INFORMATION REQUIRED Any history

Applicants With Lesions < 1 mm thick (thin lesion or low risk primary):

- Specialist Evaluation (Dermatologist, General Surgeon) within the past 6 months to include the following
 - Date of diagnosis(s).
 - Description of Jesianus to include size Lycation II, and tumor stage.
 - Treatment
 - History of recurrence(s), same site or other site.
 - Statement of prognosis from treating physician.
 - Recommendations for follow-up over the next 3 years.
 - Copy of pathology report(s) with interpretation.

Applicants With Lesions 1 - 2 mm thick (intermediate risk):

- Specialist Evaluation (Dermatologist, Oncologist, General Surgeon) within the past 6 months to include the above information.
- Copy of sentinel node biopsy report.

Applicants With Lesion > than 2 mm thick:

- Specialist Evaluation (Oncologist) within the past 6 months to include the above information.
- Copy of sentinal node biopsy report.
- · Copy of metastatic work-up.

If Applicable:

Discharge summary for all related hospitalizations.

PANCE CRITERIA	PFWT WEWER	"GUIDANCE
No history of recurrence; same site or other site. No history of metastatic disease. Treatment complete.		
Meets clearance criteria 1 - 3, AND Tumor stage_T0_/(ntraepithelial/in-situ_melanoma)_,AND_	RN	CLEAR
Occurrence greater than 2 years ago.	PCMO FOLLOW-UP Skin examination every 6-12 months.	
Meets clearance criteria 1 - 3, AND Lesion < 1 mm deep (thin lesion or low-risk primary lesion), AND Occurrence greater than 3 years ago.	RN	CLEAR
	PCMO FOLLOW-UP After diagnosis, skin examination q3 months for 2 years, of months until 5 years, and then annually thereafter.	
Meets clearance criteria 1 - 3, AND Lesion 1-2 mm deep (intermediate risk), AND Sentinel node biopsy negative, AND Occurrence greater than 3 years ago.	RN	DEFER
	PCMO FOLLOW-UP After diagnosis, skin examination q3 months for 2 years, and then annually thereafter.	
		(continued on next

Lesio	t meet clearance criteria due to one or more of the following: on < 1 mm deep (thin lesion or low-risk מות אות ביים ביים לאות של מות אות ביים ביים לאות של מות אות ביים ביים לאות מות מות אות ביים לאות מות מות מות מות מות מות מות מות מות מ	RN	DEFER lotilutofaembroendurcombiese and/or treatment complete.
•	Lesion 1-2 mm deep (intermediate risk), AND sentinel node biopsy negative, AND occurrence less than 3 years ago Lesion 1-2 mm deep (intermediate risk lesion), AND sentinel node biopsy positive, AND occurrence less than 5 years ago. Lesion > 2mm deep (thick lesion), AND sentinel node biopsy negative, AND occurrence less than 5 years ago. Treatment not complete.		
Doe	Lesion 1-2 mm deep (intermediate risk lesion), AND Sentinel node biopsy positive, AND Occurrence greater than 5 years ago.	MED ADVISOR	Risk varies - assess based of detailed history. Consider CLEAR WITH RESTRICTION; Oncologist available in country
Doe	es not meet clearance criteria due to one or more of the following: Lesion > 2mm deep (thick lesion), AND Sentinel node biopsy negative, AND Occurrence greater than 5 years ago.	MED ADVISOR	Risk varies - assess based of detailed history. Consider CLEAR WITH RESTRICTION; Oncologist available in country.
Do •	Lesion > 2mm deep (thick lesion), AND sentinel node biopsy positive. Lesion > 4 mm deep (thick or high risk lesion). History of recurrence; same site or other site. History of metastatic disease	MED ADVISOR	R DEFER/MNQ Deferral/MNQ letter require review by screening manage

DIAGNOSTIC CODES

172

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NOTES AND INSTRUCTIONS FOR REVIEWERS

Reviewers to Consider:

None

COMMENTS

Adapted from emedicine.com Malignant Melanoma. Author: Susan M Swetter, MD, Director of Pigmented Lesion and Cutaneous Melanoma Clinic, Assistant Professor, Department of Dermatology, Stanford University Medical Center/VA Palo Alto Health Care System]

Background: Melanoma is a malignancy of pigment-producing cells (melanogrytes) recomming in three skinning ears, Contract,

leptomeninges of the central nervous system (CNS), and oral and genital mucous membranes. Melanoma accounts for only 4% of all skin cancers; however, it causes the greatest number of skin cancer-related deaths worldwide. Early detection of thin cutaneous melanoma is the best means of reducing mortality.

Pathophysiology: Transformation of melanocytes to melanoma cells is understood poorly. Primary cutaneous melanoma may develop in precursor melanocytic nevi (common acquired, congenital, and atypical/dysplastic types), although more than 50% of cases are believed to arise de novo without a preexisting pigmented lesion. Melanoma is multifactorial and appears to be related to multiple risk factors including (1) fair complexion (3), pypexive shirthand, our surreupeard alicitatism high hand, our surroupeard and dysplastic moles, (4) family history of melanoma, and (5) presence of a changing mole on the skin.

History: A changing mole is the most common symptom of melanoma. Variation in color and/or increase in diameter, height, or asymmetry of borders of a pigmented lesion are noted by more than 80% of patients with melanoma at the time of diagnosis. Symptoms, such as bleeding, itching, ulceration, and pain in a pigmented lesion, are less common but warrant evaluation. Information regarding the changes noted in any of the following is relevant to the patient's history. Physician and patient education regarding the warning signs of early melanoma has been achieved successfully through the use of the ABCD criteria for a changing mole, which is as follows:

- Asymmetry
- Border notching
- · Color variegation with black, brown, red, or white hue
- Diameter >6 mm
- Consider lesions exhibiting these features to be potential melanomas, although severely atypical nevi may be difficult to distinguish clinically.

Physical: In primary cutaneous melanoma, 4 major clinical-histopathologic subtypes have been identified and include superficial spreading, nodular, lentigo maligna, and acral lentiginous melanomas.

Superficial spreading melanoma characteristics are as follows:

- Most common subtype of melanoma, occurring in approximately 70% of patients
- Most common on the trunk in men and women and on the legs in women.
- Presents as a flat or slightly elevated brown lesion, with variegate pigmentation (black, blue, or pink discoloration)
- Size of >6 mm in diameter
- · Irregular asymmetric borders

Nodular melanoma characteristics are as follows:

- · Occurs in 15-30% of patients
- Most commonly seen on the legs and trunk
- Rapid growth over weeks to months
- Presents as a dark brown-to-black papule or dome-shaped nodule, which may ulcerate and bleed with minor trauma

Lentigo maligna melanoma characteristics are as follows:

- Accounts for 4-15% of cutaneous melanoma.
- Typically located on the head, neck, and arms (sun-damaged skin) of fair-skinned older individuals (average age 65 y) (Picture 3)
- Grows slowly over 5-20 years
- Arises in only a small percentage (estimated 5-8%) of the intraepithelial precursor lesion, lentigo maligna
- In situ precursor lesion usually large (>3 cm diameter), existing for a minimum of 10-15 years, with dermal invasion characterized by development of dark brown-to-black macular pigmentation or raised blue-black nodules

Acral lentiginous melanoma characteristics are as follows:

- Least common subtype of melanoma (2-8% of melanoma in white persons)
- Accounts for 29-72% of melanoma in dark-skinned individuals (African American, Asian, and Hispanic persons)
- Occurs on the palms, soles, or beneath the nail plate (subungual variant) (Picture 2)
- Subungual melanoma presenting as diffuse nail discoloration or a longitudinal pigmented band within the nail plate
- Must be differentiated from a benign junctional melanocytic nevus of the nail bed (similar appearance)
- Pigment spread to the proximal or lateral nailfolds (Hutchinson sign, a hallmark for acral lentiginous melanoma)

Rare melanoma variants (<2% of melanomas) include the following:

- Desmoplastic/neurotropic melanoma
- Mucosal (lentiginous) melanoma
- Malignant blue nevus
- Melanoma arising in a giant congenital nevus
- Melanoma of รรซ์เกอสาร์ (ปละลาดยีเกรสาดงากล)
- Amelanotic melanoma (<2% of melanomas) characteristics are as follows:
- · Nonpigmented and appearing clinically as pink or flesh colored and often mimicking basal cell or squamous cell carcinoma
- Most commonly occurs in the setting of melanoma metastasis to the skin, presumably because of the inability of these poorly differentiated cancer cells to synthesize melanin pigment

Melanoma can occur on any skin or mucosal surface. Melanoma occurs most commonly on the trunk in white males and the lower legs and back in white females. In African American and Asian persons, the most common site is the plantar foot, followed by subungual, palmar, and mucosal sites. All except nodular melanoma are characterized by a radial growth phase, which may last for months to years before a dermal expansile nodule (vertical growth) occurs.

Lab Studies:

- The routine practice of ordering baseline and surveillance liver function tests, lactate dehydrogenase (LDH) levels, and albumin levels in patients with cutaneous melanoma has come under scrutiny with no evidence to support its usefulness in patients without signs or symptoms of disease. Likewise, studies have shown that abnormal laboratory test results are never the sole indicator of metastatic disease and that the majority of recurrences are diagnosed clinically.
- These tests may be ordered every 6-12 months in patients with deeper primary melanomas in umor nebpt An month,
- Laboratory tests should not take the place of careful history and physical examination.

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naging Studies:

- Studies have confirmed that extensive radiologic studies such as CT, MRI, positron emission tomography, ultrasonography, and bone scans, have an extremely low yield in asymptomatic patients with primary cutaneous melanoma (American Joint Committee on Cancer [AJCC] stages I and II) and are not indicated.
- Baseline metastatic staging for melanoma patients with primary tumors more than 1 mm in depth may include a chest x-ray, which
 typically is repeated every 6-12 months for routine surveillance (optional in absence of symptoms of metastatic disease).

Procedures:

- The criterion standard for melanoma diagnosis is histopathologic examination of skin or mucosal lesions that are suggestive of cancer.
- An excisional biopsy with narrow margins is preferred to ascertain the following information:
 - Assessment of tumor depth (Breslow depth)
 - Ulceration
 - Anatomic level of invasion (Clark level)
 - Presence of mitoses
 - Regression
 - Lymphatic/vessel invasion or vascular involvement
 - Host response (tumor-infiltrating lymphocytes)
- Immunohistochemical staining for lineage (S-100, homatropine methylbromide 45) or proliferation markers (proliferating cell nuclear antigen, Ki67) may be helpful in some cases for histologic differentiation from melanoma simulators.
- Generally, 2-3 mm of normal skin surrounding the pigmented lesion should be removed to provide accurate diagnosis and histologic
 microstaging. Wider margins (>1 cm) may disrupt afferent cutaneous lymphatic flow and affect the ability to identify the sentinel
 node(s) accurately in patients eligible for this staging procedure.
 - Shave biopsies of suspected melanomas are discouraged because partial removal of the primary melanoma may not provide accurate Breslow-depth measurement, which is the most important histologic prognostic factor for cutaneous melanoma

Staging: The melanoma staging system initially developed in 1983 by the AJCC and the Union Internationale Contre le Cancer (UICC) divided melanoma into 4 stages and incorporated tumor thickness and anatomic level of invasion for stages I and II (localized cutaneous disease) with the later recommendation to follow Breslow depth over Clark level when any discordance arose. Stage III disease involved transcriptional lymph nodes, and stage IV disease included distant skin, subcutaneous, nodal, visceral, skeletal, or CNS metastasis.

Major revisions in the 2002 AJCC/UICC melanoma staging system were made based on a critical analysis of prior versions of the staging. The AJCC formed an international, multidisciplinary Melanoma Staging Committee and established a new clinical-pathologic database of over 17,000 patients worldwide to test the validity of the proposed staging changes. Several important modifications in the 2002 AJCC staging system include incorporation of histologic ulceration and number of lymph nodes involved (instead of size) to better stratify metastatic risk and patient prognosis. Clark level is included only in thin primary tumors (<1 mm depth, stages IA and IB) in the revised staging system because its prognostic value is minimal in thicker primary melanoma. Microscopic regional lymph node

Table. AJCC 2002 Revised Melanoma Staging

Stage	TNM Classification	Histologic/Clinical Features	5-year Survival Rate (%)
0	Tis N0 M0	Intraepithelial/in situ melanoma	100
IA	T1a N0 M0	≤1 mm without ulceration and level II/III	<u>≥</u> 95
IB '	T1b N0 M0 T2a N0 M0	≤1 mm with ulceration or level IV/V 1.01-2 mm without ulceration	89-91
IIA	T2b N0 M0 T3a N0 M0	1.01-2 mm with ulceration 2.01-4 mm without ulceration	77-79
IIB	T3b N0 M0 T4a N0 M0	2.01-4 mm with ulceration >4 mm without ulceration	63-67
IIC	T4b N0 M0	>4 mm with ulceration	45
IIIA	T1-4a N1a M0 T1-4a N2a M0	Single regional nodal micrometastasis, nonulcerated primary 2-3 microscopic positive regional nodes, nonulcerated primary	63-69
IIIB	T1-4bN1a M0 T1-4bN2a M0 T1-4a N1b M0 T1-4a N2b M0 T1-4a/b N2c M0.	Single regional nodal micrometastasis, ulcerated primary 2-3 microscopic regional nodes, nonulcerated primary Single regional nodal macrometastasis, nonulcerated primary 2-3 macroscopic regional nodes, no ulceration of primary In-transit met/s/* and/or satellite lesion/s/ without metastatic lumphynodes.	46-53 30-50-0
IIIC	T1-4b N2a M0 T1-4b N2b M0 Any T N3 M0	Single macroscopic regional node, ulcerated primary 2-3 macroscopic metastatic regional nodes, ulcerated primary 4 or more metastatic nodes, matted nodes/gross extracapsular extension, or in-transit met(s)/satellite lesion(s) and metastatic nodes	24-29
IV	Any T any N M1a Any T any N M1b Any T any N M1c	Distant skin, subcutaneous, or nodal mets with normal LDH levels Lung mets with normal LDH All other visceral mets with normal LDH or any distant mets with elevated LDH	7-19

*metastasis

Treatment:

Medical Care: Patients with localized cute temeous disease nave been treated with adjuvant chemotherapy, nonspecific passive immunotherapy, radiation therapy, and biologic therapy. No increase in patient survival has been reported with these adjunctive therapies. Adjuvant interferon (IFN) alfa-2b and various experimental melanoma vaccines show promise in individuals with high-risk primary cutaneous melanoma and those with regional nodal disease.

Surgical Care: Surgery is the primary mode of therapy for localized cutaneous melanoma.

Surgical margins for primary melanoma

- Surgical margins of 5 mm currently are recommended for melanoma in situ, and margins of 1 cm are recommended for melanomas
 up to 1 mm in depth (low-risk primaries).
- Pradominzed prospective studies show that 2-cm margins are appropriate for tumors in the intermediate-risk group (1-4 mm in Breslow depth), although 1-cm margins have been proposed for tumors of 1- to 2-mm thickness.
- Margins of at least 2 cm are recommended for cutaneous melanomas greater than 4 mm in thickness (high-risk primaries) to
 prevent potential local recurrence in or around the scar site. A recently published retrospective study of high-risk primary melanomas
 showed that excisional margins greater than 2 cm have no effect on local recurrence, disease-free relapse, or overall survival rates;
 therefore, a 2-cm margin is appropriate in this subgroup.

Elective lymph node dissection

- Prophylactic lymph node dissection for primary cutaneous melanoma of intermediate thickness initially was believed to confer a
 survival advantage on patients with tumors 1-4 mm in depth. Subsequently, prospective randomized clinical trials have shown no
 survival benefit for elective lymphadenectomy for melanomas of varying thicknesses on the extremities and marginal, if any, benefit
 for nonextremity melanomas.
- 10-year follow-up data in 2 of the trials conducted by the World Health Organization (WHO) and Melanoma Intergroup now suggest
 a survival benefit for certain subsets of patients studied. In particular, patients in the WHO trial who had occult metastasic detected.

- Pathology/dermatopathology
- Accurate histologic microstaging of primary melanoma
- Evaluation of nodal tissue for micrometastasis
- Confirmation of diagnosis of disseminated disease
- Radiation oncology
 - Adjuvant treatment of regional nodal metastasis with extracapsular extension
 - Palliative treatment of distant metastatic disease, particularly bony metastasis or brain involvement

Medication: High-dose IFN alfa-2b is the only Food and Drug Administration—approved adjuvant therapy for high-risk resected melanoma, defined as deep primaries >4 mm in Breslow depth (AJCC stage IIB) and regional lymph node metastasis (stage III). Various trials of low-dose IFN have shown no benefit in disease-free relapse or overall survival rates. Similarly, multiple melanoma vaccine trials are in progress, predominantly for stage III and IV disease.

Follow-Up Outpatient Care:

- Moseum क्यांवारा ती प्रकार वी पारकुरांक की प्राप्त कार्या के प्रकार के प्
- Diagnosis of recurrent/metastatic disease and new primary melanoma depends on a routine evaluation schedule that varies according to the presence of the following:
 - Tumor depth (low, intermediate, or high risk)
 - Histologic ulceration
 - Lymph node status
 - Results of examination of the melanoma scar
 - Examination of regional and distant lymph node basins
 - Hepatosplenomegaly on abdominal examination
 - Mole pattern and examination of the entire cutaneous surface for new primaries

Follow-up of a Melanoma

[From National Guideline Clearinghouse; Guideline "Skin Cancer"]

- Patients with a melanoma are followed-up every 3 months until 2 years have passed from the diagnosis. Thereafter, follow-up is continued every 6 months for 5 years. The unit responsible for follow-up (hospital or primary care) can be decided on locally. It is important that the same doctor always sees the patient.
- If the patient has numerous naevi or the syndrome of hereditary dysplastic naevi, follow-up of a melanoma should take place in a dermatological unit. High-quality photographs facilitate follow-up. These patients should be followed-up throughout their life.
- At follow-up visits the general condition and symptoms are investigated, and the site of excision and local lymph nodes are palpated.
 Satellites of melanoma are usually felt as subcutaneous nodules, and they are visible under the skin as dark spots.
- A melanoma first metastasizes into regional lymph nodes, which should be followed-up carefully by palpation. If the clinical
 examination suggests the spread of a melanoma, a chest radiograph, blood count, liver function tests, and liver ultrasonography
 should be performed.
- If a melanoma has infiltrated the regional lymph nodes, they are removed surgically. A metastasized melanoma is treated by an oncologist. Cytostatics and interferon have been moderately effective in the treatment of metastasized melanoma.

A rational approach to melanoma follow-up in patients with primary cutaneous melanoma. Scottish Melanoma Group.

Dicker TJ, Kavanagh GM, Herd RM, Ahmad T, McLaren KM, Chetty U, Hunter JA. University Department of Dermatology, The Royal Infirmary of Edinburgh NHS Trust, UK.

From the Scottish Melanoma Group database for south-east Scotland we evaluated 5-year follow-up in patients with cutaneous malignant melanoma excised between 1979 and 1994 and devised an 'evidence-based' review protocol. Of the 1568 with stage I melanoma, 293 (19%) developed a recurrence, 32 had a second primary melanoma and 97 had an in-situ melanoma. The disease-free interval shortened progressively with increasing tumour thickness. Overall, 80% of recurrences were within the first 3 years, but a few patients (< 8%) had recurrences 5 or 10 years after the initial surgery. In-situ melanomas did not recur. Almost half (47%) the recurrences were noted first by the patient, and only 26% were detected first at a follow-up clinic. One hundred and thirty-nine patients (89%) were still under review when their recurrences were detected, and 102 (65%) had been seen within the previous 3 months. Questionnaires were completed by 120 patients: sun protection and avoidance, and mole examination were more likely after melanoma excision. We recommend 3-monthly review of patients with invasive lesions for the first 3 years. Thereafter, those with lesions >/= 1.0 mm need two

further annual reviews. Patients with in-situ lesions should be reviewed once, to confirm adequate excision (0.5 cm margins) and to give appropriate education. Surveillance beyond 5 years is only justified if there are special risk factors.

Prognosis: Prognosis is multifactorial and primarily depends on (1) tumor thickness, (2) presence or absence of histologic ulceration, and (3) lymph node involvement (most important).

Cutaneous melanoma (stages I and II)

- Thin primaries (< or equal to 1 mm) are associated with a 5-year survival rate of 91-95% depending on the presence or absence of histologic ulceration and Clark level >III.
- ் Intremnetinate hinkkness melanomid (பி.பி.புளார்) is associated white சி.பு. அவர் survivar ranging from 63-89%, depending on ulceration and thickness (1.01-2 mm, 2.01-4 mm) of the primary tumor.
- Patients with high-risk tumors (>4 mm) have a 5-year survival rate of 67% without ulceration, compared to 45% with an ulcerated nrimmary.
- Ulceration significantly reduces survival at each tumor stage, even when regional lymph nodes are involved.

Stage III disease

- Regional lymph node metastasis is associated with a 5-year survival rate of 13-69%, depending on the number of nodes involved, microscopic or macroscopic (matted nodes/gross extracapsular extension) disease, and ulceration of the primary melanoma. Intransit metastasis/satellite lesions are associated with 30-50% 5-year survival, with a significantly worse prognosis in the setting of concomitant regional nodal metastasis (10-30%).
- Adjuvant IFN-alfa has shown improved disease-free and overall survival for Stage III disease, and melanoma vaccines/biologic response modifiers show promise in prolonging survival.

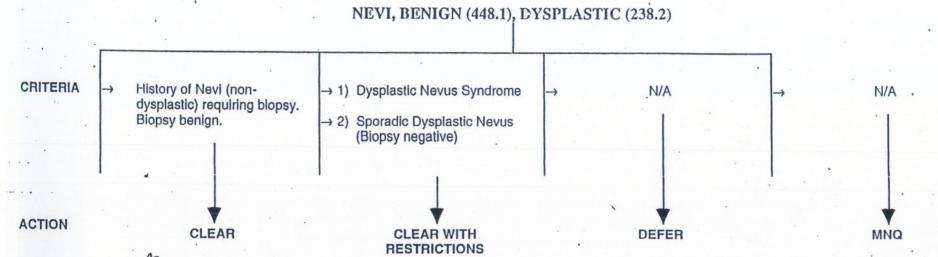
Stage IV disease

- Prognosis for distant metastatic disease is extremely poor, with a median survival rate of only 6-9 months and 5-year survival rates
 ranging from 7-19%, depending on the site(s) of metastasis. In general, patients with soft tissue, nodal, and isolated lung metastasis.
 have slightly better prognosis than those with other visceral metastasis and/or elevated lactate dehydrogenase levels. However, survival beyond one year occurs in only a minority of Stage IV patients.
- Systemic chemotherapy is the mainstay of treatment, despite low response rates (<20%), which tend to be of short duration.
- Biochemotherapy, employing standard chemotherapeutic agents with biologic response modifiers such as IL-2, interferon alfa, or GM-CSF has shown limited success in the management of unresectable stage IV melanoma, and is under further investigation.
 High dose IL-2 alone, or combined with histamine dihydrochloride, has also shown promise in patients with advanced disease.
- As with regional nodal disease, there are numerous trials investigating the use of melanoma vaccines (with or without biologic response modifiers) in the treatment of disseminated disease. It is hopeful that data from the many phase III trials in progress worldwide will show improvement in survival for patients with advanced melanoma.

Literature review available.

Reviewers:

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RATIONALE

Most Nevi are benign.

Approved BC - Derm. for annual exam. (skin checks)

Any Derm. for annual exam. (skin checks).

At risk for development of Malignant Melanoma.

MEDICAL INFORMATION NEEDED:... Generic Information

- Fuermatorogist evaluation

Biopsy report.

F/U needed 2-3 yrs.

Aggravating factors.

8/15/93

Dermatolo



