copayments of $1800 to $1900.

There are a few scenarios where the insurance coverage for tafamidis is exceptional. For example, 6 (8%) of the patients in our cohort had public employee retirement Medicare drug plans that offered more generous coverage by capping copayments for specialty tier medications such as tafamidis at a more reasonable amount, typically ranging $40 to $60 per month. Moreover, 1 (1%) of the patients with a Medicare Part D plan qualified for low-income subsidies (also known as Extra Help), which resulted in $4 copayments for tafamidis. Patients who have both Medicare Part D and Medicaid plans will also automatically qualify for the Extra Help program, which will significantly lower copayments for medications such as tafamidis.

Patisiran infusion is typically covered under Medicare Part B plans given that self-administration is not possible. Enrollees are usually responsible for 20% coinsurance of the procedure cost (ie, infusion cost and not the medication cost itself) unless they have supplemental insurance that can help with the remaining OOP costs. Our real-life examples are limited to patients with Medicare Part B plus supplemental plans that resulted in full insurance coverage with 0 copayment. If a patient has a Medicare Part B plan without a supplemental plan, then the estimated copayment would be $35 per infusion. This model is favorable for patients financially despite the inconvenience of traveling to infusion appointments every 3 weeks. Medicare Part B billing is based on J-codes in the Healthcare Common Procedure Coding System developed by the Centers for Medicare & Medicaid Services. Each J-code is a billable unit of a particular drug that includes fees for sterile compounding, administration, and health care professional services. Consequently,
this type of payment model drives up the overall cost expenditure of the health care system. For example, patisiran wholesale price is estimated at $34 000 (for the maximum dose of 30 mg) per infusion, but the actual billable amount based on the J-code can be up to 1.5 to 2.5 times higher.

**VA or Tricare**

Approximately 10% of our cohort used either VA or Tricare as their prescription insurance plans. Their copayments of tafamidis were significantly lower than those with standard Medicare drug plans. Medication copayments were typically ≤$11 per month for patients with the VA plan and ≤$33 per month for those with Tricare plans. Of note, as of 2021, the majority of VA pharmacies only have tafamidis meglumine 20 mg capsules (ie, VYNDAGEL; Pfizer, Inc) on formulary and not tafamidis 61 mg capsules (ie, VYNDAMAX; Pfizer, Inc). Initial dose is limited to tafamidis meglumine 20 mg daily instead of the recommended dose of 80 mg daily based on the VA’s criteria for use, which can be accessed by the public online.11 This document represents a national guideline proposed for VA clinicians to follow. Exceptions can be made to request initiating tafamidis meglumine 80 mg daily at the local VA system. In our experience, we have seen VA patients being prescribed tafamidis meglumine 80 mg daily with others receiving the dose at 20 mg daily. A post hoc analysis from the ATTR-ACT (Transthyretin Amyloidosis Cardiomyopathy Clinical Trial) and the

| Medication | Tafamidis | Inotersen | Patisiran |
|------------|-----------|-----------|-----------|
| Average wholesale price* | $270 000/y | $370 000/y | $581 000/y† |
| Copayment (commercial) | Fixed, highest tier | Fixed, highest tier | Fixed, highest tier |
| Copayment (Medicare) | Variable, highest tier (Part D) | Variable, highest tier (Part D) | 20% of infusion service (drug covered by Part B) |

*Obtained from Lexicomp as reference only.†This is calculated based on maximum recommended dose of 0.3 mg/kg every 3 weeks (30 mg for a patient weighing ≥100 kg requiring a total of ≈17 infusions per year). This cost does not include infusion-related costs.

Table 1. Cost of Transthyretin-Specific Treatments

Figure 1. An example of Medicare Part D coverage on the first 30-day prescription of tafamidis in 2021. True out-of-pocket: total of all the amounts in boxes highlighted in green; retail cost of tafamidis may vary (ranging anywhere from $18 000 to $20 000); $19 000 is used here as an example.
open-label phase suggest that tafamidis meglumine 80 mg daily is more beneficial compared with 20 mg daily.6,12

**Commercial Plans**
The remaining 15% of our cohort were insured with commercial prescription plans. Copayments are structured based on tiers and other variations in individual plans, making it difficult to derive a standard formula to estimate coverage. Therefore, we generally process initial prescriptions through individual commercial plans via our specialty pharmacy after prior authorization (PA) approvals to determine the individuals’ responsible copayments and refer them to financial assistance if needed.

**FINANCIAL ASSISTANCE PROGRAMS**
Given how unaffordable OOP cost can be, even after insurance covers up to 90% of medication cost, financial assistance programs are crucial in bridging the financial gap in the majority of our patients. Currently, available financial assistance programs can be divided into the following 2 main categories: charitable foundations or manufacturers’ assistance. In our cohort, two-thirds of our patients required some forms of financial assistance to secure an approved therapy for ATTR. Notably, these patients either have Medicare Part D plans or no prescription insurance. The remaining one-third of patients were able to afford their OOP cost without any forms of assistance. The eligibility of financial assistance program(s) is heavily dependent on the type of insurance and level of household income.

**Charitable Foundations**
Charitable foundations are independent 501(c)(3) nonprofit organizations dedicated to help underinsured Americans by providing financial assistance for their copayments, coinsurance, deductibles, and other health-related expenses. Currently, there are 3 disease-orientated grants13–15 specific for amyloidosis that can be used toward medication copayments, insurance premiums, travel costs, and associated medical costs (Table 2). FundFinder (https://fundfinder.panfoundation.org/) is a website we used to search for the charitable foundations mentioned in Table 2. These foundation grants can be conveniently accessed and applied online. Patients are required to provide relevant information, including diagnosis, medication, name and contact information of the prescriber, health insurance carrier, patient’s physical address, social security number, and the adjusted gross annual household income. One of the major challenges of these foundation grants is the inconsistent availability of funding. It is common to have periods of time when these foundation grants are fully depleted, resulting in temporary closure to any new or renewing applications without an expected timeline to reopening. In fact, these programs opened anywhere from 1 to 5 times in 2020 at no particular pattern and closed in a matter of hours because of high use of the available funds via easily accessible online applications. The short window of time to apply for these programs during open periods poses a tremendous challenge for patients when they are not well informed or if they lack technological resources. This is particularly important in a disease such as ATTR, where the typical demographics are elderly patients who would require significant assistance to monitor and apply for these grants. Another limiting factor is the strict income requirements, which vary based on the federal poverty level16 as shown in Tables 2 and 3. These income requirements are determined by the individual foundations with reasonable and consistent thresholds to comply to laws and regulations put forth by the Office of Inspector General and the Department of Health and Human Services such as the Anti-Kickback Statue.

In our cohort, 16 patients (22%) were able to secure 1 of the 3 foundation programs described. With Patient Access Network foundation13 and Healthwell14 the 1-time amount of $7800 and $8000, respectively, could only cover 4 to 6 months of copayments for patients. After foundation grants were depleted, the majority of

| Table 2. Available Foundation Grants to Patients With Amyloidosis13–15 |
|----------------|-----------------|-----------------|----------------|
| Eligibility criteria | PAN foundation | Healthwell | The Assistance Fund |
| Disease oriented | Yes | Yes | Yes |
| Medication required covered by insurance | Yes | Yes | Yes |
| Medicare only | Yes | No | No |
| Income falls at or below FPL* | 500% | 400%–500% | 700% |
| US citizen or permanent resident | No | N/A | Yes |
| Must receive treatment in the United States | Yes | Yes | Yes |
| Assistance amount (total) | $7800 per y | $8000 per y | No cap for the y |
| Approved period | 1 y | 1 y | 1 y |

FPL indicates federal poverty level; and PAN, Patient Access Network.
*FPL percentages are based on 2021 data.
them had to apply for manufacturer’s patient support programs for financial assistance that provided free medication (described in the next section). Only 3 (4%) patients were able to secure The Assistance Fund, which covered nearly 100% of the copayments for the entire year.

**Manufacturer’s Assistance**

Similar to other brand-name medications, manufacturers often provide copayment assistance programs to reduce patients’ copayments to an affordable amount. However, the federal Anti-Kickback Statue prohibits patients with federal health programs such as Medicare to benefit from such programs; the alternative is for the manufacturer to offer the medication free of charge (as opposed to covering part of patients’ OOP costs). In our cohort, only 16% of our patients were able to use manufacturer copayment assistance because of their commercial insurance plans. Given the patient demographics in ATTR-CM, for which the majority of the patients use Medicare, such regulations render copayment assistance programs less beneficial compared with other rare diseases with younger demographics.

Besides copayment assistance programs, manufacturers for tafamidis (VyndaLink), inotersen (Akcea Connect), and patisiran (Alnylam Assist) have patient support programs for financial assistance. If approved, these programs will directly provide free medications to eligible patients. Each program has its own set of income guidelines similar to charitable foundations that are not shared externally, which limits our ability to summarize these avenues. In our cohort, 21 (29%) patients needed manufacturer assistance for tafamidis as a result of unavailability of or ineligibility for other charitable foundation grants or manufacturers’ copayment programs. Of the 21 patients who applied for the VyndaLink program, 19 of them were approved. However, 7 of the applicants were initially denied given their income was higher than the program’s maximum income threshold for coverage. Of them, 5 were able to successfully appeal by providing additional documents of other monthly expenses to justify their need for assistance. The remaining 2 patients did not pursue the appeal process for personal reasons. Fortunately, patients on patisiran or inotersen with affordability issues were able to secure access to these medications via charitable foundations or manufacturer’s copayment programs.

As discussed previously, clinicians accrue experiences over time to preemptively predict the likelihood of successful patient access to a certain therapy solely based on type of insurance and household income. Based on what we have observed during the past 3 years, the patient group with the most difficult access barriers consists of those with Medicare Part D plans who make >400% to 700% of the federal poverty level per year (eg, $50 000 to $90 000 for a single-person household). The only option for these patients is to apply for manufacturers’ patient assistance programs directly. In all cases of tafamidis, patients were denied by the VyndaLink program because income exceeded the limits, but the majority were able to appeal as discussed previously.

In comparison, most patients diagnosed with immunoglobulin light chain amyloidosis begin therapy with a regimen consisting of cyclophosphamide, bortezomib, and dexamethasone in combination with daratumumab for the appropriate patient population. The cyclophosphamide, bortezomib, and dexamethasone regimen is available in generic formulations and is covered by most insurance providers. Daratumumab remains brand-name only (average wholesale price of $7800 to $9500 per infusion/injection), with copayment assistance programs available to patients if they have commercial insurance plans. Similar to patisiran and with rare exceptions, Medicare Part B would usually cover all the infusions or injections in the cyclophosphamide, bortezomib, and dexamethasone plus daratumumab regimen for patients with Medicare plans.

### Table 3. The 2021 Federal Poverty Guidelines* That Guide Eligibility for Foundation Grants

| Percentages above 2021 poverty guidelines* | 100%  | 400%  | 500%  | 700%  |
|------------------------------------------|-------|-------|-------|-------|
| Family size                              |       |       |       |       |
| 1                                        | $12,880 | $51,520 | $64,400 | $90,160 |
| 2                                        | $17,420 | $69,680 | $87,100 | $121,940 |
| 3                                        | $21,960 | $87,840 | $109,800 | $153,720 |
| 4                                        | $26,500 | $106,000 | $132,500 | $185,500 |
| 5                                        | $31,040 | $124,160 | $155,200 | $217,280 |
| 6                                        | $35,580 | $142,320 | $177,900 | $249,060 |
| 7                                        | $40,120 | $160,480 | $200,600 | $280,840 |
| 8                                        | $44,660 | $178,640 | $223,300 | $312,620 |
| For each additional family member         | $45,540 | $18,160 | $22,700 | $31,780 |

*Percentages for the 48 contiguous states only.
as these medications are required to be administered in an infusion center. On rare occasions, patients with amyloidosis can be treated with oral chemotherapeutic agents such as pomalidomide, which is a medication available only as brand name and has an average wholesale price of $22 871 (for a 28-day cycle).9 The financial assistance pathway is similar to that of tafamidis as previously described. However, amyloidosis and hereditary ATTR are much less common when compared with wild-type ATTR-CM. Moreover, duration of treatment is typically limited for amyloidosis rather than lifelong as in the case of ATTR.

In addition to tafamidis, inotersen, and patisiran, there are many new agents for ATTR on the horizon under investigation, including eplontersen in ATTR-CM (CARDIO-TTRansform [a study to evaluate the efficacy and safety of eplontersen in participants with transthyretin-mediated amyloid cardiomyopathy], NCT04136171) and hereditary ATTR polynuropathy (a study to evaluate the efficacy and safety of eplontersen in participants with hereditary transthyretin-mediated amyloid polynuropathy, NCT04136184), patisiran in ATTR-CM (a study to evaluate patisiran in participants with transthyretin amyloidosis with cardiomyopathy, NCT03997383), vutrisiran in hereditary ATTR polynuropathy (a study of vutrisiran [aln-trsoc02] in patients with hereditary transthyretin amyloidosis, NCT03759379) and ATTR-CM (a study to evaluate vutrisiran in patients with transthyretin amyloidosis with cardiomyopathy, NCT04153149), AG10 in ATTR-CM (efficacy and safety of ag10 in subjects with transthyretin amyloid cardiomyopathy, NCT03860935), and hereditary ATTR polynuropathy (efficacy and safety of acoramidis (AG10) in subjects with transthyretin amyloid polynuropathy, NCT04418024). There are also other agents that have not entered phase III trials yet, such as PRX004 and NTLA-2001. It is likely that these new therapeutics will continue to have a specialty tier designation if approved. The inclusion of an established and dedicated pharmacy team will guarantee the success of the program as well as patients’ access to treatment. These clinical trials are important especially in the context when all options are exhausted to procure the commercially available therapeutics. Being on 1 particular commercially available therapeutic does not preclude patients from participating in all of the clinical trials. For example, an ongoing clinical trial of eplontersen in ATTR-CM (CARDIO-TTRansform, NCT04136171) allows open-label tafamidis at any time point during the trial. It is our standard practice to screen all patients for available clinical trials and ensure all options are discussed with them. It is important that patients understand the possibility of receiving placebo treatment. We also explain to patients the option to opt out of the clinical trial at any point if circumstances change and they want to choose a different pathway for therapy.

In our cardiac amyloidosis program, a comprehensive pharmacy team (consisting of a dedicated clinical pharmacist who specializes in cardiac amyloidosis, a medication assistance team that services the entire hospital, and an on-site specialty pharmacy) is able to provide comprehensive benefit review and assessment of assistance programs for each individual patient. Figure 2 is a flowchart that illustrates the movement of a specialty prescription from a physician’s office visit to a paid claim at a specialty pharmacy. A dedicated pharmacist oversees every step to ensure the manufacturer enrollment, and PAs are completed correctly and submitted in a timely fashion. Although PAs are relatively straightforward, incorrect selection of answers to clinical criteria often results in coverage denials and subsequent treatment delays. For example, some key criteria in PAs for tafamidis require the correct diagnosis, methods of diagnosis, symptoms associated with ATTR-CM, and clinical evidence of heart failure as well as the patient’s New York Heart Association functional classification. It is important for clinicians to include these documentations clearly in clinical notes for staff who are submitting PA requests. The most common pitfall is the absence of these necessary documentations in the clinical notes used for submission. Figure 3 is a flowchart that illustrates different pathways for copayment assistance.

Figure 2. Flowchart representing stepwise processes from diagnosis to treatment.
ATTR indicates transthyretin amyloidosis; and PA, prior authorization.
based on types of insurance and levels of household income. Screening each patient’s financial profile early can prevent delays in selecting the most appropriate assistance program and securing patient access to these medications.

Specialty medications and such processes are still uncommon in cardiology. A dedicated clinical pharmacist with the expertise in this space is a tremendous asset to clinicians and patients. The pharmacist’s clinical role begins by discussing the selected ATTR treatment with the patient and how that medication fits into the overall medication regimen. Subsequently, the pharmacist oversees the entire process as previously discussed in Figures 2 and 3 to ensure the best chance of acquiring the prescribed treatment for patients. In addition, there are specific scenarios where an experienced pharmacist can steer the overall care of patients with ATTR. For example, in the case of an outpatient infusion such as patisiran, the pharmacist works with local infusion centers to adjust premedications such as corticosteroids to the minimum effective dosage needed to reduce risk of infusion-related reactions as well as titrate the weight-based dosing of patisiran. In the case of medications enrolled in the Risk Evaluation and Mitigation Strategy program, such as inotersen, the pharmacist keeps track of monitoring parameters and provides regulatory documentation. Finally, the pharmacist frequently identifies other financial assistance avenues or alternatives to expensive concurrent therapies for other indications. These financial challenges and patient-specific barriers come up infrequently in conversations with clinicians but an experienced pharmacist working with patients and establishing a bond with them can uncover these obstacles and provide solutions. Most patients are not familiar with prescriptions sent to specialty pharmacies compared with the retail settings where pickups and refills are easily accessible. Specialty drug prescriptions are processed in a centralized location by specialty pharmacies and delivered to patients strictly by mail-order services. Refilling these medications requires planning and a sufficient amount of time to maintain adherence. For most patients, these specialty prescriptions are only a few of the many medications they are taking. In our

Figure 3. Flowchart representing a simple approach to financial assistance. FPL indicates federal poverty level.
cohort, we did not observe any major adherence is-
issues with prescribed therapeutics despite the complex
process to gain access and unsustainable copayments
for some of them. Defined pathways in our health care
system should exist to support patients to navigate
these complex processes and provide them with the
means to achieve medication adherence for the best
disease outcome. Our dedicated clinical pharmacist
serves as a bridge between the amyloidosis program
and specialty pharmacies to solve pharmacy-related
issues, expedite refill requests, and provide guidance
regarding financial assistance.

With limited human resources available, not all pro-
grams will have the ability to employ a dedicated phar-
macist. However, it is possible to consider the pathway
suggested in this review and incorporate it into the
existing clinical staff’s (eg, medical assistants and/or
coordinators) workflow. Social workers and case man-
gagers are also good resources but may require train-
ing on specialty medication processes and financial
assistance programs. Training such team members
is not a simple task, but if implemented, medication
access can be substantially improvement. Simply by
familiarizing common clinical questions in PA requests,
compiling assistance information, and drafting clear
instructions for patients, the team can alleviate some
stress and time navigating these complex processes.

Toward the end of the visit, it will be helpful to quickly
assess a patient’s financial profile (ie, household in-
dom) and determine the type of insurance plans and
the preferred mail-order specialty pharmacy. This will
ensure that providers send the prescription to the
correct pharmacy (ie, specialty pharmacy) and prevent
delays in the subsequent screening for eligible assist-
tance programs based on the responsible copayments
and household income.

CONCLUSIONS

ATTR is rapidly transforming into a time-sensitive treat-
able disease with a number of currently approved thera-
pies and more on the horizon. The complexities of this
multiorgan disease, difficulties in diagnosis, and the need
for ruling out stand-alone or concomitant amyloidosis
clearly demonstrate the necessity for a focused multidisci-
plinary team approach to care for patients suspected
to have ATTR and/or amyloidosis. With the introduction
of these highly expensive novel therapeutics, the time-
sensitive nature of treatment initiation, the demographics
of the patients affected, and the complex nature of our
health care and insurance systems, a dedicated amyloi-
dosis pharmacist is an integral part of any multidiscipli-
nary amyloidosis team. Although few programs currently
incorporate such a role, as therapeutic advances in amy-
loidosis continue to evolve, the crucial role of pharmacy
team members will only increase in importance in the
multidisciplinary team and for patients trying to access
these life-saving medications.

ARTICLE INFORMATION

Affiliation
The Amyloidosis Center, Knight Cardiovascular Institute, Oregon Health &
Science University, Portland, OR.

Sources of Funding
None.

Disclosures
Dr Chen has received advisory board and consulting fees from Alnylam
and Bristol Myers Squibb. Dr Masri reports research grants from Pfizer,
Akeoa, and Urotremics (paid to Oregon Health & Science University) and
advisory board and consulting fees from Eisai, Pfizer, Ionis, Alnylam, and
Cytokinetics. Dr Chandrashekar is supported by an educational grant from
Pfizer paid to Oregon Health & Science University. K. Fischer has received
fees from Bristol Myers Squibb for speaking engagements and consulting.
The remaining authors have no disclosures to report.

REFERENCES

1. Gonzalez-Lopez E, Gallego-Delgado M, Guzzo-Merello G, de Haro-
del Moral FJ, Cobo-Marcos M, Robles C, Bornstein B, Salas C, Lara-
Pezzi E, Alonso-Pulpon L, et al. Wild-type transthyretin amyloidosis
as a cause of heart failure with preserved ejection fraction. Eur Heart J.
2015;36:2585–2594. doi: 10.1093/eurheartj/ehv338

2. Mohammed SF, Mirzoyev SA, Edwards WD, Dogan A, Grogn DR,
Dunlay SM, Roger VL, Gertz MA, Dispenzieri A, Zeidlerst SR, et al.
Left ventricular amyloid deposition in patients with heart failure and preserved
ejection fraction. JACC Heart Fail. 2020;2:113–122. doi: 10.1016/j.chff.2020.11.004

3. McHugh K, DelVore AD, Wu J, Matsouaka RA, Fonarow GC, Heidenreich
PA, Yancy CW, Green JB, Altman N, Hernandez AF. Heart failure with
preserved ejection fraction and diabetes: JACC state-of-the-art review.
J Am Coll Cardiol. 2019;73:602–611. doi: 10.1016/j.jacc.2019.11.033

4. Hsnn VS, Yanek LR, Vaishnav J, Ying W, Vaidya D, Lee YJJ, Riley SJ,
Subramanya V, Brown EE, Hopkins CD, et al. Endomyocardial biopsy
characterization of heart failure with preserved ejection fraction and
prevalence of cardioamyloidosis. JACC Heart Fail. 2020;8:712–724.
doi: 10.1016/j.jchf.2020.04.007

5. Ruberg FL, Grogan M, Hanna M, Kelly JW, Maurer MS. Transthyretin
amyloid cardiomyopathy. J Am Coll Cardiol. 2019;73:2872–2891. doi:
10.1016/j.jacc.2019.04.002

6. Maurer MS, Schwartz JH, Gundapaneni B, Elliott PM, Merlini G,
Waddington-Cruz M, Kristen AV, Grogan M, Wittlees R, Daryn T, et al.
Tafamidis treatment for patients with transthyretin amyloid cardio-
myopathy. N Engl J Med. 2018;379:1007–1016. doi: 10.1056/NEJMoa1805889

7. Benson MD, Waddington-Cruz M, Berk JL, Polydefkis M, Dyck PJ,
Wang AK, Plante-Bordeneuve V, Barroso FA, Merlini G, Obici L, et al.
Inotersen treatment for patients with hereditary transthyretin amyloidosi-
sis. N Engl J Med. 2018;379:22–31. doi: 10.1056/NEJMoa1716793

8. Adams D, Gonzalez-Duarte A, O’Riordan WD, Yang C-C, Ueda M,
Kristen AV, Toumve I, Schmidt H, Rowe I, Berk JL, et al. Patisiran, an
RNAi therapeutic, for hereditary transthyretin amyloidosis. N Engl J
Med. 2018;379:11–21. doi: 10.1056/NEJMoa1716153

9. Lexicomp Online, Lexi-Drugs Lexicomp Online, Lexi-Drugs. Available at:
https://online.lexi.com/ico/action/login. Accessed December 17, 2021.

10. Masri A, Chen H, Wong C, Fischer KL, Karam C, Gellad WF, Heitner SB.
Initial experience prescribing commercial tafamidis, the most expensive
cardiac medication in history. JAMA Cardiol. 2020;5:1066–1067. doi:
10.1001/jamacardio.2020.1738

11. VA Formulary. Available at: https://www.pbm.va.gov/apps/vanational
formulary/. Accessed December 17, 2021.

12. Daryn T, Garcia-Pavia P, Hanna M, Judge DP, Merlini G, Gundapaneni B,
Patterson TA, Riley S, Schwartz JH, Sultan MB, et al. Efficacy and safety
of tafamidis doses in the Tafamidis in Transthyretin Cardiomyopathy

Clinical Trial (ATTR-ACT) and long-term extension study. Eur J Heart Fail. 2021;23:277–285. doi: 10.1002/ejhf.2027

13. PAN Foundation. PAN Foundation. Available at: https://www.panfoundation.org/. Accessed December 17, 2021.

14. HealthWell Foundation. HealthWell Foundation. Available at: https://www.healthwellfoundation.org/. Accessed December 17, 2021.

15. The Assistance Fund—TAF. The Assistance Fund. Available at: https://tafcare.org/. Accessed December 17, 2021.

16. Annual Update of the HHS Poverty Guidelines. Available at: https://www.federalregister.gov/documents/2021/02/01/2021-01969/annual-update-of-the-hhs-poverty-guidelines. Accessed December 17, 2021.

17. Office of the Federal Register NA and RA 70 FR 70623—Publication of OIG Special Advisory Bulletin on Patient Assistance Programs for Medicare Part D Enrollees. govinfo.gov. Available at: https://www.govinfo.gov/app/details/FR-2005-11-22/https%3A%2F%2Fwww.govinfo.gov%2Fapp%2Fdetails%2FFR-2005-11-22%2F05-23038. Accessed December 17, 2021.

18. Patients and Caregivers | VyndaLink™. Available at: https://www.vyndalink.com/patient. Accessed December 17, 2021.

19. Akcea Connect. Available at: https://akceaconnect.com/. Accessed December 17, 2021.

20. Alnylam Assist Patient Support. Available at: https://dev-alnylamassist-rebuild.pantheonsite.io/. Accessed December 17, 2021.

21. Gertz MA, Dispenzieri A. Systemic amyloidosis recognition, prognosis, and therapy: a systematic review. JAMA. 2020;324:79–89. doi: 10.1001/jama.2020.5493