Familial Hypercholesterolemia – Single Site Analysis 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. I am requesting testing for a known familial <variant or variants> (test code 94878; CPT code 81403 for each known gene previously identified). Single site FH gene analysis evaluates <patient name> for pathogenic variants in the LDLR, APOB, or PCSK9 genes that are known to be present in a first-, second-, or third-degree relatives.

<Patient name> is a <age> year old <gender > with a family history of FH, including the presence of a known pathogenic variant in the <specify: LDLR, APOB, or PCSK9> gene in an affected family member. Further, <Patient name> has some risk based on my calculation of the <DLCN, Simon-Broome> score described below. <insert risk score description>Genetic testing is indicated to confirm or exclude the diagnosis of FH.

<Describe family history and the index case>

Because of the above family history, there is a reasonable probability that <Patient name> may have 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). My recommended genetic testing is the most effective and efficient way to analyze for a known familial pathogenic variant in the <specify: LDLR, APOB, or PCSK9> gene.

If a known familial variant is identified, it confirms the diagnosis of FH and the risk for extreme elevation of low density lipoprotein cholesterol (LDL-C) and resultant early CAD. Such a finding will impact my medical management of <Patient name> 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 60) (Mark). Homozygous FH patients are at even higher risk for premature CAD at an even younger age than those with heterozygous FH.

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**sative** 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	

FH is the most common inherited autosomal dominant genetic disease with a prevalence of 1:200 to 1:250 (Youngblom, Henderson), 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 evaluate family members as part of a cascade approach to identifying those with FH who can benefit from treatment. 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 recommend that genetic testing be offered to all index cases with a phenotypic diagnosis of FH and that cascade screening of first-, second-, and third-degree relatives of index cases 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 is 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 single site FH gene analysis, 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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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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