SAMPLE LETTER OF MEDICAL NECESSITY TEMPLATE

**Use of AMVUTTRA® (vutrisiran) for the cardiomyopathy of transthyretin-mediated (ATTR) amyloidosis**

**To the HCP:** The following is a sample letter of medical necessity template that can be customized based on your patient’s medical history and demographic information using your independent clinical judgment. You are responsible for providing information that completely and accurately represents your patient’s circumstances. Please note that some payers may have specific forms that must be completed in order to request prior authorization or to document medical necessity. Use of this document does not guarantee coverage or reimbursement by any third-party payer.

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| --- | --- |
| [Date] | RE: [Patient Name] |
| [Medical Director Name] | [Group Number] |
| [Payer Name] | [Policy Number] |
| [Payer Address Line 1] | [Claim Number] |
| [Payer City, State, ZIP] | [Diagnosis, ICD-10] |

Dear [Medical Director],

I am writing this letter of medical necessity to request that my patient, [insert patient name], receive AMVUTTRA® (vutrisiran), a product that is approved by the United States Food and Drug Administration (FDA) for the treatment of the cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular mortality, cardiovascular hospitalizations and urgent heart failure visits.1

Based on the clinical safety and efficacy data of AMVUTTRA, it is my medical opinion that [initiating OR continuing] treatment with AMVUTTRA concomitantly with ongoing treatment with *(name of TTR stabilizer)* for [patient’s name] is appropriate and medically necessary at this time. The costs of AMVUTTRA therapy, including all administration services, should be reimbursed. The remainder of this letter describes the patient’s medical history, prognosis, and rationale for treatment with AMVUTTRA.

***Summary of Patient’s Medical History***

***[Please complete based on your patient’s medical history; delete any categories that are not pertinent to your patient]***

**Diagnosis of ATTR Amyloidosis**

□ Date of diagnosis of ATTR amyloidosis and method(s) of diagnosis:

* Date of diagnosis of ATTR amyloidosis: [Date]
* Assessments of TTR amyloid deposition: [Please describe the method for identification of TTR amyloid deposition (e.g., bone scintigraphy scans, cardiac scintigraphy scans, biopsy, mass spectrometry)]
* Other diagnostic evaluations: [If applicable - e.g., other abnormal test findings indicative of ATTR amyloidosis; please describe]
* Other clinical signs: [If applicable, please describe]

□ Genetic testing and family history of hereditary transthyretin-mediated (hATTR) amyloidosis:

* Genetic testing: [If applicable, provide results of your patient’s genetic testing including their genotype]
* Family history: [If applicable, provide a brief description of relevant family history (e.g., affected family members, known outcomes)]

**Current Signs and/or Symptoms of Cardiomyopathy of ATTR Amyloidosis**

□ Patient has signs or symptoms consistent with the cardiomyopathy of ATTR amyloidosis:

* *Please describe signs or symptoms* 
  + *Cardiac signs / symptoms (e.g., dyspnea, fatigue, edema, increased ventricular or atrial wall thickness, other hypertrophic features on echocardiography, intolerance to antihypertensive or heart failure medications due to symptomatic hypotension or orthostasis, discrepancy between LV wall thickness on imaging and QRS voltage on electrocardiogram, atrial fibrillation, AV block or prior pacemaker implantation, persistent mild increases in troponin levels, marked ECV expansion on CMR)*
  + *Non-cardiac signs / symptoms (e.g., diarrhea, constipation, delayed gastric emptying, symptoms of polyneuropathy or* *autonomic dysfunction, bilateral carpal tunnel syndrome, lumbar spinal stenosis, hip or knee arthroplasty, history of biceps tendon rupture)*

□ Disease stage: *[New York Heart Association (NYHA) Functional Class* ***OR*** *Gillmore Stage* ***OR*** *Columbia Stage; please describe]*

□ Previous and/or current treatment: [Describe previous and current treatment strategies (include treatments for cardiomyopathy manifestations [*e.g., dyspnea, fatigue, edema*]); include the dose, start date, end date (if applicable) of each treatment, and reason for discontinuation (if applicable)]

□ Rationale for treatment modification: *[Describe reasons for intention to modify treatment by initiating OR continuing vutrisiran concomitantly with TTR stabilizer therapy]*

* Worsening in clinical status attributable to ATTR amyloidosis (including cardiomyopathy of ATTR amyloidosis or polyneuropathy of hereditary ATTR amyloidosis) while on current TTR stabilizer therapy for the cardiomyopathy of ATTR amyloidosis: *[If applicable, describe at least one of the following]:* 
  + *At least one new or worsening clinical and/or functional sign or symptom related to ATTR amyloidosis*
  + *At least one new or worsening biomarker and/or laboratory abnormality related to ATTR amyloidosis*
  + *At least one new or worsening imaging and/or ECG assessment related to ATTR amyloidosis*
* Issues with adherence to medication for the treatment of ATTR amyloidosis: *[If applicable, please describe]*

□ Rationale for continuation of care of concomitant therapy with vutrisiran plus TTR stabilizer: *[If applicable, please provide evidence demonstrating patient’s stability or improvement in signs or symptoms of ATTR-CM including, but not limited to, examples such as KCCQ (or other quality of life measures), NYHA class, 6-MWT (or other measures of functional capacity), biomarkers (e.g., NT-proBNP, troponin), PYP scan, hospitalization, etc.]*

**Prognosis**

□ Summary of professional opinion of the patient’s likely prognosis or potential disease progression without treatment with AMVUTTRA® (vutrisiran): [please describe]

**I. ATTR Amyloidosis Disease Overview**

ATTR amyloidosis is a progressive, debilitating, and ultimately fatal disease caused by misfolded transthyretin (TTR) protein.2 In ATTR amyloidosis, misfolded TTR accumulates as amyloid deposits in multiple tissues including the nerves, heart, and gastrointestinal (GI) tract, with corresponding clinical manifestations.2-4 Because TTR-derived amyloid deposits may accumulate throughout the body, a range of clinical manifestations is possible in ATTR amyloidosis, with some patients experiencing manifestations that are limited to a single organ system and others experiencing multisystemic manifestations.2,5-8

In ATTR amyloidosis with cardiomyopathy (ATTR-CM), TTR-derived amyloid deposition in the myocardium causes the myocardial tissue to stiffen and the ventricular walls to thicken in a manner that prevents normal physiological functioning of the heart.9,10 This results in progressive cardiomyopathy and heart failure with multiple associated signs and symptoms. Accordingly, ATTR-CM is a rapidly progressing, debilitating, and ultimately fatal disease, with a median survival of 2.6 to 5.8 years.11-15

**II. AMVUTTRA Efficacy and Safety in the Phase 3 HELIOS-B Trial**

Evidence for the efficacy and safety of AMVUTTRA for the treatment of ATTR-CM in adults was provided by HELIOS-B (N=654), a global, randomized, double-blind, placebo-controlled, phase 3 study in which 654 patients were equally randomized to receive vutrisiran or placebo for 33-36 months. Forty percent of the study population was receiving background treatment with the TTR stabilizer tafamidis at baseline in both the vutrisiran and placebo arms.16

In the overall population of patients, treatment with vutrisiran resulted in a lower risk of the primary composite endpoint of death from any cause and recurrent cardiovascular events compared with placebo through up to 36 months (hazard ratio in the overall population, 0.72; 95% confidence interval [CI], 0.56 to 0.93; P = 0.01) and a lower risk of the secondary endpoint of death from any cause through up to 42 months (hazard ratio, 0.65; 95% CI, 0.46 to 0.90; P = 0.01).16 Vutrisiran also provided statistically significant and clinically meaningful benefit versus placebo across all other secondary endpoints, reflecting the preservation of physical capacity (as measured by 6-minute walk test) and patient-reported health-status and health-related quality of life (as measured by Kansas City Cardiomyopathy Questionnaire overall summary score) and the prevention of heart failure worsening (as measured by New York Heart Association heart failure class).16

Vutrisiran had an acceptable safety profile in HELIOS-B. The incidence of adverse events among patients in the vutrisiran group was similar to or lower than that among the patients in the placebo group, a finding that is consistent with the known profile of the drug. No new safety signs were identified.16

**III. Rationale for Treatment**

ATTR-CM is a progressive disease. Its natural history is marked by ongoing deterioration of heart function due to cardiac deposition of TTR amyloid, leading to declines over time in physical function and quality of life. Such progression is observed in the absence of treatment, but with any approved treatments, patients may continue to experience substantial worsening of their condition and be subject to excess mortality risk.17-19

As disease progression of ATTR amyloidosis is irreversible, adding vutrisiran to ongoing TTR stabilizer therapy may be considered in the event of progression on TTR stabilizer therapy alone. Prespecified subgroup analyses for all primary and secondary endpoints in HELIOS-B demonstrated consistent clinical benefit for vutrisiran in all subgroups, including patients who were already receiving background tafamidis upon entry into HELIOS-B, with point estimates of treatment effect consistently favoring vutrisiran across these subgroups.1

***[Please include the following section on Continuation of Care if you have a patient on concomitant treatment with vutrisiran and a TTR stabilizer and are trying to maintain continuation of care without being required to discontinue one of the treatments.]***

**Continuation of Care**

Preserving continuity of care for patients currently receiving concomitant therapy with vutrisiran and a TTR stabilizer is important. Per the American College of Physicians, a reasonable effort should be made to keep patients on their current medication if they are stable.20 Patients who are clinically stable and demonstrating benefit on concomitant therapy (e.g., stable or improved functional capacity, quality of life, biomarkers) may risk unnecessary disease progression if forced to discontinue one agent. In a 12-month open-label extension of the phase 3 HELIOS-B study, in patients who crossed over from placebo to vutrisiran, an onset of relative stability in quality of life was seen as measured by KCCQ-OS. However, their scores did not return to baseline or reach the levels observed in patients initially randomized to vutrisiran, underscoring the importance of initiating treatment early and maintaining efficacious therapy.21 In a rare, progressive, and life-threatening condition with limited therapeutic options, an interruption of a regimen that has demonstrated efficacy contradicts the principle of preserving clinical stability. Upholding consistency in care is essential to maximizing long-term healthcare outcomes.

**Closing Remarks**

*[Please provide closing comments relative to this patient’s case (e.g., given the patient’s existing signs and symptoms, the rapidly progressive nature of ATTR amyloidosis, and the efficacy and safety profile of AMVUTTRA, it is medically necessary and appropriate to initiate AMVUTTRA therapy using the FDA-approved dosing regimen, OR it is medically necessary and appropriate to preserve continuation of care in the patient’s concomitant treatment with vutrisiran and a TTR stabilizer.]*

Please contact my office at [insert phone number] if more information is needed. I look forward to receiving your timely response to this claim.

Sincerely,

[Insert physician name and provider number]

[Attachments: AMVUTTRA USPI (optional), and etc.]

References

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