Meredith Loveless, MD
Attn: Medical Review
CGS Administrators, LLC
26 Century Boulevard Ste 610
Nashville, TN 37214

March 17, 2023

Dear Dr. Loveless,

On behalf of the American Society of Nuclear Cardiology and the American College of Cardiology, thank you for the opportunity to comment on the CGS Proposed Local Coverage Determination (LCD)Positron Emission Tomography (PET) Scan for Inflammation and Infection (DL39521).

ASNC is a greater than 4,700 member professional medical society, which provides a variety of continuing medical education programs related to nuclear cardiology, develops standards and guidelines for training and practice, and is a major advocate for furthering research and education in nuclear cardiology.

The American College of Cardiology (ACC) is the global leader in transforming cardiovascular care and improving heart health for all. As the preeminent source of professional medical education for the entire cardiovascular care team since 1949, and now with more than 56,000 members from over 140 countries, the ACC credentials cardiovascular professionals who meet stringent qualifications and leads in the formation of health policy, standards and guidelines. Through its world-renowned family of JACC Journals, NCDR registries, ACC Accreditation Services, global network of Member Sections, CardioSmart patient resources and more, the College is committed to ensuring a world where science, knowledge and innovation optimize patient care and outcomes. Learn more at www.ACC.org or follow @ACCinTouch.

ASNC and ACC offer comment on four clinical topics addressed in the LCD.

- **ADDITIONAL INDICATIONS**
- **CARDIAC SARCOIDOSIS**
- **INFECTION OF CARDIOVASCULAR IMPLANTABLE DEVICES**
- **VASCULAR GRAFT INFECTION**

CARDIAC SARCOIDOSIS

ASNC and ACC offer the edits below to the CGS proposed policy as written and provides explanation and supporting literature for the suggested edits below.

Clinical exam and laboratory evaluation lead to clinical suspicion of the condition and this is documented in the medical record **AND**

Non-specific or inconclusive imaging from **any one or more** echocardiography and/or CT **and/or cardiac MRI or in selected cases where other imaging is not possible or where FDG PET may be the most sensitive test (Such as patients presenting with AV block)** [6] **AND**

PET scan is conducted with cardiac preparation protocol[8,9] **AND**

The patient is being evaluated for one of the following conditions and the specific criteria has been met:

a. Infective Endocarditis: the patient has a prosthetic valve-**or where native valve endocarditis is suspected but not proven by TTE/TEE and blood cultures**

b. Device Infections (pacemaker, defibrillators, LVAD, metallic implants) suspected.

c. Aortitis and systemic vasculitis

d. Cardiac Sarcoidosis/Inflammatory cardiomyopathies:

i. The patient has risk factor cardiac sarcoidosis (such as systemic sarcoidosis with cardiac findings) or other inflammatory cardiomyopathies,

ii. a young patient **(<70 years)** with unexplained, new onset conduction system disease, heart failure without explanation)[11]

iii. Ventricular arrythmia without another explanatory cause

OR

History of systemic autoimmune disease and evidence of non coronary late gadolinium enhancement on cardiac magnetic resonance imaging

iv. For guiding subsequent treatment of proven cardiac sarcoidosis if PET scan is the primary test used to follow the patient for the **cardiac aspect of sarcoidosis/inflammatory cardiomyopathies** ~~(not in conjunction with cardiac MRI, CT or other nuclear imaging studies).~~ **These tests may be used for other purposes so it is confusing if they are not permitted in conjunction with FDG PET.**

ADDITIONAL INDICATIONS

ASNC and ACC reviewers recommend adding "device infections (pacemaker, defibrillators, LVAD, metallic implants suspected" to the list of conditions for which a patient should be undergoing evaluation for PET imaging coverage. Though transthoracic and transesophageal echocardiography are generally first line tests for suspected endocarditis and for assessing hemodynamic complications, recent literature suggests "that cardiac computed tomography (CT) or CT angiography and functional imaging with ^{18}F-fluoro-2-deoxyglucose (FDG) positron emission tomography (PET) with CT (FDG PET/CT) may have an incremental role in technically limited or inconclusive cases on echocardiography"[1] Most notably, FDG PET/CT is able to detect inflammatory cells early in the infection process before morphological damage takes place.[2]

In addition, reviewers suggest adding aortitis and systemic vasculitis to the list of conditions for which a patient should be undergoing evaluation for infection and inflammation PET coverage. In a multi societal joint procedural recommendation by the EANM, SNMMI, the PET Interest Group (PIG), and endorsed by the ASNC , FDG-PET imaging was noted to exhibit high diagnostic performance for the detection of large vessel vasculitis. FDG-PET and CTA have complementary roles in the diagnosis of large vessel vasculitis, but most importantly FDG-PET/CT(A) may be of value for evaluating response to treatment by monitoring functional metabolic information and detecting structural vascular changes.[3]

CARDIAC SARCOIDOSIS

ASNC and ACC reviewers recommend adding ventricular arrythmia without another explanatory cause to the list of conditions that would indicate PET imaging for suspected sarcoidosis is appropriate. The *Joint SNMMI–ASNC Expert Consensus Document on the Role of ^{18}F-FDG PET/CT in Cardiac Sarcoid Detection and Therapy Monitoring* confirms that postmortem studies have shown that sarcoidosis "may involve any part of the heart but most commonly involves the myocardium. Depending on the type and extent of involvement, CS can present as

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[1] Dilsizian V, Budde RPJ, Chen W, Mankad SV, Lindner JR, Nieman K. Best Practices for Imaging Cardiac Device-Related Infections and Endocarditis: A JACC: Cardiovascular Imaging Expert Panel Statement. JACC Cardiovasc Imaging. 2022 May;15(5):891-911. doi: 10.1016/j.jcmg.2021.09.029. Epub 2021 Dec 15. PMID: 34922877. *See also* Ferro P, Boni R, Slart RH, Erba PA. Imaging of Endocarditis and Cardiac Device-Related Infections: An Update. Semin Nucl Med. 2023 Mar;53(2):184-198. doi: 10.1053/j.semnuclmed.2023.01.001. Epub 2023 Feb 4. PMID: 36740487.; Ten Hove D, Wahadat AR, Slart RHJA, Wouthuyzen-Bakker M, Mecozzi G, Damman K, Witteveen H, Caliskan K, Manintveld OC, Sinha B, Budde RPJ, Glaudemans AWJM. Added value of semi-quantitative analysis of [18F]FDG PET/CT for the diagnosis of device-related infections in patients with a left ventricular assist device. Eur Heart J Cardiovasc Imaging. 2022 Dec 27:jeac260. doi: 10.1093/ehjci/jeac260. Epub ahead of print. PMID: 36573930.; Roy SG, Akhtar T, Bandyopadhyay D, Ghosh RK, Hagau R, Ranjan P, Gerard P, Jain D. The Emerging Role of FDG PET/CT in Diagnosing Endocarditis and Cardiac Device Infection. Curr Probl Cardiol. 2023 Feb;48(2):101510. doi: 10.1016/j.cpcardiol.2022.101510. Epub 2022 Nov 17. PMID: 36402219.

[2] *Id.*

[3] Slart, R.H.J.A., Writing group., Reviewer group. *et al.* FDG-PET/CT(A) imaging in large vessel vasculitis and polymyalgia rheumatica: joint procedural recommendation of the EANM, SNMMI, and the PET Interest Group (PIG), and endorsed by the ASNC. *Eur J Nucl Med Mol Imaging* **45**, 1250–1269 (2018). https://doi.org/10.1007/s00259-018-3973-8

conduction abnormalities, ventricular arrhythmias, sudden cardiac death, systolic and diastolic heart failure or valvular disorders…[4]"

As a general matter, it is important to clarify that performance of MRI does not entirely dictate the decision to perform PET or not for diagnosis of possible cardiac sarcoidosis. The cardiac magnetic resonance (CMR) imaging reflects expansion of extracellular myocardial volume due to inflammation and/or fibrosis from sarcoidosis active now or any time in the past. Sarcoidosis may be quiescent now but with residual fibrosis that would be detected by cardiac magnetic resonance imaging but not PET. The PET is really being used to image inflammation due to presently active cardiac sarcoidosis. There may often be a role to do both forms of imaging as they have complementary value in addition to the perfusion exam conducted around the time of FDG PET. Thus, it should be permissible to obtain both CMR and PET where clinically indicated. For example, in the instance below CMR was performed that is interpreted as normal but a small number of such cases may have active sarcoidosis evident on PET.

"In our study, 8 of 107 individuals had abnormal FDG uptake in the absence of LGE, although only 2 of them were ultimately categorized as having a high probability of CS on the final diagnosis. Similarly, Soussan et al24 evaluated 35 patients with suspected CS by CMR and PET and found 3 individuals with positive FDG who had negative LGE, noting that all of them were negative by the Japanese Ministry of Health, Labour, and Welfare criteria. Ohira et al7 evaluated 30 patients with suspected CS and found that 4 of 30 patients had abnormal FDG but negative CMR. In this study, the Japanese Ministry of Health, Labour, and Welfare 2006 criteria was used as the reference standard, and thus it remains unclear what proportion of individuals with isolated FDG uptake truly have CS versus having an alternative explanation for the observed FDG uptake.[5]"

Data for evaluation of sarcoidosis is still evolving as sarcoidosis is a complex disease that presents in many ways. Both PET and CMR have integral roles to play in assessment of cardiac sarcoidosis given that there is very little clinical downside to performing them given the high cost of missing the diagnosis as there are high annualized events for VT/ death.

ASNC and ACC clinical reviewers recommend deletion of the requirement that the "patient does not have any conditions that would limit the ability to interpret the PET scan including cardiac/ vascular surgery within the past three months." The data to support this condition is limited and

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[4] Chareonthaitawee P, Beanlands RS, Chen W, Dorbala S, Miller EJ, Murthy VL, Birnie DH, Chen ES, Cooper LT, Tung RH, White ES, Borges-Neto S, Di Carli MF, Gropler RJ, Ruddy TD, Schindler TH, Blankstein R; NAME OF COLLAB GROUP. Joint SNMMI-ASNC Expert Consensus Document on the Role of ^{18}F-FDG PET/CT in Cardiac Sarcoid Detection and Therapy Monitoring. J Nucl Med. 2017 Aug;58(8):1341-1353. doi: 10.2967/jnumed.117.196287. PMID: 28765228; PMCID: PMC6944184.

[5] Vita T, Okada DR, Veillet-Chowdhury M, Bravo PE, Mullins E, Hulten E, Agrawal M, Madan R, Taqueti VR, Steigner M, Skali H, Kwong RY, Stewart GC, Dorbala S, Di Carli MF, Blankstein R. Complementary Value of Cardiac Magnetic Resonance Imaging and Positron Emission Tomography/Computed Tomography in the Assessment of Cardiac Sarcoidosis. Circ Cardiovasc Imaging. 2018 Jan;11(1):e007030. doi: 10.1161/CIRCIMAGING.117.007030. PMID: 29335272; PMCID: PMC6381829.

it is possible to make the diagnosis for the diseases deemed appropriate for PET imaging in this policy within three months after cardiac/ vascular surgery.

INFECTION OF CARDIOVASCULAR IMPLANTABLE DEVICES

~~i.~~	~~Patient is unable to undergo an MRI because of their device~~
ii.	Diagnosis is inconclusive on standard imaging (echo/CT)
iii.	Additional diagnostic studies would impact clinical care (such as decision to remove device **or support prolonged antibiotic therapy or not)**

The ASNC and ACC clinical reviewers recommend the deletion of the first point under infection of cardiovascular implantable devices given that it is not related to the diagnosis of device infection with FDG PET. In addition, the reviewers recommend adding "or support prolonged antibiotic therapy or not" as a frequently occurring example of where additional diagnostic studies would impact clinical care.

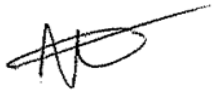
VASCULAR GRAFT INFECTION

iv.	Diagnosis is inconclusive with **one of** CTA or MRA
v.	~~No conditions that would make PET scan study less diagnosis (such as surgical adhesives/recent surgery)~~
vi.	Additional diagnostic studies would impact clinical care

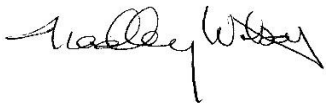
Clinical reviewers suggest deletion of subsection v. The reviewers argue that conditions such as surgical adhesives or recent surgery are not sufficient to mean that the imaging should not be done. Rather, the reviewers think that physicians should exercise caution with interpretation of the imaging.

ASNC and ACC appreciate the opportunity to provide feedback on the CGS Proposed Local Coverage Determination (LCD) Positron Emission Tomography (PET) Scan for Inflammation and Infection (DL39521). If there are any questions you have or other information we can provide please reach out to Georgia Lawrence at glawrence@asnc.org.

Sincerely,



Mouaz Al- Mallah, MD
President,
American Society of Nuclear Cardiology



B. Hadley Wilson, MD, FACC
President, American College of Cardiology