MolDX: HLA-DQB1*06:02 Testing for Narcolepsy

Noridian Healthcare Solutions, LLC

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Please Note: This is a Proposed LCD.
Proposed LCDs are works in progress and not necessarily a reflection of the current policies or practices. Proposed LCDs in an approval status display on the CMS MCD for public review.

Contractor Information

Contractor Name	Noridian Healthcare Solutions, LLC
Contract Number	01112
Contract Type	A and B MAC
Associated Contract Numbers	(A and B MAC - 01111 - J - E) Noridian Healthcare Solutions, LLC, (A and B MAC - 01211 - J - E) Noridian Healthcare Solutions, LLC, (A and B MAC - 01311 - J - E) Noridian Healthcare Solutions, LLC, (A and B MAC - 01911 - J - E) Noridian Healthcare Solutions, LLC, (A and B MAC - 01182 - J - E) Noridian Healthcare Solutions, LLC, (A and B MAC - 01212 - J - E) Noridian Healthcare Solutions, LLC, (A and B MAC - 01312 - J - E) Noridian Healthcare Solutions, LLC

Proposed LCD Information

Source LCD ID	N/A
Proposed LCD ID	DL36551

Original ICD-9 LCD ID	N/A
Proposed LCD Version	4
Proposed LCD Title	**MolDX- HLA-DQB1*06-02 Testing for Narcolepsy**
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CMS Internet Online Manual Pub. 100-04 (Medicare Claims Processing Manual), Chapter 23 (Section 10) “Reporting ICD Diagnosis and Procedure Codes”

Jurisdiction California - Northern

Super MAC Jurisdiction J - E

Coverage Guidance

Coverage Indications, Limitations and/or Medical Necessity

Indications and Limitations of Coverage

Based upon currently available information, HLA-DQB1*06:02 typing (81383) for the diagnosis or management of narcolepsy is considered experimental/investigational/unproven for all populations. Although research suggests a strong association between HLA-DQB1*06:02 and narcolepsy risk, HLA-DQB1*06:02 typing is insufficient to confirm a diagnosis of narcolepsy, rule out a diagnosis of narcolepsy or quantify risk for narcolepsy. Therefore, at this time there is no clinical utility for genetic testing or HLA-DQB1*06:02 typing in the diagnosis or treatment of narcolepsy.

Background

Narcolepsy is a sleep disorder characterized by excessive daytime sleepiness, cataplexy (sudden loss of voluntary muscle tone), and uncontrollable sleep episodes. Most cases of narcolepsy are sporadic, with symptoms beginning around the time of adolescence.

According to the International Classification of Sleep Disorders, Third Edition (ICSD-3) and the Diagnostic and Statistical Manual of Mental Disorder, Fifth Edition (DSM-5), narcolepsy is diagnosed by a combination of physical exam, medical history, polysomnogram, multiple sleep latency testing (MSLT), and low CSF hypocretin-1 levels. Current recommended treatment options include stimulants and antidepressants. At this time, treatment is aimed towards the control of symptoms and is not curative.[12]

Narcolepsy has a multifactorial etiology, likely caused by the interaction between genetic risk factors and environmental exposures. Research efforts to identify the genetic contributors to narcolepsy have focused on an association between certain human leukocyte antigen (HLA) haplotypes and narcolepsy risk. The HLA complex encodes greater than 200 genes

responsible for the recognition of foreign antigens. These genes are highly polymorphic, and certain alleles have long been known to confer risk for autoimmune disorders.

A variation of the HLA-DQB1 gene called HLA-DQB1*06:02 has been strongly associated with narcolepsy, particularly in individuals who also have cataplexy and a loss of hypocretins. Several genetic association studies in ethnically diverse populations have found a robust association between narcolepsy and the HLA-DQB1*06:02 allele. However, 15 to 25% of unaffected individuals in the general population also carry this risk haplotype, suggesting that it is necessary but not sufficient for the development of narcolepsy.[6] Additionally, persons with narcolepsy and cataplexy have been identified without the HLA-DQB1*06:02 marker.[4] More recent studies further suggest that predisposition to narcolepsy may be the result of complex genetic associations between multiple risk alleles.[11]

Despite multiple studies replicating the association between HLA-DQB1*06:02 and narcolepsy in different ethnic groups, the overall contribution of HLA variation to disease risk is low. Monozygotic twin studies have shown only partial concordance (25-31%), indicating that environmental factors play a large role in the etiology of narcolepsy.[8] Recent studies have suggested that exposure to streptococcus, H1N1, and the H1N1 vaccine may also increase the risk for narcolepsy, specifically among individuals with the HLA-DQB1*06:02 allele.[3,14,4]

Although research suggests a strong association between HLA-DQB1*06:02 and narcolepsy risk, at this time there is no evidence for any diagnostic utility of HLA typing.[5]

Proposed Process Information

Synopsis of Changes	**Changes**	**Fields Changed**
	Not Applicable	
Associated Information		

Sources of Information and Basis for Decision

1. American Academy of Sleep Medicine. The International Classification of Sleep Disorders. 2014.3rd ed.

2. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, VA: American Psychiatric Publishing. 2013.

3. Aran A, Lin L, Nevsimalova S, et al. Elevated anti-streptococcal antibodies in patients with recent narcolepsy onset. Sleep. 2009 32:979-83.

4. Han F, Lin L, Schormair B, et al. HLA DQB1*06:02 negative narcolepsy with hypocretin/orexin deficiency. Sleep. 2014.1;37(10):1601-8.

5. Hong SC, Lin L, Jeong JH, et al. A study of the diagnostic utility of HLA typing, CSF hypocretin-1 measurements, and MSLT testing for the diagnosis of narcolepsy in 163 Korean patients with unexplained excessive daytime sleepiness. Sleep. 2006. 29(11):1429-38.

6. Hor, H., Kutalik, Z., Dauvilliers, Y., et al. Genome-wide association study identifies new HLA class II haplotypes strongly protective against narcolepsy. Nature Genet. 2010. 42: 786-89,. Note: Erratum: Nature Genet. 43: 388 only, 2011.

7. Lin L, Hungs M, Mignot E. Narcolepsy and the HLA region. J Neuroimmunol. 2001. 2;117(1-2):9-20.

8. Mignot E. Genetic and familial aspects of narcolepsy. Neurology. 1998. 50(2 Suppl 1):S16-22.

9. Mignot, E., Lin, L., Rogers, W., et al. Complex HLA-DR and -DQ interactions confer risk of narcolepsy-cataplexy in three ethnic groups. Am. J. Hum. Genet. 2001. 68: 686-699.

10. Mignot, E., Hayduk, R., Black, J. et al. HLA DQB1*0602 is associated with cataplexy in 509 narcoleptic patients. Sleep 1997. 20: 1012-20.

11. Miyagawa T, Toyoda H, Hirataka A, et al. New susceptibility variants to narcolepsy identified in HLA class II region. Hum Mol Genet. 2015. 1;24(3):891-8.

12. Morgenthaler TI, Kapur VK, Brown T, et al. Standards of Practice Committee of the American Academy of Sleep Medicine. Practice parameters for the treatment of narcolepsy and other hypersomnias of central origin. Sleep. 2007. 30(12):1705-11.

13. Online Mendelian Inheritance in Man (OMIM). Narcolepsy 1. #161400. Last updated 11/13/2012.

14. Singh AK, Mahlios J, Mignot E. Genetic association, seasonal infections and autoimmune basis of narcolepsy. J Autoimmun. 2013. 43:26-31.

15. Tafti M, Hor H, Dauvilliers Y, et al. DQB1 locus alone explains most of the risk and protection in narcolepsy with cataplexy in Europe. Sleep. 2014. 37:19–25.

	Meeting Date	Meeting Information	State
Open Meetings	02/04/2016	Four Points by Sheraton Hotel 1617 1st Avenue San Diego, CA 92101	American Samoa, California - Entire State, Guam, Hawaii, Nevada, Northern Mariana Islands, California - Northern, California - Southern

	Meeting Date	Meeting Information	State
Part B MAC Contractor Advisory Committee (CAC) Meetings	02/17/2016	Los Angeles	California - Entire State, California - Northern, California - Southern
	02/12/2016	Honolulu	Hawaii
	02/18/2016	Las Vegas	Nevada

Comment Period Start Date	02/04/2016
Comment Period End Date	04/10/2016
Released to Final LCD Date	Not yet released.
Reason for Proposed LCD	Creation of Uniform LCDs... Creation of Uniform LCDs With Other MAC Jurisdiction
Proposed LCD Contact	Noridian Healthcare Solutions, LLC JE Part B Contractor Medical Director(s) Attention: Draft LCD Comments PO Box 6783 Fargo, North Dakota 58108-6783 policyb.drafts@noridian.com
Coding Information	

Bill Type Codes

Revenue Codes

Group 1: Paragraph
N/A

CPT/HCPCS Codes

Group 1: Codes

81383	HLA CLASS II TYPING, HIGH RESOLUTION (IE, ALLELES OR ALLELE GROUPS); ONE ALLELE OR ALLELE GROUP (EG, HLA-DQB1*06:02P), EACH

Does the CPT 30% Coding Rule Apply?

No

ICD-10 Codes that Support Medical Necessity

Group 1: Paragraph
N/A

Group 1: Codes

G47.411	Narcolepsy with cataplexy
G47.419	Narcolepsy without cataplexy
G47.421	Narcolepsy in conditions classified elsewhere with cataplexy

Note: Performance is optimized by using code ranges.

ICD-10 Codes that DO NOT Support Medical Necessity

Group 1: Paragraph

Group 1: Codes

Note: Performance is optimized by using code ranges.

Additional ICD-10 Information

Associated Documents

There are no attachments for this LCD.

This LCD version has no Related Local Coverage Documents.

This LCD version has no Related National Coverage Documents.