HLA-DQ Genotyping Analysis

I. *HLA-DQA1* and *HLA-DQB1* genotyping analysis to rule out celiac disease (CD) is considered **medically necessary** when:

   A. The member is being evaluated for celiac disease, **AND**

   B. The member meets at least one of the following:

      1. Had an inconclusive serology (antibody) result, **OR**

      2. Had an inconclusive histology (biopsy) result, **OR**

      3. Started a gluten-free diet before evaluation for celiac disease, **AND**

   C. *HLA-DQA1* and *HLA-DQB1* genotyping analysis has not been previously performed.

II. *HLA-DQA1* and *HLA-DQB1* genotyping analysis to rule out celiac disease is considered **investigational** for all other indications.

RATIONALE AND REFERENCES

HLA-DQ Genotyping Analysis

American College of Gastroenterology (ACG)

The ACG guidelines addressing the diagnosis and management of celiac disease (CD) (2023) state that genetic testing for CD-compatible HLA haplotype is not required for diagnosis in all cases but may be helpful in selected situations such as in the context of serology-histology discrepancy. If negative, celiac disease is ruled out. HLA testing is also central to the approach to CD testing for individuals who have already started a GFD (gluten free diet) before evaluation; in the presence of a CD-compatible haplotype, a gluten challenge can be offered (p. 63-64).

Rubio-Tapia A, Hill ID, Semrad C, et al. American College of Gastroenterology Guidelines Update: Diagnosis and Management of Celiac Disease. Am J Gastroenterol. 2023;118(1):59-76. doi:10.14309/ajg.0000000000002075. Erratum in: Am J Gastroenterol. 2024 Jul 1;119(7):1441. doi: 10.14309/ajg.0000000000002210.

American Gastroenterological Association (AGA)

The AGA clinical practice update on diagnosis and monitoring of celiac disease (2019) states that HLA testing has value in its negative predictive value to rule out CD in patients who are seronegative but have histologic changes or did not have serology at the time of diagnosis. HLA testing may be reserved for second line evaluation of patients with an equivocal diagnosis (inconclusive serology, histology or prior gluten free diet).

Husby S, Murray JA, Katzka DA. AGA Clinical Practice Update on Diagnosis and Monitoring of Celiac Disease-Changing Utility of Serology and Histologic Measures: Expert Review. Gastroenterology. 2019;156(4):885-889. doi:10.1053/j.gastro.2018.12.010

U.S. Preventive Services Task Force (USPSTF)

In 2017, the USPSTF released guidelines on screening adults and children for celiac disease (CD). These guidelines reviewed the use of tTG IgA testing followed by an intestinal biopsy to screen asymptomatic patients. Genotype testing was not discussed. The overall conclusion of this review was that the current balance of evidence was insufficient to assess benefits and harms resulting from screening for CD (p. 1252).

US Preventive Services Task Force, Bibbins-Domingo K, Grossman DC, et al. Screening for Celiac Disease: US Preventive Services Task Force Recommendation Statement. JAMA. 2017;317(12):1252-1257. doi:10.1001/jama.2017.1462