Familial Hypercholesterolemia – Panel Testing
Letter of Medical Necessity

<Date>

ATTN: <Medical Director/ Physician Name>, M.D.
<Institution/Insurance Company>
<Street Address>
<City>**,** <State>, <Zip>

RE: <Patient Name>
DOB: <MM/DD/YYYY>
Member ID: <Insurance ID Number>
Group #: <Enter Group #>

Dear Medical Director:

I am writing this letter on behalf of my patient <patient name> to request authorization for genetic testing for Familial Hypercholesterolemia (FH) to be performed by Quest Diagnostics. This diagnostic panel test (test code 94877; CPT codes 81405, 81406x2, 81479) evaluates <patient name> for pathologic variants in the *LDLR*, *APOB*, and *PCSK9* genes associated with up to 70-95% of patients with FH, though reports vary (Khera, Henderson, Youngblom).

<Patient name> is a <age> year old <gender > with a suspected diagnosis of FH. Based on the <DLCN, Simon-Broome> score described below, genetic testing is indicated to confirm the diagnosis. <insert risk score description> <Patient name> has the following clinical and laboratory findings that support the suspected diagnosis:
1. < Clinical or Lab finding #1 with ICD-10 code>
2. < Clinical or Lab finding #2 with ICD-10 code>
3. < Clinical or Lab finding #3 with ICD-10 code>

<Patient name> also has a family history suggestive of FH, although the diagnosis has not been conclusively made in any close family member:
<Add family history if relevant>

Because of the above findings, there is a reasonably high probability that <Patient name> has FH. Evidence based clinical practice guidelines now offer clear treatment choices for reducing the risk of future morbidity and extending longevity when FH is recognized and treated (Goldberg, FH Foundation). This multi-gene test is the most effective and efficient way to analyze the genes implicated in FH.

If a variant is identified in 1 or more genes on the FH panel, it confirms the diagnosis of FH, helping to clarify <Patient name's> risk for extreme elevation of low density lipoprotein cholesterol (LDL-C) and resultant early CAD. Such a finding will change my medical management of this patient to mitigate these risks, possibly including initiating or increasing statin therapy and lifestyle counseling (Nordestgaard, Wiegman).

Background for Genetic Testing
A pathogenic variant results in a lifetime of exposure to extremely elevated levels of plasma LDL-C. Defects in FH genes impair the liver's LDL-C metabolism, causing the elevation in circulating LDL-C. The cumulative lifetime burden of elevated LDL-C increases the risk for premature CAD and resultant myocardial infarction (MI) (men-50% higher by age 50; women 30% higher by age

DLCN adult criteria for diagnosing heterozygous FH (Henderson, Nordestgaard,)

Criteria	*Points*
Family History	
FDR with premature CHD	1
FDR w/LDL-C >95th %ile	1
FDR w/tendon xanthoma and/or corneal arcus	2
Children <18 with LDL-C above 95th %ile	2
Clinical History	
Premature CHD	2
Premature PVD or **c**erebral **vascular disease**	1
Physical Exam	
Tendon xanthoma	6
Corneal arcus <45 years	4
LDL-C results	
>325 mg/dL	8
251-325 mg/dL	5
191-250 mg/dL	3
155-190 mg/dL	1
Molecular mutation	
LDLR, APOB, or PCSK9 cau**sativ**e mutation	8

Scoring	*Points*
Definitive FH diagnosis	>8
Probable FH diagnosis	6-8
Possible FH diagnosis	3-5
Unlikely FH diagnosis	0-2

FDR=First-degree relative

60) (Mark). Homozygous FH patients are at even higher risk for premature CAD at an even younger age than those with heterozygous FH.

FH is the most common inherited autosomal dominant genetic disease with a prevalence of 1:200 to 1:250 (Henderson, Youngblom), yet it continues to be underdiagnosed and undertreated (Goldberg, Nordestgaard). In the United States approximately 1.3 million people have FH; however, in most countries <1% are properly diagnosed (Nordestgaard).

High suspicion for FH exists when family, clinical, and laboratory findings are combined using the Dutch Lipid Clinic Network (DLCN) and a high score is identified. The DLCN criteria are summarized in the table. The Simon Broome Register Group criteria appear similar to the DLCN criteria in predicting FH although it is simpler, when applied to at least the UK population (Gidding).

Over the 6 years of cited references in this letter, the literature shows increasing acceptance of genetic testing to clarify and solidify the diagnosis of both index cases with a high probability for FH and for evaluating family members as part of a cascade approach. Genetic testing improves the diagnostic accuracy for FH (Watts) and is included in the DLCN and Simon-Broome algorithms for FH diagnosis (Henderson) and is now found in internationally recognized guidelines. When genetic testing is positive, diagnosis of FH is nearly certain.

The International FH Guidelines state: the most reliable FH diagnostic criteria include both phenotypic and genetic testing; genetic testing should ideally be offered to all index cases with a phenotypic diagnosis of FH and that cascade screening be performed with a combination of lipid and DNA testing, starting with first-degree relatives and extending to biologic second-and third-degree relatives, as appropriate. (Watts) The National Lipid Association states that genetic screening may be useful when the clinical diagnosis is uncertain (Goldberg). The European Atherosclerosis Society indicates that when a causative mutation is identified in an index patient, genetic cascade testing of family members, initially first-degree relatives followed by biologic second-degree relatives is both cost-effective and drives appropriate treatment for identified patients (Nordestgaard).

Testing Venue
I am specifying Quest Diagnostics as the performing laboratory because of Quest's extensive experience in molecular genetics. They offer a very sensitive and cost-effective test for FH.

Informed Consent
The patient has provided informed consent after being counseled about the risks associated with the genes on the FH panel, the meaning of possible test results, and available management options.

Please contact me if you need additional information to certify this request.

Thank you,

<Physician Name>, MD

NPI #: <Physician NPI#>
Contact information:
< Address>
<City>**,** <State>, <Zip>
Contact Phone No.: <phone number>

References

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6. Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease: consensus statement of the European Atherosclerosis Society. *Eur Heart J* 2013;34:3478-3490a.
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8. Watts GF, Gidding S, Wierzbicki AS, et al. Integrated guidance on the care of familial hypercholesterolemia from the International FH Foundation. *J Clin Lipidol* 2014;8:148-172.
9. Wiegman A, Gidding SS, Watts GF, et al. Familial hypercholesterolemia in children and adolescents: gaining decades of life by optimizing detection and treatment. *Eur Heart J* 2015;36:2425-2437.
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