The Royal College of Pathologists
Pathology: the science behind the cure

Standards and datasets for reporting cancers

Dataset for histopathological reporting of conjunctival melanoma and conjunctival melanocytic intraepithelial lesions

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Authors: Yamini Krishna, Liverpool Clinical Laboratories
Sarah Coupland, Liverpool Clinical Laboratories
Hardeep Singh Mudhar, Royal Hallamshire Hospital, Sheffield

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Produced by	Dr Yamini Krishna is a consultant histopathologist at the National Specialist Ophthalmic Pathology Service (Liverpool), Liverpool Clinical Laboratories, University Hospitals of Liverpool Group; and is the RCPath Subspecialty Advisor for Ophthalmic Pathology. Professor Sarah Coupland is a consultant histopathologist at the National Specialist Ophthalmic Pathology Service (Liverpool), Liverpool Clinical Laboratories, University Hospitals of Liverpool Group; and is George Holt Chair of Pathology, University of Liverpool. Dr Hardeep Singh Mudhar is a consultant histopathologist at the National Specialist Ophthalmic Pathology Service (Sheffield), Department of Histopathology, Royal Hallamshire Hospital.
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Comments	This document replaces the 1st edition of *Dataset for histopathological reporting of conjunctival melanoma and melanosis* published in 2007. In accordance with the College's pre-publications policy, this document was on the Royal College of Pathologists' website for consultation from 14 July to 11 August 2025. Responses and authors' comments are available to view at: www.rcpath.org/profession/publications/documents-in-development.html. **Dr Brian Rous** **Clinical Lead for Guideline Review**

The Royal College of Pathologists
6 Alie Street, London E1 8QT
Tel: 020 7451 6700
Fax: 020 7451 6701
Web: www.rcpath.org

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Foreword

The cancer datasets published by the Royal College of Pathologists (RCPath) are a combination of textual guidance, educational information and reporting proformas. The datasets enable pathologists to report the most clinically relevant information on cancer specimens, including grade and stage, in a consistent manner, in compliance with international standards and provide prognostic information thereby and allowing clinicians to provide a high standard of care for patients and appropriate management for specific clinical circumstances. This guideline has been developed to cover most common circumstances. However, we recognise that guidelines cannot anticipate every pathological specimen type and clinical scenario. Occasional variation from the practice recommended in this guideline may therefore be required to report a specimen in a way that maximises benefit to the patient.

Each dataset contains core data items (see Appendix C) that are mandated for inclusion in the Cancer Outcomes and Services Dataset (COSD – previously the National Cancer Data Set) in England. Core data items are supported by robust published evidence and are required for cancer staging, optimal patient management and prognosis. Core data items meet the requirements of professional standards. It is recommended that at least 95% of reports on cancer resections should record a full set of core data items. Other non-core data items are described. These may be included to provide a comprehensive report or to meet local clinical or research requirements. All data items should be clearly defined to allow the unambiguous recording of data.

The following stakeholders were contacted to consult on this document:

- British Association for Ophthalmic Pathology
- National Specialist Ophthalmic Pathology Service in England, and its equivalent in Glasgow, Scotland
- UK ocular oncologists working in specialised commissioned ocular oncology centres in Liverpool, London, Sheffield and Glasgow.

The information used to develop this dataset was obtained by undertaking a systematic search of the PubMed database, previous recommendations of the RCPath, and local guidelines in the UK. Key search terms used for electronic searches included ‘conjunctival melanoma’, ‘conjunctival primary acquired melanosis,’ ‘conjunctival melanocytic intraepithelial neoplasia’ and ‘conjunctival melanocytic intraepithelial lesions’ and dates

searched were between January 1984 and June 2025. Published evidence was evaluated using modified SIGN guidance (see Appendix D).[1] Consensus of evidence in the guideline was achieved by expert review. Gaps in the evidence were identified by College members via feedback received during consultation.

No major organisational changes have been identified that would hinder the implementation of the dataset.

A formal revision cycle for all cancer datasets takes place on a 3-yearly basis. However, each year, the College will ask the authors of the dataset, in conjunction with the relevant sub-specialty adviser to the College, to consider whether the dataset needs to be revised. A full consultation process will be undertaken if major revisions are required, i.e. revisions to core data items (the only exception being changes to international tumour grading and staging schemes that have been approved by the Specialty Advisory Committee on Cellular Pathology and affiliated professional bodies; these changes will be implemented without further consultation). If minor revisions or changes to non-core data items are required, an abridged consultation process will be undertaken, whereby a short note of the proposed changes will be placed on the College website for 2 weeks for fellows' attention. If members do not object to the changes, the short notice of change will be incorporated into the dataset and the full revised version (incorporating the changes) will replace the existing version on the College website.

The dataset has been reviewed by the Professional Guidelines team, Working Group on Cancer Services and Lay Advisory Group and was placed on the College website for consultation with the membership from 14 July to 11 August 2025. All comments received from the Working Group and membership were addressed by the authors to the satisfaction of the Chair of the Working Group and the Clinical Lead for Guideline Review.

This dataset was developed without external funding to the writing group. The College requires the authors of datasets to provide a list of potential conflicts of interest; these are monitored by the Professional Guidelines team and are available on request. The authors have declared no conflicts of interest.

List of abbreviations

Alpha-thalassaemia mental retardation X-linked	ATRX
B-Raf proto-oncogene	BRAF
Mitogen-activated protein kinase/extracellular signal-related kinase	MEK
Neurofibromatosis type 1	NF1
Programmed cell death ligand 1	PDL-1
Rat sarcoma oncogene	RAS
Telomerase reverse transcriptase	TERT

1 Introduction

Conjunctival melanoma occurs most frequently in fair-skinned populations, with the overall incidence being approximately 0.46 cases per 1,000,000 persons per year, representing about 0.25% of melanomas at all sites and 5% of all ocular melanomas.[2,3] It is a mucosal melanoma with histological and biological similarities to cutaneous melanoma and similar genetic alterations.[4,5] These include UV-related driver mutations in the *BRAF, NF1 and RAS* genes and copy number variations.[6–15] *BRAF* and *NRAS* mutations are present in approximately 30% and 14–25% of conjunctival melanoma, respectively.[8,11,13,15]

Conjunctival melanoma affects any part of the conjunctiva (i.e. bulbar, palpebral and forniceal conjunctiva), as well as the caruncle, and invades the neighbouring structures in advanced cases.[16,17] There is no standardised treatment; however, management includes surgical excision +/− adjuvant cryotherapy, topical chemotherapy, brachytherapy, proton beam radiotherapy or photon external beam radiation and, in advanced cases with local tissue invasion, radical orbital exenteration.[13,15,17,18]

Poor prognostic indicators for nodal and systemic metastases include non-bulbar locations, multifocality, ulceration, increased tumour thickness and high mitotic activity.[19–24] Metastases to the lymph nodes are common (~25%) but metastases may also involve the liver, lungs, brain and skin.[19,20]

Despite recent successes with targeted and immunotherapies in cutaneous melanoma, data on conjunctival melanoma treated with similar therapies (anti-BRAF/anti-MEK/anti-PDL1) are promising but limited.[13,15,25–29]

The majority (~70%) of conjunctival melanoma cases develop from conjunctival melanocytic intraepithelial lesions (C-MIL), while a smaller proportion develop from pre-existing naevi or are *de novo.*[16,21,22,30] C-MIL, a preinvasive disease, encompasses a spectrum of morphological changes ranging from melanocytic hyperplasia through degrees of melanocytic atypia to melanoma in situ.[31] Various terminologies and classification systems have been proposed for C-MIL, each with their strengths and weaknesses. The most widely used include the primary acquired melanosis (PAM) with atypia system[32] (clinical descriptive system) and the conjunctival melanocytic intraepithelial neoplasia (C-MIN) system.[17]

In 2018, the 4th edition of the WHO Classification of Eye Tumours' proposed the C-MIL classification, simplifying the grading of these lesions and capturing their risk of disease

progression to invasive melanoma.[33] This comprised: low-grade C-MIL, high-grade C-MIL and conjunctival melanoma in situ. The system was validated in 2021 and it was found that all 3 classification systems (C-MIL, C-MIN and PAM) had comparable accuracy in their ability to identify lesions with potential for recurrence.[34] In 2022, the editorial panel of the 5th edition of the WHO decided to revise the classification scheme because the low-grade C-MIL in the fourth edition incorporated both non-neoplastic (benign melanosis) and neoplastic melanocytic proliferations, and further simplified high-grade C-MIL to include all PAM with moderate/severe atypia, C-MIN score >5 and melanoma in situ. This led to the current system as summarised in Table 1,[31] which was validated by a large international collaborative study and found to have substantial interobserver agreement, good reproducibility, be predictive of recurrence and invasive disease and, importantly, inform clinical treatment thresholds.[35]

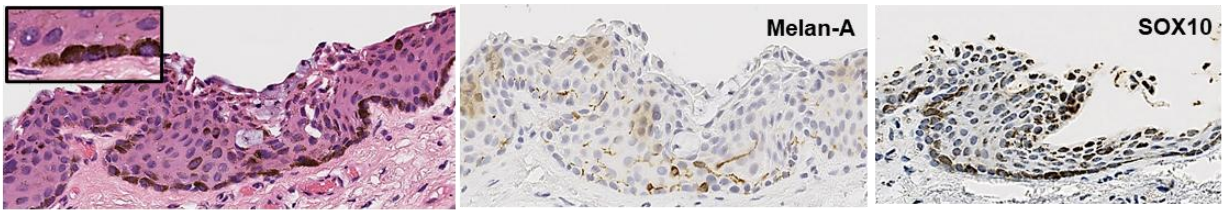
Table 1: WHO 2022 classification of C-MIL.[31]

WHO	Acceptable alternative terminology	Increased cellularity	Histologic features	Risk of association with or progression to invasive melanoma
Not applicable	Bening melanosis c-MIN (grades 0–1) PAM without atypia	No/minimal	Conjunctival hypermelanosis (increased pigment in epithelial cells without melanocytic hyperplasia or atypia). Slight or focal melanocytic hyperplasia without atypia (parabasal melanocytes with condensed round nuclei, smaller than basal epithelial cell, inconspicuous nucleoli and inconspicuous cytoplasm) may be seen.	None
Low-grade C-MIL	PAM with mild atypia c-MIN (grades 2–4)	Yes	Predominantly basilar melanocytic proliferation with low-grade atypia (dendritic or small to moderate size polyhedral, usually non-epithelioid melanocytes with round to irregular nuclear contours, often nuclear hyperchromasia, inconspicuous nucleoli, and inconspicuous or scant cytoplasm).	Lower

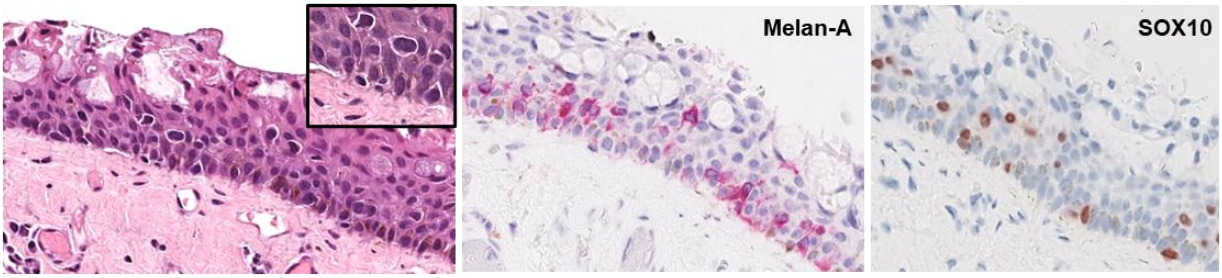
High-grade C-MIL	PAM with moderate to severe atypia c-MIN (grades 5–10)	Yes	More confluent basilar and significant non-basilar proliferation of melanocytes with high-grade atypia (moderate to severe), evidence of intraepithelial nested and/or pagetoid growth, and epithelioid cell cytomorphology.	Higher
	Melanoma in situ	Yes	The term melanoma in situ may be used for (1) the most atypical high-grade C-MILs involving close to full thickness of the epithelium, (2) histologically obvious melanomas without documented evidence of subepithelial invasion.	Highest

Photomicrographs demonstrating the C-MIL scoring grades are presented in Figure 1.[35]

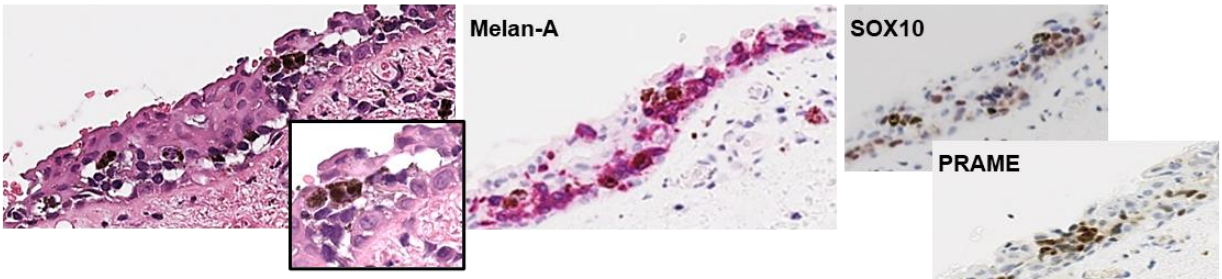
Figure 1: Photomicrographs showing the H&E section and corresponding immunohistochemistry for each of the C-MIL scoring grades.[35]



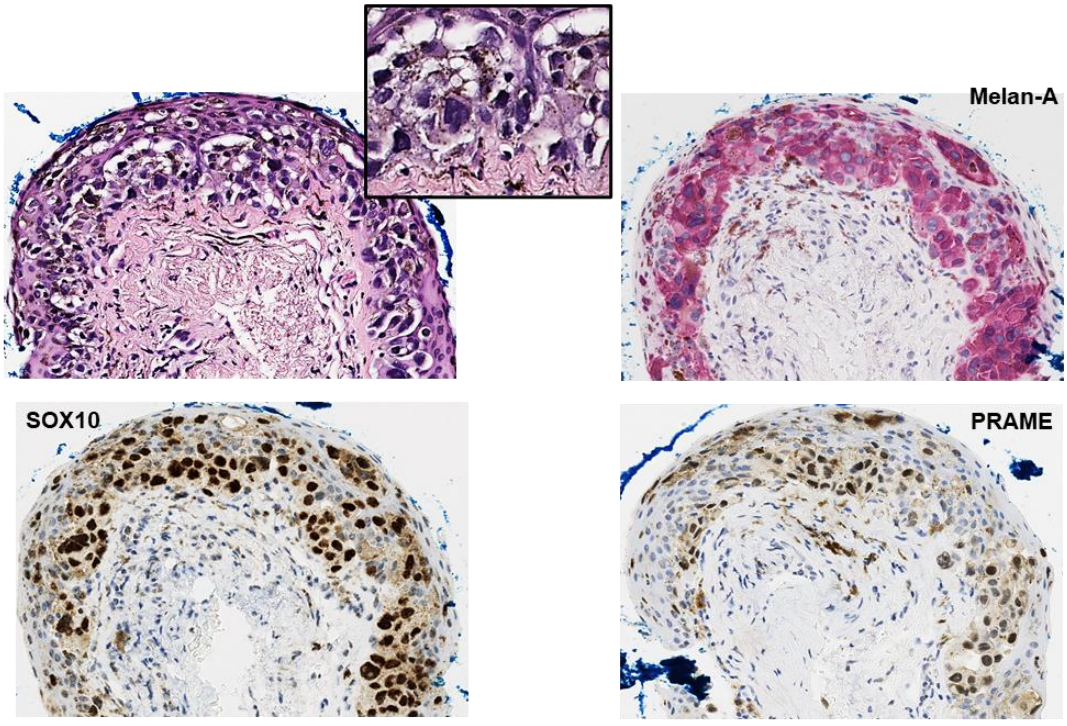
A: Benign melanosis



B: Low Grade C-MIL



C: High Grade C-MIL with focal melanoma in situ



D: High Grade C-MIL with extensive melanoma in situ

These proposals for the reporting of conjunctival melanoma and C-MIL should be implemented in order to:

- achieve consistency/standardisation in the histological reporting of conjunctival melanoma and C-MIL, with respect to report content and terminology. This will facilitate collaboration between cancer centres and cancer networks
- provide accurate data for cancer registration
- provide prognostic information to clinicians and patients
- potentially assist in selecting patients for future trials of adjuvant therapy
- provide data for clinical audit and effectiveness
- allow accurate and equitable comparison of surgical and adjuvant treatment practice in different units and the comparison of patients in clinical trials
- provide a database for research.

The synoptic proforma (Appendix C) is based on the 5th edition of WHO Classification of Eye Tumours,[36] the TNM Classification of Malignant Tumours (8th edition)[37] from the Union for International Cancer Control (UICC) and the Cancer Staging Manual (8th edition)[38] from the American Joint Committee on Cancer (AJCC). The synoptic proforma may be used as the main reporting format or may be combined with free text.

The data have been divided into core and non-core. Core data represents a minimum standard required for patient management and are judged, based on the available published literature, to be the most statistically robust. Non-core data can be included for completeness of the report, to reflect local practice. Non-core data are judged to be of lesser prognostic significance or have not been as thoroughly statistically validated as core data.

The sections on dissection technique are for guidance only and are not meant to be prescriptive. Further guidelines on how to dissect ophthalmic specimens for the diagnosis of conjunctival melanoma and C-MIL can be found in the references at the end of this document.

1.1 Target users and health benefits of this guideline

The target primary users of the dataset are trainee and consultant cellular pathologists reporting ophthalmic pathology and, on their behalf, the suppliers of IT products to

laboratories. The secondary users are surgeons, specialist nurses, medical and surgical oncologists, and radiologists. It may also be of use to cancer registries.

2 Clinical information required on the request form

For suspected melanocytic lesions of the conjunctiva, it is essential that the following specific data items are known before histopathological reporting:

- the age and sex of the patient (conjunctival melanoma is more common in older adults)
- laterality of eye on which operated
- clinical details, such as racial background (conjunctival hypermelanosis; benign melanosis)[31]
- whether the lesion is congenital or acquired
- the precise anatomical site of the lesion (lesions in the fornix and tarsal conjunctiva are more likely to be melanoma)
- any previous diagnosis of a C-MIL or conjunctival melanoma (retrospective review and evolution of pathology)
- any previous treatment of a C-MIL or conjunctival melanoma
- a detailed diagram indicating locations of multiple conjunctival mapping biopsies.

3 Specimen receipt and preparation

4 types of specimen may be received from patients suspected of having conjunctival melanocytic lesions, usually in 10% buffered formalin. These are: excisional biopsies, incisional biopsies, multiple incisional ‘mapping’ biopsies and exenterations for advanced/uncontrolled conjunctival melanoma.

Incisional and excisional biopsies are best placed flat on a piece of card by the surgeon. If this is not done, it is recommended the specimen be flattened in this manner to minimise tangential section artefact, which can falsely upgrade melanocytic lesions at histological interpretation.[39] Very small biopsies should also be placed in a tissue biopsy ‘Cellsafe’ cassette.

Exenteration specimens are typically sent in 10% buffered formalin and usually require 48 hours fixation before macroscopic description and dissection. Exenterations may be complete or limited. Complete exenteration comprises removal of the eyelids, globe, optic nerve, extraocular muscles, orbital fat and periosteum. For orientation purposes, the lashes of the upper lid are longer than those of the lower lid and the upper lid possesses a fold/lid crease; the medial canthus has the caruncle and puncta.

4 Specimen handling and block selection

4.1 Macroscopic description

For incisional and excisional biopsies, record the overall length, width and depth of each specimen, followed by the size of any apparent lesions. With multiple incisional 'mapping' procedure, to assess the extent of melanocytic lesions, margins are not an issue as the mapping is simply establishing the extent of the lesions. Therefore, these specimens do not require painting. Clinically, C-MIL are usually flat, brown/black and mottled, but a non-pigmented variant – so-called melanosis with atypia sine pigmento – does exist.[31,40,41] Invasive conjunctival melanoma is often indicated by a firm thickening or nodule. It is good practice to paint the margins of an excisional biopsy, to aid in margin status assessment at microscopy, unless this would compromise accurate embedding of the specimen.

Exenteration is performed for advanced conjunctival melanoma and/or after failed previous localised treatment.[42,43] The following measurements are usually taken: maximum antero-posterior, horizontal (medial to lateral) and vertical (superior to inferior). Any relevant external features are described, e.g. whether the exenteration specimen includes eyelids, the location and dimensions of the melanoma and its distance from the surgical margins. The external soft tissue margins should be painted in suitable dye for margin assessment and orientation purposes. The specimen is usually 'bread-sliced' in the sagittal plane, starting either at the lateral or medial side and ending at the opposite side. It is helpful to note which slices have tumour present, the overall dimensions of the tumour, the involvement of orbital adnexal structures and/or globe, and the distance of surgical margins from the melanoma.

4.2 Block taking

4.2.1 Incisional or multiple mapping incisional biopsies

These can be processed whole, along their longest margin if less than 3 mm. If greater than 3 mm in length, they can be bread-sliced across their width.

4.2.2 Excisional biopsies

It is good practice to paint the margins, unless this would compromise accurate embedding of the specimen. The specimen is bread-sliced along the length (as for cutaneous melanoma excisions, see RCPath's *Dataset for histopathological reporting of primary cutaneous malignant melanoma and regional lymph nodes*).[44] If the excision includes the limbus, the slices should ideally pass through the limbal margin, so that the lesion's relationship to the cornea can be ascertained.

4.2.3 Exenterations

The specimen is usually 'bread-sliced' in the sagittal direction starting either at the lateral or medial side and ending at the opposite side. While the medial and lateral slices usually do not require megablock cassettes, the more central slices typically do. The surgical margin of the optic nerve is embedded separately. If bone is attached to the specimen, it should be removed, decalcified and then processed. The medial nasolacrimal duct resection margin is sampled as C-MIL and melanoma can involve this margin.[45] Finding this margin is facilitated by probing the lacrimal puncta.

Please see the macroscopic description above (section 4.1). Involvement of any orbital adnexal structures and/or globe and the closest surgical margin (orbital soft tissue and/or cutaneous) should be represented in the block taking.

5 Core data items

5.1 Macroscopic core data items

5.1.1 Location of tumour

For incisional and excisional biopsies, the clinical details will usually indicate the site of the biopsy. For exenterations, inspection of the specimen will indicate the site of the lesion.

Primary conjunctival melanoma located at unfavourable sites, such as the fornix, palpebral conjunctiva, caruncle, plica semilunaris and corneal stroma, is associated with a higher

recurrence rate and a higher rate of metastatic death compared with favourable sites such as the bulbar and limbal conjunctiva.[30,36,42,43,46–50]

[Level of evidence – B]

5.1.2 Size of melanoma

Melanomas larger than 10 mm in greatest width and those that are pathological stage pT3 and above have a greater local recurrence rate and higher death rate from metastatic tumour.[36,51–53] More recently, however, clinical staging refers to the number of involved quadrants and pathological staging gives importance to tumour thickness (the latter is described in the microscopic core data).[15,22,30,36,47,54]

[Level of evidence – B]

5.1.3 Multifocality

Multifocal primary conjunctival melanomas are associated with a higher rate of recurrence and metastatic death than unifocal tumours due to the difficulty in adequately/completely treating multifocal lesions.[15,16,24,36,46,48,55]

[Level of evidence – B]

5.2 Microscopic core data

5.2.1 Conjunctival melanocytic intraepithelial lesions

Benign melanosis is diagnosed in 2 circumstances: 1) hypermelanosis or increased pigment in epithelial keratinocytes without melanocytic hyperplasia or atypia, and 2) focal basal layer confined melanocytic hyperplasia without atypia. Current evidence suggests that benign melanosis has no risk of progression to invasive melanoma.[31–33,35]

Cytological features of low-grade C-MIL include dendritic or small polyhedral melanocytes with nuclear hyperchromasia, inconspicuous nucleoli and scant cytoplasm. Those of high-grade C-MIL are severely atypical large pleomorphic epithelioid cells with copious cytoplasm and prominent eosinophilic nucleoli. The range of atypical architectural patterns include linear hyperplasia of the basal melanocytes (low-grade C-MIL) to a confluent lentiginous spread, intraepithelial nests, pagetoid growth and full-thickness epithelial involvement by atypical melanocytes, i.e. high-grade C-MIL, which also incorporates melanoma in situ. Nests, pagetoid spread and confluent growth extend upward from the basal epithelium, displacing squamous and/or goblet cells; however, there should be no evidence of invasive growth.[31–33,35,56–58] The cytological and architectural features of C-

MIL, along with the equivalent PAM and C-MIN grading, and their risk of progression to invasive melanoma are summarised in Table 1.[31] Epithelioid cell morphology with cytological atypia, nesting and pagetoid spread are associated with an increased risk of recurrence and a 75–90% chance of progression to invasive melanoma.[18,31–36,56–58]

The assessment of the extent of involvement of the epithelium by atypical melanocytes can be facilitated by immunohistochemistry with markers against MelanA, SOX10, S100, HMB45, MITF and/or PRAME proteins.[31,35,59] Photomicrographs demonstrating the C-MIL scoring grades (H&E and corresponding immunohistochemistry) are presented in Figure 1.[35]

Description of the status of margins of excision should be provided for excisional biopsies as incompletely excised C-MIL can recur or in some cases progress to invasive melanoma.[31–36]

[Level of evidence – B]

5.2.2 Invasive melanoma

Approximately 75% of conjunctival melanomas arise from C-MIL, while a smaller proportion develop from pre-existing naevi or are de novo.[16,20,21,30] Melanomas arising de novo seem to have a worse outcome than those arising from C-MIL or naevi.[16] However, this observation may be biased because clinical and histological findings can be contradictory and precursors (C-MIL and naevi) may be overlooked or be difficult to characterise.[13,15]

[Level of evidence – B]

5.2.3 Thickness of invasive melanoma

The thickness of invasive melanoma is measured from the top of the conjunctival epithelium to the deepest invasive melanocyte (Jakobiec modification of the Breslow thickness). It is recorded in millimetres to the first decimal point (as for cutaneous melanoma). Tumour thickness can be measured using a microscope vernier scale, an eyepiece graticule or a validated digital pathology measurement tool.[60]

The thickness of invasive melanoma has prognostic significance, with a greater thickness increasing the risk for metastasis, similar to cutaneous melanoma.[6,15,23,24,32,36,47] The most recent pTNM pathological classification for primary conjunctival melanoma states a critical thickness of 2 mm and tumour location as key factors for upstaging (Appendix A). Since metastatic potential is related to tumour thickness, histologically determined invasive

tumour thickness would play an important part in triaging patients for sentinel lymph node biopsies.[15,24,36,47,53]

Occasionally, areas of substantia propria inflammation can obscure foci of invasion. In these circumstances, applying immunohistochemical melanocytic markers can often help detect the obscured invasive melanoma cells.

[Level of evidence – B]

5.2.4 Cell types within the invasive melanoma

Tumours with an epithelioid cell component exhibit a higher recurrence rate and a higher tumour-related mortality compared to those composed of pure spindle cells.[23,24,36,47]

[Level of evidence – B]

5.2.5 Ulceration

Ulceration or significant epithelial sloughing/loss has also been associated with a higher recurrence rate, metastases and increased tumour-associated mortality, similar to cutaneous melanoma.[15,19–24,32,36]

[Level of evidence – B]

5.2.6 Mitotic rate

Increased mitoses (>5.5 mitoses/mm^2) have been reported to be associated with nodal metastasis.[23,24,36]

[Level of evidence – B]

5.2.7 Lymphatic/blood vessel invasion

Tumours exhibiting lymphatic invasion are associated with a higher rate of death from metastatic melanoma.[17]

Lymph node metastases are common (~25–52%; preauricular, parotid, submandibular and/or cervical nodes, depending on conjunctival melanoma location) but metastasis may also involve the liver, lungs, brain and skin (11–42%).[15,19–24,36,47] The reported usefulness of sentinel lymph node biopsy is still variable (in terms of clinical management and sensitivity of pickup) but it has been shown to be of prognostic value for conjunctival melanomas >2 mm thickness and/or >10 mm in diameter.[24,36,47,53]

[Level of evidence – B]

5.2.8 Anatomical structures infiltrated

A non-bulbar conjunctival location (forniceal, palpebral or caruncular) or invasion of the eyelid, eyeball and orbit have a greater cumulative probability of recurrence, increased risk for nodal and systemic metastases, and greater 5-year and 10-year disease-specific mortality rates of approximately 14–27% and 25–35%, respectively.[16,19–24,46–48,50,61]

[Level of evidence – B]

5.2.9 Status of excision margins

Ill-defined and/or multifocal lesions are difficult to treat and, therefore, insufficient treatment or incomplete excision is not uncommon. Excision margins involved by melanoma are positively correlated with local tumour recurrence, higher risk of metastasis and higher tumour-associated mortality.[19,36,50,62]

[Level of evidence – B]

6 Non-core data items

Some of these items have not yet been validated or there is insufficient robust statistical evidence to include them in the core data.

6.1 Macroscopic

Items include:

- dimensions of specimen
- colour of lesion.

6.2 Microscopic

For invasive melanoma: growth phase, perineural invasion, tumour regression, microsatellites, tumour infiltrating lymphocytes, tumour-associated macrophages, presence or absence of co-existing naevus.

7 Genetic studies

The use of genetics for prognostication in conjunctival melanoma is currently limited. UV signatures, driver mutations and copy number variations in multiple chromosomes have been described, with high-frequency mutations in the *NF1* (33–50%), *BRAF* (29–46%), *NRAS* (11–26%) and *ATRX* (25%) genes.[6–13,15,63–69] *NRAS* mutations are associated with

higher metastatic risk.[8,9] *TERT promoter* mutations have also been identified in up to 54% of conjunctival melanomas and even in PAM with atypia (~8%).[8,9,70–72] While activating *TERT promoter* mutations are associated with a poor prognosis, mutually exclusive inactivating *ATRX* mutations appear to be associated with a better prognosis.[8,12,27,70]

Despite recent successes with targeted and immunotherapies in cutaneous melanoma, data on conjunctival melanoma treated with similar therapies (anti-BRAF/anti-MEK/anti-PDL1) are promising but limited, with only those from small case series or single case studies in patients with inoperable disease or as first-line therapy prior to surgery in advanced cases.[13,15,25,26,29,73–86] Although *BRAF* mutational status is currently not predictive of outcome in conjunctival melanoma, it is worth assessing for *BRAF V600* mutations as it may become a future prognostic factor with promising results being reported with BRAF and MEK inhibitor combination therapies.

8 Reporting of frozen sections

Not applicable. It is not recommended that surgical margins for C-MIL or conjunctival melanoma are assessed using frozen sections.

9 Criteria for audit

The following are recommended by the RCPath as key assurance indicators[87] (see *Key assurance indicators for pathology services*) and key performance indicators[88] (see *Key performance indicators – Proposals for implementation*).

- Cancer resections should be reported using a template or proforma, including items listed in the English COSD, which are, by definition, core data items in RCPath cancer datasets. English trusts were required to implement the structured recording of core pathology data in the COSD
  - standard: 95% of reports must contain structured data
- Histopathology cases that are reported, confirmed and authorised within 7 and 10 calendar days of the procedure
  - standard: 80% of cases must be reported within 7 calendar days and 90% within 10 calendar days.

10 References

1. Palmer K, Nairn M, Guideline Development Group. Management of acute gastrointestinal blood loss: summary of SIGN guidelines. *BMJ* 2008;337:a1832.

2. Triay E, Bergman L, Nilsson B, All-Ericsson C, Seregard S. Time trends in the incidence of conjunctival melanoma in Sweden. *Br J Ophthalmol* 2009;93:1524–1528.

3. Virgili G, Parravano M, Gatta G, Capocaccia R, Mazzini C, Mallone S *et al*. Incidence and survival of patients with conjunctival melanoma in Europe. *JAMA Ophthalmol* 2020;138:601–608.

4. Rodrigues M, Koning L, Coupland SE, Jochemsen AG, Marais R, Stern MH *et al*. So close, yet so far: Discrepancies between uveal and other melanomas. A position paper from UM Cure 2020. *Cancers (Basel)* 2019;11:1032.

5. Mikkelsen LH, Larsen AC, von Buchwald C, Drzewiecki KT, Prause JU, Heegaard S. Mucosal malignant melanoma – a clinical, oncological, pathological and genetic survey. *APMIS* 2016;124:475–486.

6. Kenawy N, Kalirai H, Sacco JJ, Lake SL, Heegaard S, Larsen AC *et al*. Conjunctival melanoma copy number alterations and correlation with mutation status, tumor features, and clinical outcome. *Pigment Cell Melanoma Res* 2019;32:564–575.

7. Cisarova K, Folcher M, El Zaoui I, Pescini-Gobert R, Peter VG, Royer-Bertrand B *et al*. Genomic and transcriptomic landscape of conjunctival melanoma. *PLoS Genet* 2020;16:e1009201.

8. Lally SE, Milman T, Orloff M, Dalvin LA, Eberhart CG, Heaphy CM *et al*. Mutational landscape and outcomes of conjunctival melanoma in 101 patients. *Ophthalmology* 2022;129:679–693.

9. Larsen AC, Dahl C, Dahmcke CM, Lade-Keller J, Siersma VD, Toft PB *et al*. BRAF mutations in conjunctival melanoma: investigation of incidence, clinicopathological features, prognosis and paired premalignant lesions. *Acta Ophthalmol* 2016;94:463–470.

10. Scholz SL, Cosgarea I, Susskind D, Murali R, Moller I, Reis H *et al*. NF1 mutations in conjunctival melanoma. *Br J Cancer* 2018;118:1243–1247.

11. Gardrat S, Houy A, Brooks K, Cassoux N, Barnhill R, Dayot S *et al*. Definition of biologically distinct groups of conjunctival melanomas according to etiological factors and implications for precision medicine. *Cancers (Basel)* 2021;13:3836.

12. van Poppelen NM, van Ipenburg JA, van den Bosch Q, Vaarwater J, Brands T, Eussen B *et al*. Molecular genetics of conjunctival melanoma and prognostic value of TERT promoter mutation analysis. *Int J Mol Sci* 2021;22:5784.

13. Brouwer NJ, Verdijk RM, Heegaard S, Marinkovic M, Esmaeli B, Jager MJ. Conjunctival melanoma: New insights in tumour genetics and immunology, leading to new therapeutic options. *Prog Retin Eye Res* 2022;86:100971.

14. Krauthammer M, Kong Y, Bacchiocchi A, Evans P, Pornputtapong N, Wu C *et al*. Exome sequencing identifies recurrent mutations in NF1 and RASopathy genes in sun-exposed melanomas. *Nat Genet* 2015;47:996–1002.

15. Butt K, Hussain R, Coupland SE, Krishna Y. Conjunctival melanoma: A clinical review and update. *Cancers (Basel)* 2024;16:3121.

16. Shields CL, Markowitz JS, Belinsky I, Schwartzstein H, George NS, Lally SE *et al*. Conjunctival melanoma: outcomes based on tumor origin in 382 consecutive cases. *Ophthalmol* 2011;118:389–395.

17. Damato B, Coupland SE. Conjunctival melanoma and melanosis: a reappraisal of terminology, classification and staging. *Clin Exp Ophthalmol* 2008;36:786–795.

18. Shields JA, Shields CL, Mashayekhi A, Marr BP, Benavides R, Thangappan A *et al*. Primary acquired melanosis of the conjunctiva: risks for progression to melanoma in 311 eyes. The 2006 Lorenz E. Zimmerman lecture. *Ophthalmology* 2008;115:511–519.

19. Brouwer NJ, Marinkovic M, van Duinen SG, Bleeker JC, Jager MJ, Luyten GPM. Treatment of conjunctival melanoma in a Dutch referral centre. *Br J Ophthalmol* 2018;102:1277–1282.

20. Esmaeli B, Wang X, Youssef A, Gershenwald JE. Patterns of regional and distant metastasis in patients with conjunctival melanoma: experience at a cancer center over four decades. *Ophthalmol* 2001;108:2101–2105.

21. Missotten GS, Keijser S, De Keizer RJ, De Wolff-Rouendaal D. Conjunctival melanoma in the Netherlands: a nationwide study. *Invest Ophthalmol Vis Sci* 2005;46:75–82.

22. Shields CL, Kaliki S, Al-Dahmash SA, Lally SE, Shields JA. American Joint Committee on Cancer (AJCC) clinical classification predicts conjunctival melanoma outcomes. *Ophthalmic Plast Reconstr Surg* 2012;28:313–323.

23. Esmaeli B, Roberts D, Ross M, Fellman M, Cruz H, Kim SK, Prieto VG. Histologic features of conjunctival melanoma predictive of metastasis and death (an American Ophthalmological thesis). *Trans Am Ophthalmol Soc* 2012;110:64–73.

24. Esmaeli B, Rubin ML, Xu S, Goepfert RP, Curry JL, Prieto VG *et al*. Greater Tumor thickness, ulceration, and positive sentinel lymph node are associated with worse prognosis in patients with conjunctival melanoma: Implications for future AJCC classifications. *Am J Surg Pathol* 2019;43:1701–1710.

25. Sagiv O, Thakar SD, Kandl TJ, Ford J, Sniegowski MC, Hwu WJ, Esmaeli B. Immunotherapy with programmed cell death 1 inhibitors for 5 patients with conjunctival melanoma. *JAMA Ophthalmol* 2018;136:1236–1241.

26. Finger PT, Pavlick AC. Checkpoint inhibition immunotherapy for advanced local and systemic conjunctival melanoma: a clinical case series. *J Immunother Cancer* 2019;7:83.

27. Chang E, Demirci H, Demirci FY. Genetic aspects of conjunctival melanoma: A review. *Genes (Basel)* 2023;14:1668.

28. Esmaeli B, Sagiv O. Targeted biological drugs and immune check point inhibitors for locally advanced or metastatic cancers of the conjunctiva, eyelid, and orbit. *Int Ophthalmol Clin* 2019;59:13–26.

29. Rossi E, Maiorano BA, Pagliara MM, Sammarco MG, Dosa T, Martini M *et al*. Dabrafenib and trametinib in BRAF mutant metastatic conjunctival melanoma. *Front Oncol* 2019;9:232.

30. Larsen AC, Dahmcke CM, Dahl C, Siersma VD, Toft PB, Coupland SE *et al*. A retrospective review of conjunctival melanoma presentation, treatment, and outcome and an investigation of features associated with BRAF mutations. *JAMA Ophthalmol* 2015;133:1295–1303.

31. Coupland SE, Milman T, Verdijk RM, Brouwer NJ. Conjunctival melanocytic intraepithelial lesions. *In:* WHO Classification of Tumours Editorial Board (eds) *Eye Tumours*. Lyon, France: International Agency for Research on Cancer, 2023.

32. Folberg R, McLean IW. Primary acquired melanosis and melanoma of the conjunctiva: terminology, classification, and biologic behavior. *Hum Pathol* 1986;17:652–654.

33. Eberhart C, Coupland SE, Folberg R, Margo C, Rao N. Conjunctival melanocytic intraepithelial neoplasia. In: *WHO Classification of Tumours of the Eye*. Lyon, France: International Agency for Research on Cancer, 2018.

34. Milman T, Eiger-Moscovich M, Henry RK, Folberg R, Coupland SE, Grossniklaus HE *et al*. Validation of the newly proposed World Health Organization Classification System for Conjunctival Melanocytic Intraepithelial Lesions: A comparison with the C-MIN and PAM classification schemes. *Am J Ophthalmol* 2021;223:60–74.

35. Mudhar HS, Krishna Y, Cross S, Auw-Haedrich C, Barnhill R, Cherepanoff S *et al*. A multicenter study validates the WHO 2022 Classification for Conjunctival Melanocytic Intraepithelial Lesions with Clinical and Prognostic Relevance. *Lab Invest* 2024;104:100281.

36. Moulin A, Brouwer NJ, Ferreira TA, Jager MJ, Verdijk RM. Conjunctival melanoma. *In*: WHO Classification of Tumours Editorial Board (eds) *Eye Tumours*. Lyon, France: International Agency for Research on Cancer, 2023.

37. Brierley JD, Gospodarowicz M, Wittekind C. *TNM Classification of Malignant Tumours (8th edition)*. Oxford, UK: Wiley-Blackwell, 2017.

38. Amin MB, Edge S, Greene F, Byrd DR, Brookland RK, Washington MK *et al*. (eds). *AJCC Cancer Staging Manual (8th edition)*. Cham, Switzerland: Springer.

39. Jakobiec FA, Folberg R, Iwamoto T. Clinicopathologic characteristics of premalignant and malignant melanocytic lesions of the conjunctiva. *Ophthalmol* 1989;96:147–166.

40. Jakobiec FA, Rini FJ, Fraunfelder FT, Brownstein S. Cryotherapy for conjunctival primary acquired melanosis and malignant melanoma. Experience with 62 cases. *Ophthalmol* 1988;95:1058–1070.

41. Griffith WR, Green WR, Weinstein GW. Conjunctival malignant melanoma originating in acquired melanosis sine pigmento. *Am J Ophthalmol* 1971;72:595–599.

42. Paridaens AD, McCartney AC, Minassian DC, Hungerford JL. Orbital exenteration in 95 cases of primary conjunctival malignant melanoma. *Br J Ophthalmol* 1994;78:520–528.

43. Shields CL, Shields JA, Gunduz K, Cater J, Mercado GV, Gross N, Lally B. Conjunctival melanoma: risk factors for recurrence, exenteration, metastasis, and death in 150 consecutive patients. *Arch Ophthalmol* 2000;118:1497–1507.

44. The Royal College of Pathologists. *Dataset for histopathological reporting of primary cutaneous malignant melanoma and regional lymph nodes*. Available at: www.rcpath.org/profession/guidelines/cancer-datasets-and-tissue-pathways.html

45. Paridaens AD, McCartney AC, Lavelle RJ, Hungerford JL. Nasal and orbital recurrence of conjunctival melanoma 21 years after exenteration. *Br J Ophthalmol* 1992;76:369–371.

46. Paridaens AD, Minassian DC, McCartney AC, Hungerford JL. Prognostic factors in primary malignant melanoma of the conjunctiva: a clinicopathological study of 256 cases. *Br J Ophthalmol* 1994;78:252–259.

47. Jain P, Finger PT, Damato B, Coupland SE, Heimann H, Kenawy N *et al*. Multicenter, international assessment of the eighth edition of the American Joint Committee on Cancer Cancer Staging Manual for Conjunctival Melanoma. *JAMA Ophthalmol* 2019;137:905–911.

48. Anastassiou G, Heiligenhaus A, Bechrakis N, Bader E, Bornfeld N, Steuhl KP. Prognostic value of clinical and histopathological parameters in conjunctival melanomas: a retrospective study. *Br J Ophthalmol* 2002;86:163–167.

49. Damato B, Coupland SE. An audit of conjunctival melanoma treatment in Liverpool. *Eye (Lond)* 2009;23:801–809.

50. Werschnik C, Lommatzsch PK. Long-term follow-up of patients with conjunctival melanoma. *Am J Clin Oncol* 2002;25:248–255.

51. Seregard S, Kock E. Conjunctival malignant melanoma in Sweden 1969-91. *Acta Ophthalmol (Copenh)* 1992;70:289–296.

52. Lommatzsch PK, Lommatzsch RE, Kirsch I, Fuhrmann P. Therapeutic outcome of patients suffering from malignant melanomas of the conjunctiva. *Br J Ophthalmol* 1990;74:615–619.

53. Cohen VM, Tsimpida M, Hungerford JL, Jan H, Cerio R, Moir G. Prospective study of sentinel lymph node biopsy for conjunctival melanoma. *Br J Ophthalmol* 2013;97:1525–1529.

54. Vora GK, Demirci H, Marr B, Mruthyunjaya P. Advances in the management of conjunctival melanoma. *Surv Ophthalmol* 2017;62:26–42.

55. Shields CL, Chien JL, Surakiatchanukul T, Sioufi K, Lally SE, Shields JA. Conjunctival tumors: Review of clinical features, risks, biomarkers, and outcomes – The 2017 J. Donald M. Gass Lecture. *Asia Pac J Ophthalmol (Phila)* 2017;6:109–120.

56. Sugiura M, Colby KA, Mihm MC, Jr., Zembowicz A. Low-risk and high-risk histologic features in conjunctival primary acquired melanosis with atypia: Clinicopathologic analysis of 29 cases. *Am J Surg Pathol* 2007;31:185–192.

57. Zembowicz A, Mandal RV, Choopong P. Melanocytic lesions of the conjunctiva. *Arch Pathol Lab Med* 2010;134:1785–1792.

58. Maly A, Epstein D, Meir K, Pe'er J. Histological criteria for grading of atypia in melanocytic conjunctival lesions. *Pathology* 2008;40:676–681.

59. Mudhar HS, Milman T, Stevenson S, Watson M, Kim J, Magan T et al. PRAME expression by immunohistochemistry and reverse transcription quantitative PCR in conjunctival melanocytic lesions-a comprehensive clinicopathologic study of 202 cases and correlation of cytogenetics with PRAME expression in challenging conjunctival melanocytic lesions. *Hum Pathol* 2023;134:1–18.

60. Jakobiec FA. Conjunctival melanoma. *Arch Ophthalmol* 1980;98:1378–1384.

61. Lim M, Tatla T, Hersh D, Hungerford J. Patterns of regional head and neck lymph node metastasis in primary conjunctival malignant melanoma. *Br J Ophthalmol* 2006;90:1468–1471.

62. Cohen VML, O'Day RF. Management issues in conjunctival tumours: Conjunctival melanoma and primary acquired melanosis. *Ophthalmol Ther* 2019;8:501–510.

63. Lake SL, Jmor F, Dopierala J, Taktak AF, Coupland SE, Damato BE. Multiplex ligation-dependent probe amplification of conjunctival melanoma reveals common BRAF V600E gene mutation and gene copy number changes. *Invest Ophthalmol Vis Sci* 2011;52:5598–5604.

64. Goldenberg-Cohen N, Cohen Y, Rosenbaum E, Herscovici Z, Chowers I, Weinberger D *et al*. T1799A BRAF mutations in conjunctival melanocytic lesions. *Invest Ophthalmol Vis Sci* 2005;46:3027–3030.

65. Cao J, Heijkants RC, Jochemsen AG, Dogrusoz M, de Lange MJ, van der Velden PA *et al*. Targeting of the MAPK and AKT pathways in conjunctival melanoma shows potential synergy. *Oncotarget* 2017;8:58021–58036.

66. Griewank KG, Westekemper H, Murali R, Mach M, Schilling B, Wiesner T *et al*. Conjunctival melanomas harbor BRAF and NRAS mutations and copy number changes similar to cutaneous and mucosal melanomas. *Clin Cancer Res* 2013;19:3143–3152.

67. El Zaoui I, Bucher M, Rimoldi D, Nicolas M, Kaya G, Pescini Gobert R *et al*. Conjunctival melanoma targeted therapy: MAPK and PI3K/mTOR pathways inhibition. *Invest Ophthalmol Vis Sci* 2019;60:2764–2772.

68. Francis JH, Grossniklaus HE, Habib LA, Marr B, Abramson DH, Busam KJ. BRAF, NRAS, and GNAQ mutations in conjunctival melanocytic nevi. *Invest Ophthalmol Vis Sci* 2018;59:117–121.

69. Gear H, Williams H, Kemp EG, Roberts F. BRAF mutations in conjunctival melanoma. *Invest Ophthalmol Vis Sci* 2004;45:2484–2488.

70. van Ipenburg JA, Naus NC, Dubbink HJ, van Ginderdeuren R, Missotten GS, Paridaens D, Verdijk RM. Prognostic value of TERT promoter mutations in conjunctival melanomas in addition to clinicopathological features. *Br J Ophthalmol* 2021;105:1454–1461.

71. Griewank KG, Murali R, Schilling B, Scholz S, Sucker A, Song M et al. TERT promoter mutations in ocular melanoma distinguish between conjunctival and uveal tumours. *Br J Cancer* 2013;109:497–501.

72. Koopmans AE, Ober K, Dubbink HJ, Paridaens D, Naus NC, Belunek S *et al*. Prevalence and implications of TERT promoter mutation in uveal and conjunctival melanoma and in benign and premalignant conjunctival melanocytic lesions. Invest *Ophthalmol Vis Sci* 2014;55:6024–6030.

73. Demirci H, Demirci FY, Ciftci S, Elner VM, Wu YM, Ning Y et al. Integrative exome and transcriptome analysis of conjunctival melanoma and its potential application for personalized therapy. *JAMA Ophthalmol* 2019;137:1444–1448.

74. Pahlitzsch M, Bertelmann E, Mai C. Conjunctival melanoma and BRAF inhibitor therapy. *J Clin Exp Ophthalmol* 2014;5:1–4.

75. Hong BY, Ford JR, Glitza IC, Torres Cabala CA, Tetzlaff M, Prieto VG *et al*. Immune checkpoint inhibitor therapy as an eye-preserving treatment for locally advanced conjunctival melanoma. *Ophthalmic Plast Reconstr Surg* 2021;37:e9–e13.

76. Dagi Glass LR, Lawrence DP, Jakobiec FA, Freitag SK. Conjunctival melanoma responsive to combined systemic BRAF/MEK inhibitors. *Ophthalmic Plast Reconstr Surg* 2017;33:e114–e116.

77. Kim JM, Weiss S, Sinard JH, Pointdujour-Lim R. Dabrafenib and trametinib for BRAF-mutated conjunctival melanoma. *Ocul Oncol Pathol* 2020;6:35–38.

78. Kini A, Fu R, Compton C, Miller DM, Ramasubramanian A. Pembrolizumab for recurrent conjunctival melanoma. *JAMA Ophthalmol* 2017;135:891–892.

79. Weber JL, Smalley KS, Sondak VK, Gibney GT. Conjunctival melanomas harbor BRAF and NRAS mutations – Letter. *Clin Cancer Res* 2013;19:6329–6330.

80. Maleka A, Astrom G, Bystrom P, Ullenhag GJ. A case report of a patient with metastatic ocular melanoma who experienced a response to treatment with the BRAF inhibitor vemurafenib. *BMC Cancer* 2016;16:634.

81. Pinto Torres S, Andre T, Gouveia E, Costa L, Passos MJ. Systemic treatment of metastatic conjunctival melanoma. *Case Rep Oncol Med* 2017;2017:4623964.

82. Chaves LJ, Huth B, Augsburger JJ, Correa ZM. Eye-sparing treatment for diffuse invasive conjunctival melanoma. *Ocul Oncol Pathol* 2018;4:261–266.

83. Kiyohara T, Tanimura H, Miyamoto M, Shijimaya T, Nagano N, Nakamaru S *et al*. Two cases of BRAF-mutated, bulbar conjunctival melanoma, and review of the published literature. *Clin Exp Dermatol* 2020;45:207–211.

84. Chang M, Lally SE, Dalvin LA, Orloff MM, Shields CL. Conjunctival melanoma with orbital invasion and liver metastasis managed with systemic immune checkpoint inhibitor therapy. *Indian J Ophthalmol* 2019;67:2071–2073.

85. Miura S, Onishi M, Watabe D, Amano H. Conjunctival malignant melanoma treated successfully with BRAF inhibitor: encorafenib plus binimetinib. *Dermatol Online J* 2022;28:17.

86. Fan K, Waninger JJ, Yentz S, McLean S, Demirci H. Neoadjuvant immune checkpoint inhibition in metastatic conjunctival melanoma. *Ophthalmic Plast Reconstr Surg* 2023;39:e152–e155.

87. The Royal College of Pathologists. *Key assurance indicators for pathology services*. Accessed January 2025. Available at: www.rcpath.org/profession/guidelines/kpis-for-laboratory-services.html

88. The Royal College of Pathologists. *Key performance indicators*. Accessed January 2025. Available at: www.rcpath.org/profession/guidelines/kpis-for-laboratory-services.html

Appendix A TNM Classification of conjunctival melanomas (UICC TNM 8)

This should be used for all tumours diagnosed after 1 January 2018.

Primary tumour (pT)

pTX Primary tumour cannot be assessed

pT0 No evidence of primary tumour

pTis Melanoma confined to the conjunctival epithelium (in situ)*

pT1 Melanoma of the bulbar conjunctiva

pT1a Tumour 2.0 mm or less in thickness with invasion of the substantia propria

pT1b Tumour more than 2.0 mm in thickness with invasion of the substantia propria

pT2 Melanoma of the palpebral, forniceal or caruncular conjunctiva

pT2a Tumour 2.0 mm or less in thickness with invasion of the substantia propria

pT2b Tumour more than 2.0 mm in thickness with invasion of the substantia propria

pT3 Melanoma invades the eye, eyelid, nasolacrimal system or orbit

pT3a Invades the globe

pT3b Invades the eyelid

pT3c Invades the orbit

pT3d Invades the paranasal sinus and/or nasolacrimal duct or lacrimal sac

pT4 Melanoma invades the central nervous system

*pTis: Melanoma in situ (please see Table 1) includes the term high-grade C-MIL replacing greater than 75% of the normal epithelial thickness, with cytological features of epithelioid cells, including abundant cytoplasm, vesicular nuclei or prominent nucleoli, and/or presence of intraepithelial nests of atypical cells.

Regional lymph nodes (pN)

pNX Regional lymph nodes cannot be assessed

pN0 No regional lymph node metastasis

pN1 Regional lymph node metastasis

Distant metastasis (pM)

pM0 No evidence of distance metastasis

pM1 Distant metastasis

Stage group: No stage grouping is recommended at this time.

Histopathologic type: This categorisation applies only to melanoma of the conjunctiva.

Histopathologic grade: This grade represents the origin of the primary tumour.

GX Origin cannot be assessed

G0 Primary acquired melanosis without cellular atypia

G1 Conjunctival naevus

G2 C-MIL low- or high-grade (epithelial disease only)

G3 C-MIL low- or high-grade and invasive melanoma

G4 De novo malignant melanoma

Appendix B SNOMED T and M CODES

Sites and subsites for description and their associated SNOMED 'T' codes

T-AA860	Conjunctiva
T-AA861	Plica semilunaris
T-AA862	Caruncle
T-AA880	Bulbar conjunctiva
T-AA863	Conjunctiva fornix-superior
T-AA864	Conjunctiva fornix-inferior
T-AA870	Tarsal conjunctiva

Common SNOMED 'M' codes used in conjunctiva melanoma and melanosis

M-87203	Malignant melanoma
M-87413	Melanoma arising in melanosis
M-57210	Melanosis
M-87200	Naevus
M-87206	Melanoma metastasis

SNOMED P (Procedure) codes

These are used in SNOMED 2 and SNOMED 3 to distinguish biopsies and exenterations, to indicate the nature of the procedure.

Local P codes should be recorded. At present, P codes vary according to the SNOMED system in use in different institutions.

Appendix C Reporting proforma for conjunctival melanoma and conjunctival melanocytic intraepithelial lesions

Surname …… Forename(s) …… Sex ……

Date of birth …… Hospital …… Hospital no. …… NHS no. ……

Date of receipt …… Date of reporting …… Report no. ……

Pathologist …… Surgeon ……

Macroscopic description

For incisional biopsies

Part	Laterality (L/R)	Location	Size of biopsy (mm)	Description of biopsy

For excisional biopsies

Laterality: Right □ Left □

Dimension of specimen(s)……

Location of tumour: Bulbar □ Palpebral □ Fornix □ Caruncle □

Plica semilunaris □ Limbus □ Cornea □ Unspecified □

Tumour characteristics: Unifocal tumour □ Multifocal tumour □

Size of tumour(s)……mm

Non-conjunctival structures involved (specify)……

Microscopic description

(Please see Table 1 for reference, also included at the end of this appendix).

Benign melanosis: Present □ (For incisional, specify which parts ……) Absent □
Low-grade C-MIL: Present □ (For incisional, specify which parts ……) Absent □
High-grade C-MIL: Present □ (For incisional, specify which parts ……) Absent □
Invasive melanoma: Present □ (For incisional, specify which parts……..) Absent □

Maximum invasive melanoma thickness ……mm

Epithelioid cells present in invasive melanoma: yes □ no □

Blood vessel/lymphatic invasion: yes □ no □

Ulceration: yes □ no □

Mitotic rate (for excisional biopsy) …… mm^2

Anatomical structures involved by invasive melanoma (specify): …….

Other features …….

Excision margins

Distance to nearest peripheral margin by invasive melanoma is ……mm
(clear □ involved □ for incisional, specify which parts ……)

Distance to nearest deep margin by invasive melanoma is…….mm
(clear/involved – for incisional, specify which parts ……..)

Distance to nearest peripheral margin by low/high grade C-MIL …….mm
(excision biopsies only: clear/involved).

Comments

Pathological staging (excision specimens only) pT pN pM
(UICC TNM 8th edition)

SNOMED codes T……. / M…….

Signature……. Date…….

Table 1: WHO 2022 classification of C-MIL.[31]

WHO	Acceptable alternative terminology	Increased cellularity	Histologic features	Risk of association with or progression to invasive melanoma
Not applicable	Bening melanosis c-MIN (grades 0–1) PAM without atypia	No/minimal	Conjunctival hypermelanosis (increased pigment in epithelial cells without melanocytic hyperplasia or atypia). Slight or focal melanocytic hyperplasia without atypia (parabasal melanocytes with condensed round nuclei, smaller than basal epithelial cell, inconspicuous nucleoli and inconspicuous cytoplasm) may be seen.	None
Low-grade C-MIL	PAM with mild atypia c-MIN (grades 2–4)	Yes	Predominantly basilar melanocytic proliferation with low-grade atypia (dendritic or small to moderate size polyhedral, usually non-epithelioid melanocytes with round to irregular nuclear contours, often nuclear hyperchromasia, inconspicuous nucleoli, and inconspicuous or scant cytoplasm).	Lower
High-grade C-MIL	PAM with moderate to severe atypia c-MIN (grades 5–10)	Yes	More confluent basilar and significant non-basilar proliferation of melanocytes with high-grade atypia (moderate to severe), evidence of intraepithelial nested and/or pagetoid growth, and epithelioid cell cytomorphology.	Higher
	Melanoma in situ	Yes	The term melanoma in situ may be used for (1) the most atypical high-grade C-MILs involving close to full thickness of the epithelium, (2) histologically obvious melanomas without documented evidence of subepithelial invasion.	Highest

Appendix D Reporting proforma for conjunctival melanoma and conjunctival melanocytic intraepithelial lesions in list format

Element name	Values	Implementation notes
Laterality	Single selection value list: • Right • Left	
Dimension of specimen(s)	Free text	
Location of tumour	Single selection value list: • Bulbar • Palpebral • Fornix • Caruncle • Plica semilunaris • Limbus • Cornea • Unspecified	
Tumour characteristics	Single selection value list: • Unifocal tumour • Multifocal tumour	
Size of tumour(s)	Size in mm	
Non-conjunctival structures involved (specify)	Free text	
Benign melanosis	Single selection value list: • Present • Absent	
For incisional, specify which parts	Free text	
Low-grade C-MIL	Single selection value list: • Present • Absent	
For incisional, specify which parts	Free text	
High-grade C-MIL	Single selection value list: • Present • Absent	

For incisional, specify which parts	Free text	
Invasive melanoma	Single selection value list: • Present • Absent	
For incisional, specify which parts	Free text	
Maximum invasive melanoma thickness	Size in mm	
Epithelioid cells present in invasive melanoma	Single selection value list: • Yes • No	
Blood vessel/lymphatic invasion	Single selection value list: • Yes • No	
Ulceration	Single selection value list: • Yes • No	
Mitotic rate (for excisional biopsy)	Size in mm^2	
Anatomical structures involved by invasive melanoma (Specify)	Free text	
Other features	Free text	
Distance to nearest peripheral margin by invasive melanoma is	Size in mm	
	Single selection value list: • Clear • Involved	
For incisional, specify which parts	Free text	
Distance to nearest deep margin by invasive melanoma is	Size in mm	
	Single selection value list: • Clear • Involved	
For incisional, specify which parts	Free text	

Distance to nearest peripheral margin by low/ high grade C-MIL	Size in mm	
	Single selection value list: • Clear • Involved	
UICC TNM version 8 pM stage	Single selection value list: • pT • pN • pM	
SNOMED topography code	May have multiple codes. Look up from SNOMED tables.	

Appendix E Summary table – Explanation of grades of evidence

(modified from Palmer K *et al. BMJ* 2008;337:1832)

Grade (level) of evidence	Nature of evidence
Grade A	At least 1 high-quality meta-analysis, systematic review of randomised controlled trials or a randomised controlled trial with a very low risk of bias and directly attributable to the target population or A body of evidence demonstrating consistency of results and comprising mainly well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias, directly applicable to the target cancer type.
Grade B	A body of evidence demonstrating consistency of results and comprising mainly high-quality systematic reviews of case-control or cohort studies and high-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal, and which are directly applicable to the target population or Extrapolation evidence from studies described in A.
Grade C	A body of evidence demonstrating consistency of results and including well-conducted case-control or cohort studies and high-quality case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal, and which are directly applicable to the target population or Extrapolation evidence from studies described in B.
Grade D	Non-analytic studies such as case reports, case series or expert opinion or Extrapolation evidence from studies described in C.
Good practice point (GPP)	Recommended best practice based on the clinical experience of the authors of the writing group.

Appendix F AGREE II guideline monitoring sheet

The guidelines of the Royal College of Pathologists comply with the AGREE II standards for good quality clinical guidelines. The sections of this guideline that indicate compliance with each of the AGREE II standards are indicated in the table.

AGREE standard	Section of guideline
Scope and purpose	
1 The overall objective(s) of the guideline is (are) specifically described	Foreword
2 The health question(s) covered by the guideline is (are) specifically described	1
3 The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described	Foreword, 1
Stakeholder involvement	
4 The guideline development group includes individuals from all the relevant professional groups	Foreword
5 The views and preferences of the target population (patients, public, etc.) have been sought	Foreword
6 The target users of the guideline are clearly defined	Foreword, 1
Rigour of development	
7 Systematic methods were used to search for evidence	Foreword
8 The criteria for selecting the evidence are clearly described	Foreword
9 The strengths and limitations of the body of evidence are clearly described	Foreword
10 The methods for formulating the recommendations are clearly described	Foreword
11 The health benefits, side effects and risks have been considered in formulating the recommendations	Foreword, 1
12 There is an explicit link between the recommendations and the supporting evidence	2–8
13 The guideline has been externally reviewed by experts prior to its publication	Foreword
14 A procedure for updating the guideline is provided	Foreword
Clarity of presentation	
15 The recommendations are specific and unambiguous	2–8
16 The different options for management of the condition or health issue are clearly presented	2–8
17 Key recommendations are easily identifiable	2–8
Applicability	

18	The guideline describes facilitators and barriers to its application	Foreword
19	The guideline provides advice and/or tools on how the recommendations can be put into practice	Appendices A–D
20	The potential resource implications of applying the recommendations have been considered	Foreword
21	The guideline presents monitoring and/or auditing criteria	9
Editorial independence		
22	The views of the funding body have not influenced the content of the guideline	Foreword
23	Competing interest of guideline development group members have been recorded and addressed	Foreword