


Agency medical director comments

PET Scans for Lymphoma – Re-Review

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November 16, 2018




PET Scans

HTCC Determination November 18, 2011

HTCC Reimbursement Determination

- ❖ **Limitations of Coverage**
 - Positron Emission Tomography (PET) scans for Lymphoma is a covered benefit when the following conditions are met:
 - One scan for initial treatment planning;
 - Additional scans for restaging with clinical suspicion of disease progression or treatment failure subject to agency approval;
 - No coverage for routine surveillance
- ❖ **Non-Covered Indicators**
 - N/A


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PET Scans for Lymphoma Re-review

- This topic was last reviewed in 2011
- The decision for re-review was based on more recent literature evaluating the effectiveness of PET +/- CT across stages of treatment:
 - Initial staging
 - Interim treatment
 - Prognosis during and at the end of treatment
 - End of treatment status
 - End of treatment confirmed relapse
 - Surveillance: evaluation of asymptomatic patients in remission

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Key Questions

In patients with histologically proven lymphoma undergoing PET/CT at any time after initial diagnosis:

1. What is the evidence of clinical effectiveness of ^{18}F FDG PET/CT results?
2. What is the evidence of the safety of ^{18}F FDG PET/CT imaging?
3. What is the evidence that ^{18}F FDG PET/CT imaging has differential efficacy or safety issues in subpopulations?
4. What is the evidence of cost-effectiveness of ^{18}F FDG PET/CT imaging?

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PET Scans for Lymphoma

Diffuse Large
B Cell
Lymphoma

Hodgkin
Lymphoma

Anaplastic
Large Cell
Lymphoma

Follicular
Lymphoma

Small
Lymphocytic
Lymphoma

Manohar K, Mittal BR, Bhattacharya A, Malhotra P, Varma S. Fluoro-deoxy-glucose positron emission tomography/computed tomography in lymphoma: A pictorial essay. Indian J Nucl Med 2013;28:85-92

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Lymphoma Types

Classic Hodgkin Lymphoma

Type	Histologic Features	Frequency	Prognosis
Nodular sclerosis	Bands of fibrosis, lacunar cells	Most frequent type (80-80%), more common in women	Good, most are stage I or II
Mixed cellularity	Composed of many different cells	Most frequent in older persons, second most frequent overall (15-30%)	Fair, most are stage III
Lymphocyte rich	Mostly reactive lymphocytes and many Reed-Sternberg cells	Uncommon (5%), Older adults	Good to excellent
Lymphocyte depletion	Many Reed-Sternberg cells and variants	Rare (<1%)	Poor, most are stage III or IV
Lymphocyte predominance	Mostly B-cells and few Reed-Sternberg variant cells	Uncommon (5%)	Good, most are stage I or II

Abdulkarim Aldosari

Non-Hodgkin Lymphoma, Subtypes

Amitage JO, et al. J Clin Oncol. 1998; 16:2780-2795.(1)


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Agency Medical Director Concerns

SAFETY =	Medium
EFFICACY =	High
COST =	Medium


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Diagnosis Codes - Lymphoma

ICD-9/10	Diagnosis Code Description
C81 - C88.9	
C81	Hodgkin lymphoma
C82	Follicular lymphoma
C83	Non-follicular lymphoma
C84	Mature T/NK-cell lymphomas
C85	Other specified and unspecified types of non-Hodgkin lymphoma
C86	Other specified types of T/NK-cell lymphoma
C88	Malignant immunoproliferative diseases and certain other B-cell lymphomas
200.0-202.98	
200	Lymphosarcoma and reticulosarcoma and other specified malignant tumors of lymphatic tissue
201	Hodgkin's disease
202	Other malignant neoplasm of lymphoid and histiocytic tissue

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Procedure Codes

Analysis failed to identify claims w/CPT: 78812 or 78813
 Procedure codes paired w/modifier PI or PS

TYPE	CPT	Procedure Code Description
PET/CT	78814	Positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; limited area (e.g., chest, head/neck)
PET/CT	78815	Positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; skull base to mid-thigh
PET/CT	78816	Positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; whole body
PET	A9597	Positron emission tomography radiopharmaceutical, diagnostic, for tumor identification, not otherwise classified
Modifier	Modifier Code Description	
PI	PET or Pet/CT to inform the initial treatment strategy of tumors that are biopsy proven or strongly suspected of being cancerous based on other diagnostic testing.	
PS	PET or Pet/CT to inform the subsequent treatment strategy of cancerous tumors when the beneficiary's treating physician determines that the PET study is needed to inform subsequent antitumor strategy.	

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Aggregate Utilization 2015 – 2017

PET Scans for Lymphoma

Initial Treatment Planning and Subsequent Treatment Strategy Scans


PEBB/UWP (Public Employees Benefit Board Uniform Medical Plan); PEBB Medicare, the Department of Labor and Industries (L&I) workers' compensation plan; and the Managed Care Medicaid and the Medicaid Fee-for-Service

Year	Unique Patients	SCANS*	Total Paid Amount – Technical and Professional
2015	46	49	\$39,237
2016	227	273	\$232,448
2017	224	255	\$205,509

* Range of scans/patients: 1 – 6.

Some participating agencies incurred less than the minimum allowable utilization required for public reporting, therefore all utilization is displayed in aggregate.


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Current State Agency Policy

PEBB (Regence) –	Covered
Medicaid FFS/ Managed Care –	Covered
Labor and Industries –	Covered

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Other Payers

Covered:

- **CMS NCD:** allows initial staging, 3 during treatment, none for surveillance
- **Regence:** use AIM Specialty Health criteria which allows 1-5 by lymphoma type
- **Aetna:** coverage diagnosis*, staging, restaging
- **Cigna:** covers 2-3, more for Hodgkin lymphoma, not surveillance

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Findings: Early Hodgkin Lymphoma


Accuracy:

- Initial staging outperforms CT
- Interim: no new studies since 2011
- End of treatment: many false positives
- Prognostic accuracy during, (interim) treatment: NPV 93%
- Prognostic accuracy after 1st treatment: neither sensitive nor specific
- Inter-rater reliability in adults: moderate to substantial

Pediatric:

- Insufficient information

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Findings: Early Hodgkin Lymphoma

Prognostic influence:

- Use in initial staging to inform prognosis: insufficient evidence but need a baseline for comparison
- Use to upstage or downstage: mixed results, actual changes in therapy were few. No patient oriented outcomes
- Use to inform treatment escalation, (PET-adapted) when PET+
 - Improved 5 year survival, progression free and overall
 - NNH = 25 for grade 3 or 4 toxicity with escalation
- Use to inform treatment de-escalation, (PET-adapted) PET –
 - Little difference in survival when radiation therapy omitted in OS, suggested difference in PFS
 - Insufficient information about toxicity difference
 - Follow up not long enough to look at secondary malignancies

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Findings: Advanced Hodgkin Lymphoma


Advanced Hodgkin lymphoma, aHL:

- Interim and end of treatment PET/CT to assess for treatment escalation PET +, NS difference in survival or toxicity
- Interim and end of treatment PET/CT to assess for treatment de-escalation PET-, omission of radiation therapy did not worsen survival time and toxicity less

Relapsed, recurrent HL or NHL:

- Insufficient evidence

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Findings: Aggressive Non-Hodgkin Lymphoma


Accuracy diffuse large B cell lymphoma, (DLBCL):

- Diagnosis: mixed findings
- Staging: no new studies, low specificity from 2011
- Interim and end of treatment testing: wide ranging false positive rate
- Surveillance: low positive predictive value

Prognostic value:

- Interim: wide range of sensitivity and specificity
- End of treatment: PET+ associated with lower PFS, OS

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Findings: Aggressive Non-Hodgkin Lymphoma


Prognostic influence

- Initial: PET/CT diffuse large B cell lymphoma, (DLBCL): 10% of patients were upstaged; studies observational
- Interim PET-adapted therapy for PET-: no difference in overall survival w/o radiation when used in early stage non-bulky DLBCL so may be helpful in avoiding radiation

Relapse surveillance:

- Improved detection when use directed by clinical symptoms


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Safety

Event	Radiation reading, millisievert (mSv)
Single dose, fatal within weeks	10,000
Typical dosage recorded in those Chernobyl workers who died within a month	6,000
Single doses which would kill half of those exposed to it within a month	5,000
Single dosage which would cause radiation sickness, including nausea, lower white blood cell count. Not fatal	1,000
Accumulated dosage estimated to cause a fatal cancer many years later in 5% of people	1,000
Max radiation levels recorded at Fukushima plant yesterday, per hour	400
Exposures of Chernobyl residents who were relocated after the blast in 1986	350
Recommended limit for radiation workers every five years	100
Lowest annual dose at which any increase in cancer is clearly evident	100
CT scan: heart	16
CT scan: abdomen & pelvis	15
Dose in full-body CT scan	10
Airline crew flying New York to Tokyo polar route, annual exposure	9
Natural radiation we're all exposed to, per year	2
CT scan: head	2
Spine x-ray	1.5
Radiation per hour detected at Fukushima site, 12 March	1.015
Mammogram breast x-ray	0.4
Chest x-ray	0.1
Dental x-ray	0.005


<https://www.theguardian.com/news/datablog/2011/mar/15/radiation-exposure-levels-guide>
<https://www.imagewisely.org/Imaging-Modalities/Nuclear-Medicine/Optimizing-Oncologic-FDG-PETCT-Scans>



Key Questions 3 and 4

- **No studies to inform difference of impacts on sub-groups**
 - Insufficient information to direct use in children
- **Cost effectiveness studies either of poor quality or evaluated limited use cases from which conclusions can not be made**

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Summary

Staging PET/CT	Interim PET/CT	End of Treatment PET/CT Prognosis	Surveillance
Hodgkin Lymphoma	Hodgkin Lymphoma	Hodgkin Lymphoma	Hodgkin Lymphoma
<u>Aggressive NHL</u> DLBCL Follicular lymphoma Burkitt lymphoma	<u>Aggressive NHL</u> DLBCL Follicular lymphoma Burkitt lymphoma	<u>Aggressive NHL</u> DLBCL Follicular lymphoma Burkitt lymphoma	<u>Aggressive NHL</u> DLBCL Lymphocytic lymphoma Burkitt lymphoma
T-cell lymphoma Extranodal marginal zone Small lymphocytic lymphoma	T-cell lymphoma Extranodal marginal zone Small lymphocytic lymphoma	T-cell lymphoma, Extranodal marginal zone Small lymphocytic lymphoma	T-cell lymphoma, Extranodal marginal zone Small lymphocytic lymphoma

FDG-avid

FDG non avid


Evidence +

Not supported

Mixed evidence

Insufficient


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Summary

- There are multiple lymphoma types
- Evidence supports the use of 18FDG-PET/CT for the accurate diagnosis and staging of some lymphomas
- Evidence supports 18FDG-PET/CT use at interim and end of treatment periods to help determine intensity of treatment and inform prognosis for certain types of lymphoma
- Evidence does not support 18FDG-PET/CT use for routine surveillance to assess recurrence in asymptomatic persons
- Implementing coverage to match evidence levels across all the lymphoma types would be extraordinarily burdensome to providers and the agencies

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Agency Medical Director Recommendations PET Scans for Lymphoma


Covered with conditions:

- Up to 4 scans per active occurrence of lymphoma. (This number is the same as allowed by the NDC.)
 - Scans should be done no sooner than 3 weeks after chemotherapy and 8-12 weeks after radiation or combined chemo and radiation therapy.

Relapse*: Covered when relapse is suspected in the presence of clinical symptoms

Surveillance: Not covered

* Relapse is not covered in the NDC₂₂



Questions?

More Information:

<https://www.hca.wa.gov/about-hca/health-technology-assessment/positron-emission-tomography-pet-scans-lymphoma>

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