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Approval and implementation dates for specific health plans may vary. Please consult the applicable health plan for more details.

Clinical Appropriateness Guidelines

Genetic Testing

Appropriate Use Criteria: Polygenic Risk Scores in Genetic Testing

Table of Contents

Description and Application of the Guidelines

The Carelon Clinical Appropriateness Guidelines (hereinafter “the Carelon Clinical Appropriateness Guidelines” or the “Guidelines”) are designed to assist providers in making the most appropriate treatment decision for a specific clinical condition for an individual. As used by Carelon, the Guidelines establish objective and evidence-based criteria for medical necessity determinations where possible. In the process, multiple functions are accomplished:

- To establish criteria for when services are medically necessary (i.e., in general, shown to be effective in improving health outcomes and considered the most appropriate level of service)
- To assist the practitioner as an educational tool
- To encourage standardization of medical practice patterns
- To curtail the performance of inappropriate and/or duplicate services
- To advocate for patient safety concerns
- To enhance the quality of health care
- To promote the most efficient and cost-effective use of services

The Carelon guideline development process complies with applicable accreditation standards, including the requirement that the Guidelines be developed with involvement from appropriate providers with current clinical expertise relevant to the Guidelines under review and be based on the most up-to-date clinical principles and best practices. Relevant citations are included in the References section attached to each Guideline. Carelon reviews all of its Guidelines at least annually.

Carelon makes its Guidelines publicly available on its website twenty-four hours a day, seven days a week. Copies of the Carelon Clinical Appropriateness Guidelines are also available upon oral or written request. Although the Guidelines are publicly-available, Carelon considers the Guidelines to be important, proprietary information of Carelon, which cannot be sold, assigned, leased, licensed, reproduced or distributed without the written consent of Carelon.

Carelon applies objective and evidence-based criteria, and takes individual circumstances and the local delivery system into account when determining the medical appropriateness of health care services. The Carelon Guidelines are just guidelines for the provision of specialty health services. These criteria are designed to guide both providers and reviewers to the most appropriate services based on a patient’s unique circumstances. In all cases, clinical judgment consistent with the standards of good medical practice should be used when applying the Guidelines. Guideline determinations are made based on the information provided at the time of the request. It is expected that medical necessity decisions may change as new information is provided or based on unique aspects of the patient’s condition. The treating clinician has final authority and responsibility for treatment decisions regarding the care of the patient and for justifying and demonstrating the existence of medical necessity for the requested service. The Guidelines are not a substitute for the experience and judgment of a physician or other health care professionals. Any clinician seeking to apply or consult the Guidelines is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient’s care or treatment.

The Guidelines do not address coverage, benefit or other plan specific issues. Applicable federal and state coverage mandates take precedence over these clinical guidelines. If requested by a health plan, Carelon will review requests based on health plan medical policy/guidelines in lieu of the Carelon Guidelines. Pharmaceuticals, radiotracers, or medical devices used in any of the diagnostic or therapeutic interventions listed in the Guidelines must be FDA approved or conditionally approved for the intended use. However, use of an FDA approved or conditionally approved product does not constitute medical necessity or guarantee reimbursement by the respective health plan.

The Guidelines may also be used by the health plan or by Carelon for purposes of provider education, or to review the medical necessity of services by any provider who has been notified of the need for medical necessity review, due to billing practices or claims that are not consistent with other providers in terms of frequency or some other manner.

General Clinical Guideline

Clinical Appropriateness Framework

Critical to any finding of clinical appropriateness under the guidelines for a specific diagnostic or therapeutic intervention are the following elements:

- Prior to any intervention, it is essential that the clinician confirm the diagnosis or establish its pretest likelihood based on a complete evaluation of the patient. This includes a history and physical examination and, where applicable, a review of relevant laboratory studies, diagnostic testing, and response to prior therapeutic intervention.
- The anticipated benefit of the recommended intervention should outweigh any potential harms that may result (net benefit).
- Current literature and/or standards of medical practice should support that the recommended intervention offers the greatest net benefit among competing alternatives.
- Based on the clinical evaluation, current literature, and standards of medical practice, there exists a reasonable likelihood that the intervention will change management and/or lead to an improved outcome for the patient.

If these elements are not established with respect to a given request, the determination of appropriateness will most likely require a peer-to-peer conversation to understand the individual and unique facts that would supersede the requirements set forth above. During the peer-to-peer conversation, factors such as patient acuity and setting of service may also be taken into account.

Simultaneous Ordering of Multiple Diagnostic or Therapeutic Interventions

Requests for multiple diagnostic or therapeutic interventions at the same time will often require a peer-to-peer conversation to understand the individual circumstances that support the medical necessity of performing all interventions simultaneously. This is based on the fact that appropriateness of additional intervention is often dependent on the outcome of the initial intervention.

Additionally, either of the following may apply:

- Current literature and/or standards of medical practice support that one of the requested diagnostic or therapeutic interventions is more appropriate in the clinical situation presented; or
- One of the diagnostic or therapeutic interventions requested is more likely to improve patient outcomes based on current literature and/or standards of medical practice.

Repeat Diagnostic Intervention

In general, repeated testing of the same anatomic location for the same indication should be limited to evaluation following an intervention, or when there is a change in clinical status such that additional testing is required to determine next steps in management. At times, it may be necessary to repeat a test using different techniques or protocols to clarify a finding or result of the original study.

Repeated testing for the same indication using the same or similar technology may be subject to additional review or require peer-to-peer conversation in the following scenarios:

- Repeated diagnostic testing at the same facility due to technical issues
- Repeated diagnostic testing requested at a different facility due to provider preference or quality concerns
- Repeated diagnostic testing of the same anatomic area based on persistent symptoms with no clinical change, treatment, or intervention since the previous study

- Repeated diagnostic testing of the same anatomic area by different providers for the same member over a short period of time

Repeat Therapeutic Intervention

In general, repeated therapeutic intervention in the same anatomic area is considered appropriate when the prior intervention proved effective or beneficial and the expected duration of relief has lapsed. A repeat intervention requested prior to the expected duration of relief is not appropriate unless it can be confirmed that the prior intervention was never administered.

Polygenic Risk Scores in Genetic Testing

Description and Scope

Polygenic risk scores (PRS) involve the aggregation of common, low penetrance variants into a weighted risk score in order to calculate the inherited component of an individual's lifetime risk of a disease. This guideline addresses the use of genetic testing for application to polygenic risk scores.

For specific test modalities, see separate guidelines Chromosomal Microarray Analysis, and Whole Exome Sequencing and Whole Genome Sequencing. For testing associated with reproduction, see Carrier Screening in the Prenatal Setting guideline.

For testing associated with hereditary cancer syndromes, see Hereditary Cancer Testing guideline.

For testing of tumor biomarkers, see Somatic Tumor Testing guideline.

For single gene testing and other hereditary conditions, see the Inherited Conditions guideline.

Clinical Indications

Polygenic risk scores in genetic testing

Not Medically Necessary:

The use of polygenic risk scores is considered **not medically necessary** for all indications.

Rationale

In contrast to Mendelian disorders and monogenic traits, there are a large number of complex traits (such as eye color) and conditions that are multifactorial (such as diabetes mellitus and coronary artery disease) and ultimately determined by variations occurring in many different genes that have smaller effect sizes.[1] Genome-wide association studies conducted over the past decade have examined the role of common, low penetrance genetic variants in disease risk, identifying associations of these individual common variants or single-nucleotide polymorphisms (SNP), with a small increased risk in disease. More than 70,000 associations between SNPs and traits are now documented (www.ebi.ac.uk/gwas/).[2] Polygenic risk scores (PRS) involve the aggregation of these common, low penetrance variants into a weighted risk score in order to calculate the inherited component of an individual's lifetime risk of a disease.[3] Non-genetic factors such as lifestyle, behavioral factors, and environmental exposures are also known to contribute to the risk of many conditions. There have been a variety of methods for calculating a PRS and combining this information with other known risk factors for illness (including age). Important caveats thus far are that most of the data have been derived from individuals of European ancestry, and the clinical utility of a PRS depends on its accuracy and also the existence of interventions that individuals can and would act upon to reduce disease risk.[2] Another caveat is that it is incorrect to assume that odds ratios derived from PRS that are important etiologically are also directly useful in risk prediction and population screening.[4] PRS is not ready for clinical implementation currently, but large clinical trials are underway to evaluate the clinical utility of various polygenic risk scores.[3]

References

1. Sugrue LP, Desikan RS. What Are Polygenic Scores and Why Are They Important? JAMA. 2019;321(18):1820-1. Epub 2019/04/09. PMID: 30958510
2. Hunter DJ, Drazen JM. Has the Genome Granted Our Wish Yet? N Engl J Med. 2019;380(25):2391-3. Epub 2019/05/16. PMID: 31091368
3. Zeinomar N, Chung WK. Cases in Precision Medicine: The Role of Polygenic Risk Scores in Breast Cancer Risk Assessment. Ann Intern Med. 2021;174(3):408-12. Epub 2020/12/01. PMID: 33253037
4. Wald NJ, Old R. The illusion of polygenic disease risk prediction. Genet Med. 2019;21(8):1705-7. Epub 2019/01/13. PMID: 30635622

Codes

The following code list is not meant to be all-inclusive. Authorization requirements will vary by health plan. Please consult the applicable health plan for guidance on specific procedure codes.

Specific CPT codes for services should be used when available. Nonspecific or not otherwise classified codes may be subject to additional documentation requirements and review.

CPT/HCPCS

81479	Unlisted molecular pathology procedure
81493	Coronary artery disease, mRNA, gene expression profiling by real-time RT-PCR of 23 genes, utilizing whole peripheral blood, algorithm reported as a risk score
0289U	Neurology (Alzheimer disease), mRNA, gene expression profiling by RNA sequencing of 24 genes, whole blood, algorithm reported as predictive risk score - MindX Blood Test™ - Memory/Alzheimer's
0294U	Longevity and mortality risk, mRNA, gene expression profiling by RNA sequencing of 18 genes, whole blood, algorithm reported as predictive risk score - MindX Blood Test™ - Longevity

History

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