



S I G N

**PROPOSED REVIEW OF SIGN GUIDELINE
CONSULTATION FORM**

Title of guideline	SIGN 72: Cutaneous melanoma	
Date of publication	July 2003	
SIGN scoping search – sources	<p>MeSH headings for the condition specified and any common variations as free text, plus terms for the interventions and care processes discussed in the guideline</p> <p>Sources: Guidelines: NICE; National Library for Health guidelines finder; National Guidelines Clearinghouse; GIN Web site. Technology appraisals: NICE; UK HTA database (Southampton); INAHTA database. Cochrane reviews: Cochrane Library. Other good quality systematic reviews: UK HTA database (Southampton); DARE. RCTs: MEDLINE</p>	
SIGN scoping search - summary	<p>Guidelines – 12 HTAs – 1 Cochrane reviews – 6 Other good quality systematic reviews – 18 RCTs - 1769</p>	
Other guidelines/HTAs	<p>Counseling to prevent skin cancer: recommendations and rationale of the U.S. Preventive Services Task Force. MMWR Recomm Rep 2003 Oct 17;52(RR-15):13-7. [27 references]</p> <p>Dutch Working Group on Melanoma. Skin melanoma. Utrecht, The Netherlands: Association of Comprehensive Cancer Centres (ACCC); 2006.</p> <p>Finnish Medical Society Duodecim. Skin cancer. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2005 May 25 [Various].</p> <p>From L, Marrett L, Johnston M, Mai V, Fong J, Rosen C, Bak K, Sibbald G, Skin Cancer Screening Guideline Panel. Screening for skin cancer: a clinical practice guideline. Toronto (ON): Cancer Care Ontario (CCO); 2006 Mar 15. 32 p. (Evidence-based series; no. 15-1). [70 references]</p> <p>NICE. Improving Outcomes for People with Skin Tumours including Melanoma Guidance type: Cancer service guidance February 2006.</p> <p>New Zealand Guidelines Group. Clinical Guidelines on the Management of Melanoma in Australia and New Zealand. Wellington; The Group: 2008.</p> <p>Petrella T, Quirt I, Verma S, Haynes A, Charette M, Bak K, Melanoma Disease Site Group. Single-agent interleukin-2 in the treatment of metastatic melanoma: a clinical practice guideline. Toronto (ON): Cancer Care Ontario (CCO); 2006 Mar 20. 32 p. (Evidence-based series; no. 8-5).</p> <p>Quirt I, Verma S, Petrella T, Bak K, Charette M, Melanoma Disease Site Group. Temozolomide for the treatment of metastatic melanoma: a clinical practice guideline. Toronto (ON): Cancer Care Ontario (CCO); 2006 Mar 20. 25 p. (Evidence-based series; no. 8-4). [38 references]</p> <p>Roberts DL, Anstey AV, Barlow RJ, Cox NH, Newton Bishop JA, Corrie PG, Evans J, Gore ME, Hall PN, Kirkham N. U.K. guidelines for the management of cutaneous melanoma. Br J Dermatol 2002 Jan;146(1):7-17. [60 references]</p> <p>U.S. Preventive Services Task Force. Screening for skin cancer: U.S.</p>	
File name : SIGN72 melanoma review	Version 0.1	13/01/2012
Produced by: Roberta James	Page 1 of 7	Review date: November 2012

Preventive Services Task Force recommendation statement. *Ann Intern Med* 2009 Feb 3;150(3):188-93.

Verma S, Petrella T, Hamm C, Bak K, Charette M, Melanoma Disease Site Group. Biochemotherapy for the treatment of metastatic malignant melanoma: a clinical practice guideline. Toronto (ON): Cancer Care Ontario (CCO); 2007 Apr 30. 25 p. (Evidence-based series; no. 8-3).

Verma S, Quirt I, McCreedy D, Bak K, Charette M, Iscoe N, Melanoma Disease Site Group. Systemic adjuvant therapy for patients at high risk for recurrent melanoma: a clinical practice guideline. Toronto (ON): Cancer Care Ontario (CCO); 2005 Aug 30. 39 p. (Evidence-based series; no. 8-1). [61 references]

Adjuvant systemic therapy of melanoma. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 93-4. [4 references]

American Society of Plastic Surgeons. Evidence-based clinical practice guideline: treatment of cutaneous melanoma. Arlington Heights (IL): American Society of Plastic Surgeons; 2007 May. 14 p. [81 references]

Appropriate investigations. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 55-62. [37 references]

Biopsy. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 35-9. [14 references]

Congenital melanocytic naevi. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 63-7. [18 references]

Classification and staging of melanoma. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 23-6. [3 references]

Clinical diagnosis. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 27-34. [51 references]

Complementary and alternative medicine. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 163-8. [13 references]

Follow-up. In: Australian Cancer Network Melanoma Guidelines Revision

File name : SIGN72 melanoma review	Version 0.1	13/01/2012
Produced by: Roberta James	Page 2 of 7	Review date: November 2012

Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 121-6. [27 references]

Histopathological reporting of cutaneous melanoma. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 41-54. [39 references]

Identification and management of high-risk individuals. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 15-21. [15 references]

Management of locoregionally recurrent melanoma. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 87-91. [10 references]

Management of regional lymph nodes in melanoma. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 79-85. [16 references]

Melanoma in children. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 145-9. [30 references]

Occult melanoma. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 141-2. [4 references]

Palliative care in melanoma. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 113-7. [30 references]

Petrella T, Walker-Dilks C. PET imaging in melanoma: recommendations. Toronto (ON): Cancer Care Ontario (CCO); 2009 Jan 19. 24 p. (Recommendation report - PET; no. 3). [19 references]
<http://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=43131>

Population-based whole-body skin screening for melanoma. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 5-13. [63 references]

Pregnancy and melanoma (including hormone replacement therapy and oral contraceptives). In: Australian Cancer Network Melanoma Guidelines

File name : SIGN72 melanoma review	Version 0.1	13/01/2012
Produced by: Roberta James	Page 3 of 7	Review date: November 2012

	<p>Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 151-6. [53 references]</p> <p>Prevention. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 1-4. [20 references]</p> <p>Prognostic factors and survival outcomes in cutaneous melanoma. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 157-62. [43 references]</p> <p>Psychosocial issues in melanoma. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 101-11. [34 references]</p> <p>Treatment of desmoplastic melanoma. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 129-30. [3 references]</p> <p>Treatment of disseminated melanoma. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 95-100. [46 references]</p> <p>Treatment of primary melanoma. In: Australian Cancer Network Melanoma Guidelines Revision Working Party. Clinical practice guidelines for the management of melanoma in Australia and New Zealand. Wellington (NZ): The Cancer Council Australia, Australian Cancer Network, Sydney and New Zealand Guidelines Group; 2008. p. 73-7. [26 references]</p> <p>U.S. Preventive Services Task Force. Screening for skin cancer: U.S. Preventive Services Task Force recommendation statement. <i>Ann Intern Med</i> 2009 Feb 3;150(3):188-93. [12 references]</p> <p>Canadian Coordinating Office for Health Technology Assessment. Metastatic melanoma vaccines. <i>Ottawa: Canadian Coordinating Office for Health Technology Assessment (CCOHTA).2006:5.</i></p>
Main conclusions from new evidence	<ul style="list-style-type: none"> ▪ A Cochrane and another systematic review of chemoimmunotherapy (a combination of chemotherapy with interferon-alpha or interleukin-2 or both) versus chemotherapy found no survival benefit and increased toxicity with chemoimmunotherapy, concluding that "The standard of care remains single-agent DTIC, and the role of immunotherapy remains in doubt." <i>The guideline recommends DTIC (grade A) as the standard single agent of choice) and states that multiple drug regimens including those with tamoxifen and interferon alpha do not improve survival and are not recommended outside of clinical trials.</i> ▪ The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of using a whole-body skin examination by a primary care clinician or patient skin self-examination for the early

detection of cutaneous melanoma, basal cell cancer, or squamous cell skin cancer in the adult general population. *The guideline makes no recommendation on screening for melanoma.*

- RCP/BAD guidelines (The prevention, diagnosis, referral and management of melanoma of the skin, 2007) recommend urgent referral to a dermatologist for the following:
 - a new mole which is growing quickly over the age of puberty
 - a long-standing mole which is changing progressively in shape or colour regardless of age
 - any mole which has three or more colours or has lost its symmetry
 - any new nodule which is growing and is pigmented or vascular in appearance
 - a new pigmented line in a nail
 - something growing under a nail
 - a mole which has changed in appearance and which is also itching or bleeding.

The SIGN guideline recommends a different 7-point or ABCDE checklist (grade D) and does not make a recommendation concerning urgent referral.

- Previous reviewers of scoping reports for this guideline have indicated that the section on sentinel lymph node biopsy (SLNB) should be updated. One reviewer cited Morton et al., Sentinel-Node Biopsy or Nodal Observation in Melanoma, NEJM 2006: 355(13):1307-17. This randomised study of 1269 patients concluded, "The staging of intermediate-thickness (1.2 to 3.5 mm) primary melanomas according to the results of sentinel-node biopsy provides important prognostic information and identifies patients with nodal metastases whose survival can be prolonged by immediate lymphadenectomy." Evidence about the prognostic power of polymerase chain reaction of SLN in patients with cutaneous melanoma is probably inadequate to support the use of PCR status in clinical decision-making. *The guideline recommends SLNB should be considered as a staging technique in patients with a primary melanoma ≥ 1 mm thick or a primary melanoma < 1 mm thick of Clark level 4 (grade B).*
- A Cochrane review of statins and fibrates found that the melanoma outcomes data collected did not exclude the possibility that these drugs prevent melanoma. There was a 10% and 42% reduction for participants on statins and fibrates, respectively; however these results were not statistically significant. Until further evidence is established, limiting exposure to ultraviolet radiation remains the most effective way to reduce the risk of melanoma. *The guideline does not address pharmacological prevention.*
- A systematic review found that excision margins in excess of 1 cm had no effect on disease-free or overall survival, recurrence, or metastases for melanoma less than 2 mm in thickness. *The guideline recommends: in pT1 (melanoma 0 to 1 mm thickness) a surgical excision margin of 1 cm (B); in pT2 (melanoma 1 to 2 mm thickness) a surgical excision margin of 1 to 2 cm (B) and in pT3 (melanoma 2 to 4 mm thickness) a surgical excision margin of 2 cm (B).*
- The current evidence, summarised in a systematic review, is insufficient to confirm that elective lymph node dissection (ELND) does not improve survival in patients with melanoma. *The guideline recommends that elective lymph node dissection should not be routinely performed in patients with primary melanoma (B).*
- There is currently insufficient evidence to support adding tamoxifen to chemotherapy regimens for people with metastatic malignant melanoma. They authors of a systematic review believe there is no evidence to support a large-scale trial of tamoxifen in people with melanoma. *The guideline quotes studies that reach similar conclusions.*

	<ul style="list-style-type: none"> Melanoma vaccines have led to encouraging preliminary results, but results from phase III trials are required before these vaccines are considered as viable treatment options. Guideline makes a <i>GPP</i> that <i>patients should be entered into vaccine clinical trials as appropriate.</i> 	
New areas that could be added to the guideline	<ul style="list-style-type: none"> Discussion of pharmacological prevention. Melanoma genetics. Psychological interventions. Criteria for urgent referral. 	
Summary of the recommendations that could be updated	Section:	
	<ul style="list-style-type: none"> It may be possible to update the recommendation against ELND. The role of SLNB and nature of the biopsy may be updated. 	4.3.4 4.3.5
	<ul style="list-style-type: none"> It may be possible to update the evidence on the role of vaccines. 	6.22

Please answer the following questions as fully as possible:

Specialties:	General Practice (1), Pathology (1), Dermatology (2), Other (2)	
1(a) Is there still a requirement for an evidence-based guideline on this topic?	Yes	
1(b) If no, should the guideline be withdrawn?	n/a	
2(a) Based on the information given above, and your own clinical judgement, does the guideline require revision in the light of new evidence? <i>Please give details.</i>	<p>Section 2: Need to update section on genetics. Would also be appropriate to make mention of conflicting advice on sun protection and vitamin D lack. Include public screening for melanoma.</p> <p>Section 3: Update diagnostic tools to include evaluation of nodules as opposed to flat melanomas.</p> <p>Section 3.2 on clinical diagnosis should include a section on referral.</p> <p>Section 7: Update in follow up regimens.</p> <p>Section 8: Management of stage IV disease needs updating to include chemotherapy/immunotherapy, vaccine experience, tamoxifen.</p>	
2(b) If no, is there a need to scope for new evidence on a yearly basis?	Annually is too short a time interval. Criteria for urgent referral would be the most important part of the guideline that needs to be updated.	
2(c) Do you agree with the assessment of the impact of the new evidence and its likely effect on recommendations?	Yes	
2(d) If yes, please suggest clinical questions that could be addressed in the revision?	<p>Which lesions require referral in general practice?</p> <p>Revision of indications for SNLB plus comment about adverse events , variation in positivity rates</p> <p>Comment on further evidence for use of dermoscopy</p> <p>Benefits from clinical nurse specialist role in melanoma</p> <p>Effective follow up techniques</p> <p>Update to information to patients sections to take account of web based sources.</p>	
3(a) Please list any additions to the remit of the guideline that you think would be beneficial		
File name : SIGN72 melanoma review	Version 0.1	13/01/2012
Produced by: Roberta James	Page 6 of 7	Review date: November 2012

Section 2.4.4 covers public education to promote early detection. I would be interested to know if there was any qualitative if not quantitative research into the effects or benefits of a public awareness campaign which is provided in Australia as an important part of health education to promote early detection.

At no point have I seen advances in melanoma progress so rapidly; we now have a new melanoma staging system (AJCC 7) and of course the changes in genetics have been profound with the identification of c-kit mutations in acral lesions and b-raf mutations in superficial spreading lesions in sun-exposed skin all proving to be very important. New therapeutic modalities that are based on this genetic information are continuing apace with the use of imatinib and b-raf antagonists proving valuable. Refinements to surgery (especially sentinel nodes), imaging (such as PET scanning) and ongoing clinical trials are also important. Also questions on vitamin D and adjuvant interferon.

Cost-effectiveness evidence in the guideline related to the areas of screening, sentinel lymph node biopsy, adjuvant interferon, and follow-up of stage I/II patients. The information presented above did not specifically relate to new evidence from a literature search on cost-effectiveness but it is likely that there is some new evidence on some of these topics that could be used to refresh the guideline if it is being revised.

Cost benefit analysis, early vs later diagnosis

3(b) Please list any sections of the guideline that are no longer required	
Section 7.4 figure 1 is referenced 1988. More up-to-date data on the recurrence rate and the initial Breslow thickness at presentation should be included.	
4 Please tick your preferred option for reviewing this guideline	
a. there is no new evidence that will affect existing recommendations and the guideline should not be reviewed at this time	
b. some recommendations will change in the light of the new evidence and elements of the guideline should be reviewed	✓

5 SIGN COUNCIL			Date: 11/11/2011
Revalidate	Refresh	Revise	Remove
	✓		