### NCCN Guidelines Version 1.2018 Panel Members

#### Uveal Melanoma

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**Expert Disclosures**

© Ophthalmology

† Medical oncology

▷ Internal medicine

□ Dermatology

¶ Surgery/Surgical oncology

≥ Pathology

¥ Patient advocacy

♣ Hematology/Hematology oncology

§ Radiotherapy/Radiation oncology

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© Ophthalmology

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¥ Patient advocacy

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§ Radiotherapy/Radiation oncology

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NCCN Guidelines Version 1.2018 Sub-Committee
Uveal Melanoma

NCCN Guidelines Panel Disclosures

NCCN Guidelines Version 1.2018 Table of Contents
Uveal Melanoma

NCCN Uveal Melanoma Panel Members
NCCN Uveal Melanoma Subcommittee Members

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Clinical Trials: NCCN believes that the best management for any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
To find clinical trials online at NCCN Member Institutions, click here: nccn.org/clinical_trials/physician.html.

NCCN Categories of Evidence and Consensus: All recommendations are category 2A unless otherwise indicated.
See NCCN Categories of Evidence and Consensus.

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NCCN Guidelines Version 1.2018
Uveal Melanoma

CLINICAL PRESENTATION

- Suspicous pigmented uveal tumor of ciliary body and/or choroida
  - Symptoms may include:
    - Vision loss
    - Vision changes (e.g., blurred vision, photopsia, floaters, metamorphopsia)
  - May be asymptomatic
  - Assessment of risk factors for developing uveal melanomab

WORKUP AND DIAGNOSIS

- Clinical evaluation, including:
  - H&P, including history of prior or current cancers (outside the eye)
  - Color fundus photography
  - Ultrasound of eye and orbit
  - Comprehensive eye exam: Examine the front and back of eye (biomicroscopy)
    - Dilated fundus exam (indirect ophthalmoscopy)
    - Measure vision acuity
    - Measure and document location and the size of the tumor (diameter, thickness)
    - Assess and document if present:
      - Subretinal fluid
      - Orange pigment
  - Additional testing options include:
    - Autofluorescence of the ocular fundus
    - Optical coherence tomography
    - Retinal fluorescein angiography of the ocular fundus
    - Transillumination
    - MRI occasionally needed to confirm diagnosis
    - Consider biopsy if needed to confirm diagnosisc or for prognostic analysis for risk stratificationd

CLINICAL STAGING

- Diagnosis uncertain and/or <3 risk factors for growthe
- Uveal melanoma

Observe and re-evaluate for growth or features of malignancyf
- Every 1–4 monthsg until clinically stable
- Then close follow-up for 5 yearsg
- Then annually thereafter

See Workup and Staging for uveal melanoma (UM-2)

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

aThis guideline does not include the management of iris melanoma.
bSee Risk Factors for Development of Uveal Melanoma (UM-A).
cBiopsy is usually not necessary for initial diagnosis of uveal melanoma and selection of first-line treatment, but may be useful in cases of uncertainty regarding diagnosis, such as for amelanotic tumors, or retinal detachment.
dBiopsy of the primary tumor does not impact outcome, but may provide prognostic information that can help inform frequency of follow-up and may be needed for eligibility for clinical trials. Specimen should be sent for histology, chromosome analysis, and/or gene expression profiling. The risks/benefits of biopsy for prognostic analysis should be carefully considered and discussed.
eRisk factors or growth of small melanocytic tumors: presence of symptoms, tumor thickness >2 mm, tumor diameter >5 mm, presence of subretinal fluid and orange pigment, tumor margin within 3 mm of optic disk, ultrasound hollowness, absence of halo.
fThe recommendation to “observe and re-evaluate” consists of tests listed under “Workup and Diagnosis” that would help to clarify if there is progression and determine the natural history of the indeterminate lesion.
gFrequency of evaluation should depend on index of suspicion, patient age, and medical frailty.
**WORKUP AND STAGING**

- Ocular imaging if not previously done:
  - If large tumor, close to nerve or suspicion of extraocular involvement, MRI of orbit with and without IV contrast
  - Assess and document, if present:
    - Ciliary body involvement
    - Extraocular extension
  - Extraocular imaging:
    - Baseline imaging to screen for distant disease
  - Consider biopsy of primary tumor for prognostic analysis

- Metastasis

**TUMOR SIZE**

- **Largest diameter 5–16 mm and thickness <2.5 mm**
- **Largest diameter ≤18 mm and thickness 2.5–10 mm**
- **Largest diameter >18 mm [any thickness] or Thickness >10 mm [any diameter] or Thickness >8 mm with optic nerve involvement [any diameter]**

**PRIMARY TREATMENT**

**Options:**
- Brachytherapy plaque
- Particle beam radiation
- Laser ablation in highly select patients

**Options:**
- Brachytherapy plaque
- Particle beam radiation
- Enucleation

**Options:**
- RT
  - Particle beam radiation (preferred)
  - Stereotactic radiosurgery (SRS)
- Enucleation

---

**Note:** All recommendations are category 2A unless otherwise indicated.

**Clinical Trials:** NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.
ADDITIONAL PRIMARY TREATMENT

Extraocular extension at the time of enucleation

- Microscopically positive or close margins after enucleation (but no clinical, intraoperative, or radiographic evidence of gross residual disease in the orbit)
- Visible extraocular tumor or suspicion of gross disease in the orbit

| Observe or Map biopsy and/or Consider RT to orbit (particle beam or photon beam)\(^n\) |
| Biopsy extraocular tissue if possible and one or more of the following: • Intraoperative cryotherapy • Orbital exenteration • RT to orbit (particle beam or photon beam)\(^n\) |

All others

\(^n\)See Principles of Radiation Therapy (UM-B).

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### NCCN Guidelines Version 1.2018
#### Uveal Melanoma

<table>
<thead>
<tr>
<th>RISK OF DISTANT METASTASIS&lt;sup&gt;w&lt;/sup&gt;</th>
<th>SYSTEMIC IMAGING BASED ON RISK STRATIFICATION&lt;sup&gt;l&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low risk:</strong></td>
<td>• Imaging to evaluate signs or symptoms as clinically indicated</td>
</tr>
<tr>
<td>• Class 1A&lt;sup&gt;x&lt;/sup&gt;</td>
<td>• Consider surveillance imaging&lt;sup&gt;y&lt;/sup&gt;</td>
</tr>
<tr>
<td>• Disomy 3</td>
<td></td>
</tr>
<tr>
<td>• Gain of chromosome 6p</td>
<td></td>
</tr>
<tr>
<td>• <strong>EIF1AX</strong> mutation</td>
<td></td>
</tr>
<tr>
<td>• T1 (AJCC) (See ST-1 and ST-2)</td>
<td></td>
</tr>
<tr>
<td>• Spindle cells</td>
<td></td>
</tr>
<tr>
<td><strong>Medium risk:</strong></td>
<td></td>
</tr>
<tr>
<td>• Class 1B&lt;sup&gt;x&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>• <strong>SF3B1</strong> mutation</td>
<td></td>
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<tr>
<td>• T2 and T3 (AJCC) (See ST-1 and ST-2)</td>
<td></td>
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<tr>
<td>• Mixed histology (spindle and epithelioid cells)</td>
<td></td>
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<tr>
<td><strong>High risk:</strong></td>
<td></td>
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<tr>
<td>• Class 2&lt;sup&gt;x&lt;/sup&gt;</td>
<td></td>
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<tr>
<td>• Monosomy 3</td>
<td>• Imaging to evaluate signs or symptoms every 6–12 months for 10 years, then as clinically indicated</td>
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<tr>
<td>• Gain of chromosome 8q</td>
<td></td>
</tr>
<tr>
<td>• <strong>BAP1</strong> mutation</td>
<td></td>
</tr>
<tr>
<td>• <strong>PRAME</strong> mutation</td>
<td></td>
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<tr>
<td>• T4 (AJCC) (See ST-1 and ST-2)</td>
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<tr>
<td>• Epithelioid cells</td>
<td></td>
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<tr>
<td>• Extraocular extension</td>
<td></td>
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<tr>
<td>• Ciliary body involvement</td>
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</table>

<sup>1</sup>The most frequent sites of metastasis are liver, lungs, skin/soft tissue, and bones. At minimum, all patients should have contrast-enhanced MR or ultrasound of the liver, with modality preference determined by expertise at the treating institution. Additional imaging modalities may include chest/abdominal/pelvic CT with contrast. However, screening should limit radiation exposure whenever possible. Scans should be performed with IV contrast unless contraindicated.

<sup>2</sup>The affected eye should be imaged with color fundus photography and ultrasonography every 3–6 months for 3–5 years, then every 6–12 months thereafter, if stable. The frequency of follow-up should depend on the size and location (eg, juxtapapillary location, ciliary body involvement) of the tumor at presentation. Radiation-related retinopathy and other treatment-related complications often occur between 18 months to 3 years after treatment.

<sup>3</sup>The contralateral eye is not at increased risk of uveal melanoma, and can be followed with routine ophthalmologic care.

<sup>4</sup>Recognizing that there are limited options for systemic recurrence and that regular imaging may cause patient anxiety, some patients may elect to forgo surveillance imaging.

<sup>5</sup>Additional risk factors for recurrence: Juxtapapillary location and ciliary body involvement.

<sup>6</sup>Liver function tests (LFTs) may be considered as part of follow-up, although some studies showed poor sensitivity for early detection of liver metastases.

<sup>7</sup>If biopsy not performed, then follow medium- or high-risk pathways, depending on whether any high-risk features are present.


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**Clinical Trials:** NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.
Recurrence or metastasis

WORKUP

- H&P
- Biopsy if clinically appropriate
- Ocular orbital imaging if not previously done
- Imaging to evaluate extent of local recurrence and/or for baseline staging

Extraocular involvement

- Surgical resection
  - ± RT to orbit (particle beam or photon beam)
  - ± cryotherapy to orbital tumor

Intraocular recurrence (limited to eye, no orbital involvement)

- RT (plaque brachytherapy or particle beam)
  or
  - Enucleation
  or
  - Laser ablation

Orbital involvement in patients with prior enucleation

- Surgical resection
  or
  - Cryotherapy to orbital tumor
  and/or
  - RT to orbit (particle beam or photon beam)

Distant metastatic disease

(See UM-6)

\[^n^\]See Principles of Radiation Therapy (UM-B).

\[^2^\]Extraocular recurrence or metastasis should be confirmed histologically whenever possible or if clinically indicated. Biopsy techniques may include FNA or core. Obtain tissue for genetic analysis (screening for mutations that may be potential targets for treatment or determine eligibility for a clinical trial) from either biopsy of the metastasis (preferred) or archival material if the patient is being considered for targeted therapy. Consider broader genomic profiling if the test results might guide future decisions or eligibility for participation in a clinical trial.

\[^aa^\]Intraocular recurrence can often be diagnosed and managed without a biopsy.

\[^bb^\]The most frequent sites of metastasis are liver, lungs, skin/soft tissue, and bones. At minimum, all patients should have contrast-enhanced MR or ultrasound of the liver, with modality preference determined by expertise at the treating institution. Additional imaging may include chest/abdominal/pelvic CT with contrast and/or whole-body FDG PET/CT; however, screening should limit radiation exposure whenever possible. Brain MRI with IV contrast may be performed if neurologic symptoms are present, but routine CNS imaging is not recommended. Scans should be performed with IV contrast unless contraindicated.

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WORKUP  |  TREATMENT OF METASTATIC DISEASE
---|---
**Distant metastatic disease**
- Biopsy if clinically appropriate
- LDH
- Imaging for baseline staging and to evaluate specific signs and symptoms

**One or more of the following options:**
- Clinical trial (preferred)
-  
  - Liver-directed therapies:
    - Regional isolation perfusion of the liver
    - Chemoembolization
    - Radioembolization
- Therapies for systemic disease:
  - Systemic therapy
  - Consider resection and/or RT (photon beam or SRS) for limited or symptomatic disease
- Best supportive/palliative care (See NCCN Guidelines for Palliative Care)

**Clinical trial (preferred) or Observation (See Follow-up UM-4)**

**No evidence of disease**

**Imaging** to assess response or progression

**Residual or progressive disease**

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RISK FACTORS FOR DEVELOPMENT OF UVEAL MELANOMA

- Patients with the following risk factors are at increased risk of developing uveal melanoma:
  - Choroidal nevi
  - Ocular/oculodermal melanocytosis (hyperpigmentation of episclera, uvea, and skin)
  - Familial uveal melanoma (e.g., germline \textit{BAP1} mutation, neurofibromatosis [NF-1], dysplastic nevus syndrome [BK-mole])
- The presence of cutaneous melanoma does not increase the risk of uveal melanoma.

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Plaque Brachytherapy

- Plaque brachytherapy is a common form of definitive radiotherapy for the primary tumor.\(^1\) A prospective trial found no difference in cause-specific survival among patients with tumors 2.5–10 mm in apical height and ≤16 mm in maximum basal diameter randomized to plaque brachytherapy or enucleation.\(^2\)
- Plaque brachytherapy is appropriate for patients with tumors ≤18 mm in largest base diameter, ≤10 mm in thickness.
- Plaque brachytherapy is appropriate as an upfront therapy after initial diagnosis, or after local recurrence following a prior local therapy.
- Plaque brachytherapy should be performed by an experienced multidisciplinary team including an ophthalmic oncologist, radiation oncologist, and brachytherapy physicist.\(^3\)
- Tumor localization for brachytherapy may be performed using indirect ophthalmoscopy, transillumination, light pipe diathermy, and/or ultrasound (intraoperative and/or preoperative).\(^4\) MRI may be used for preoperative planning.
- Using 125Iodine Collaborative Ocular Melanoma Study (COMS) plaques with 85 Gy should be prescribed to the apex of the tumor at low dose rate (≥0.6 Gy/h). The plaque margin on the tumor border should be ≥2 mm when feasible (diameter of plaque ≥4 mm larger than largest base diameter of tumor). The exception is for tumors near the optic nerve where it may be impossible to achieve adequate coverage of the margins. The largest commercially available brachytherapy plaque is 22 mm in diameter; thus, plaque brachytherapy is recommended only for tumors with largest basal diameter ≤18 mm.
- Using other radioisotopes (eg, 106ruthenium, 103palladium, 90strontium, 60cobalt, 131cesium), or non-COMS 125iodine plaques, 60–100 Gy may be prescribed at low dose rate to the tumor apex; alternatively, a minimum dose may be prescribed to the base of the tumor. The plaque margin on the tumor border may vary for other radioisotopes.
- Round plaques are most commonly used, although non-round plaques (eg, notched) can be considered for tumors in specific locations (eg, peripapillary).
Particle Beam Therapy

- Particle beam therapy is a common form of definitive radiotherapy for the primary tumor. A prospective trial found no difference in cause-specific survival among patients with tumors ≤15 mm in maximum basal diameter and ≤11 mm in apical height randomized to plaque brachytherapy or particle beam therapy.
- Particle beam therapy is appropriate as upfront therapy after initial diagnosis, after margin-positive enucleation, or for intraocular or orbital recurrence.
- Particle beam therapy should be performed by an experienced multidisciplinary team including an ophthalmic oncologist, radiation oncologist, and particle beam physicist.
- Tumor localization for particle beam therapy may be performed using indirect ophthalmoscopy, transillumination, and/or ultrasound (intraoperative and/or preoperative), MRI, and/or CT.
- For intraocular tumors:
  - Using protons, 50–70 cobalt Gray equivalent (CGyE) in 4–5 fractions should be prescribed to encompass the planning target volume surrounding the tumor.
  - Using carbon ions, 60–85 CGyE in 5 fractions should be prescribed to encompass the planning target volume surrounding the tumor.
  - Fiducial markers (tantalum clips) are encouraged to permit eye and tumor position verification for image-guided radiotherapy delivery.
  - Volumetric planning in 3 dimensions (with or without CT and/or MRI) is encouraged to maximize radiation delivery to tumor and minimize radiation delivery to organs and tissues at risk of injury from radiation.
PRINCIPLES OF RADIATION THERAPY

Stereotactic Radiosurgery (SRS)
- SRS is the least often used and non-preferred form of definitive radiotherapy for the treatment of primary or recurrent intraocular tumors. Few prospective studies have assessed the efficacy and safety of radiosurgery.\[10,11\]
- Tumor localization, fiducial marker use, and planning for SRS are generally consistent with particle beam therapy approaches.
- Using fractionated SRS: 45–70 Gy in 2–5 fractions should be prescribed.
- Using single-fraction SRS: 18–45 Gy in 1 fraction should be prescribed.

Photon Beam Radiotherapy
- Photon beam radiotherapy is a preferred option as an adjuvant to surgery for orbital involvement.
  - Adjuvant radiotherapy can be used in patients at risk for local recurrence (margin-positive enucleation or exenteration) or regional recurrence (resected regional metastases).
  - A dose of 20–30 Gy in 5 fractions should be prescribed to the clinical target volume at risk for recurrence\[12,13\] using intensity-modulated techniques with image guidance.
  - Photon beam radiotherapy can be used for treatment of distant metastases at risk for causing symptoms or for palliation of symptomatic distant metastases.
    - Doses of 8–30 Gy in 1–10 fractions should be prescribed to the appropriate target volume\[14\] using appropriate 3-D or intensity-modulated radiation therapy (IMRT) techniques with or without image guidance.

Radioembolization
- Selective internal radiation therapy for patients with liver metastases using $^{90}$Ytrrium has been reported in retrospective studies.\[15\]
- Further study is required to determine the appropriate patients for and risks and benefits of this approach.

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**PRINCIPLES OF RADIATION THERAPY**

(References)


SYSTEMIC THERAPY FOR METASTATIC OR UNRESECTABLE DISEASE¹
(Clinical Trial Preferred)

Consider one or more of the following options:

**Immunotherapy**
- Anti PD-1 monotherapy
  - Pembrolizumab²,³
  - Nivolumab²,³
  - Nivolumab/ipilimumab²,³
  - Ipilimumab²,³

**Cytotoxic Regimens**
- Dacarbazine
- Temozolomide
- Paclitaxel
- Albumin-bound paclitaxel
- Carboplatin/paclitaxel

**Targeted Therapy**²,⁴
- Trametinib

¹When available and clinically appropriate, enrollment in a clinical trial is recommended. The literature is not directive regarding the specific systemic agent(s) offering superior outcomes, but does provide evidence that uveal melanoma is sensitive to some of the same systemic therapies used to treat cutaneous melanoma. Although uveal melanomas have lower response rates to systemic therapies than cutaneous melanoma, individual patients on occasion may derive substantial benefit. The agents listed above have been used with some success in patients with uveal melanoma.

²See Management of Toxicities Associated with Immunotherapy and Targeted Therapy from the NCCN Guidelines for Melanoma (cutaneous) (ME-I).

³See NCCN Guidelines for Management of Immunotherapy-Related Toxicities.

⁴The listed systemic therapy options do not cover BRAF or KIT mutated tumors. In general, uveal melanomas rarely have BRAF or KIT mutations.

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SYSTEMIC THERAPY FOR METASTATIC OR UNRESECTABLE DISEASE (REFERENCES)

**Immunotherapy**

**Pembrolizumab and Nivolumab**

**Nivolumab/ipilimumab**

**Ipilimumab**
SYSTEMIC THERAPY FOR METASTATIC OR UNRESECTABLE DISEASE (REFERENCES)

**Cytotoxic Regimens**

**Dacarbazine**

**Temozolomide**

**Paclitaxel**

**Albumin-bound paclitaxel**

**Paclitaxel/carboplatin**

**Targeted Therapy**

**Trametinib**
## Table 1
American Joint Committee on Cancer (AJCC) Definitions of TNM for Choroidal and Ciliary Body Melanoma (8th ed., 2017)
Definition of Primary Tumor (T)

<table>
<thead>
<tr>
<th>T Category</th>
<th>T Criteria</th>
</tr>
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<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor size category 1</td>
</tr>
<tr>
<td>T1a</td>
<td>Tumor size category 1 without ciliary body involvement</td>
</tr>
<tr>
<td>T1b</td>
<td>Tumor size category 1 with ciliary body involvement</td>
</tr>
<tr>
<td>T1c</td>
<td>Tumor size category 1 without ciliary body involvement but with extraocular extension ≤5 mm in largest diameter</td>
</tr>
<tr>
<td>T1d</td>
<td>Tumor size category 1 with ciliary body involvement and extraocular extension ≤5 mm in largest diameter</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor size category 2</td>
</tr>
<tr>
<td>T2a</td>
<td>Tumor size category 2 without ciliary body involvement</td>
</tr>
<tr>
<td>T2b</td>
<td>Tumor size category 2 with ciliary body involvement</td>
</tr>
<tr>
<td>T2c</td>
<td>Tumor size category 2 without ciliary body involvement but with extraocular extension ≤5 mm in largest diameter</td>
</tr>
<tr>
<td>T2d</td>
<td>Tumor size category 2 with ciliary body involvement and extraocular extension ≤5 mm in largest diameter</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor size category 3</td>
</tr>
<tr>
<td>T3a</td>
<td>Tumor size category 3 without ciliary body involvement</td>
</tr>
<tr>
<td>T3b</td>
<td>Tumor size category 3 with ciliary body involvement</td>
</tr>
<tr>
<td>T3c</td>
<td>Tumor size category 3 without ciliary body involvement but with extraocular extension ≤5 mm in largest diameter</td>
</tr>
<tr>
<td>T3d</td>
<td>Tumor size category 3 with ciliary body involvement and extraocular extension ≤5 mm in largest diameter</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor size category 4</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumor size category 4 without ciliary body involvement</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor size category 4 with ciliary body involvement</td>
</tr>
<tr>
<td>T4c</td>
<td>Tumor size category 4 without ciliary body involvement but with extraocular extension ≤5 mm in largest diameter</td>
</tr>
<tr>
<td>T4d</td>
<td>Tumor size category 4 with ciliary body involvement and extraocular extension ≤5 mm in largest diameter</td>
</tr>
<tr>
<td>T4e</td>
<td>Any tumor size category with extraocular extension &gt;5 mm in largest diameter</td>
</tr>
</tbody>
</table>

1. Primary ciliary body and choroidal melanomas are classified according to the four tumor size categories defined in Figure 1. (See ST-4)
2. In clinical practice, the largest tumor basal diameter may be estimated in optic disc diameters (DD; average: 1 DD = 1.5 mm), and tumor thickness may be estimated in diopters (average: 2.5 diopters = 1 mm). Ultrasonography and fundus photography are used to provide more accurate measurements.
3. When histopathologic measurements are recorded after fixation, tumor diameter and thickness may be underestimated because of tissue shrinkage.

---

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**Clinical Trials:** NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.
Table 1 (continued)
Definition of Primary Tumor (T)

<table>
<thead>
<tr>
<th>T Category</th>
<th>T Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor size category 1</td>
</tr>
<tr>
<td>T1a</td>
<td>Tumor size category 1 without ciliary body involvement and extraocular extension</td>
</tr>
<tr>
<td>T1b</td>
<td>Tumor size category 1 with ciliary body involvement</td>
</tr>
<tr>
<td>T1c</td>
<td>Tumor size category 1 without ciliary body involvement but with extraocular extension ≤5 mm in largest diameter</td>
</tr>
<tr>
<td>T1d</td>
<td>Tumor size category 1 with ciliary body involvement and extraocular extension ≤5 mm in largest diameter</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor size category 2</td>
</tr>
<tr>
<td>T2a</td>
<td>Tumor size category 2 without ciliary body involvement and extraocular extension</td>
</tr>
<tr>
<td>T2b</td>
<td>Tumor size category 2 with ciliary body involvement</td>
</tr>
<tr>
<td>T2c</td>
<td>Tumor size category 2 without ciliary body involvement but with extraocular extension ≤5 mm in largest diameter</td>
</tr>
<tr>
<td>T2d</td>
<td>Tumor size category 2 with ciliary body involvement and extraocular extension ≤5 mm in largest diameter</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T Category</th>
<th>T Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>T3</td>
<td>Tumor size category 3</td>
</tr>
<tr>
<td>T3a</td>
<td>Tumor size category 3 without ciliary body involvement and extraocular extension</td>
</tr>
<tr>
<td>T3b</td>
<td>Tumor size category 3 with ciliary body involvement</td>
</tr>
<tr>
<td>T3c</td>
<td>Tumor size category 3 without ciliary body involvement but with extraocular extension ≤5 mm in largest diameter</td>
</tr>
<tr>
<td>T3d</td>
<td>Tumor size category 3 with ciliary body involvement and extraocular extension ≤5 mm in largest diameter</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor size category 4</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumor size category 4 without ciliary body involvement and extraocular extension</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor size category 4 with ciliary body involvement</td>
</tr>
<tr>
<td>T4c</td>
<td>Tumor size category 4 without ciliary body involvement but with extraocular extension ≤5 mm in largest diameter</td>
</tr>
<tr>
<td>T4d</td>
<td>Tumor size category 4 with ciliary body involvement and extraocular extension ≤5 mm in largest diameter</td>
</tr>
<tr>
<td>T4e</td>
<td>Any tumor size category with extraocular extension &gt;5 mm in largest diameter</td>
</tr>
</tbody>
</table>

Note:
1. Primary ciliary body and choroidal melanomas are classified according to the four tumor size categories defined in Figure 1. (See ST-4)
2. In clinical practice, the largest tumor basal diameter may be estimated in optic disc diameters (DD; average: 1 DD = 1.5 mm), and tumor thickness may be estimated in diopters (average: 2.5 diopters = 1 mm). Ultrasonography and fundus photography are used to provide more accurate measurements.
3. When histopathologic measurements are recorded after fixation, tumor diameter and thickness may be underestimated because of tissue shrinkage.

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### Table 1 (continued)

**Choroidal/Ciliary Body Melanomas**

#### Definition of Regional Lymph Node (N)

<table>
<thead>
<tr>
<th>N Category</th>
<th>N Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node involvement</td>
</tr>
<tr>
<td>N1</td>
<td>Regional lymph node metastases or discrete tumor deposits in the orbit</td>
</tr>
<tr>
<td>N1a</td>
<td>Metastasis in one or more regional lymph node(s)</td>
</tr>
<tr>
<td>N1b</td>
<td>No regional lymph nodes are positive, but there are discrete tumor deposits in the orbit that are not contiguous to the eye (choroidal and ciliary body).</td>
</tr>
</tbody>
</table>

#### Definition of Distant Metastasis (M)

<table>
<thead>
<tr>
<th>M Category</th>
<th>M Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant metastasis by clinical classification</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
<tr>
<td>M1a</td>
<td>Largest diameter of the largest metastasis ≤3.0 cm</td>
</tr>
<tr>
<td>M1b</td>
<td>Largest diameter of the largest metastasis 3.1–8.0 cm</td>
</tr>
<tr>
<td>M1c</td>
<td>Largest diameter of the largest metastasis ≥8.1 cm</td>
</tr>
</tbody>
</table>

#### Histologic Grade (G)

<table>
<thead>
<tr>
<th>G</th>
<th>G Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>GX</td>
<td>Grade cannot be assessed</td>
</tr>
<tr>
<td>G1</td>
<td>Spindle cell melanoma (&gt;90% spindle cells)</td>
</tr>
<tr>
<td>G2</td>
<td>Mixed cell melanoma (&gt;10% epithelioid cells and &lt;90% spindle cells)</td>
</tr>
<tr>
<td>G3</td>
<td>Epithelioid cell melanoma (&gt;90% epithelioid cells)</td>
</tr>
</tbody>
</table>

**Note:** Because of the lack of universal agreement regarding which proportion of epithelioid cells classifies a tumor as mixed or epithelioid, some ophthalmic pathologists currently combine grades 2 and 3 (non-spindle, i.e. epithelioid cells detected) and contrast them with grade 1 (spindle, i.e., no epithelioid cells detected).

#### AJCC PROGNOSTIC STAGE GROUPS

**Choroidal and Ciliary Body Melanomas**

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>T1a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T1b–d</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T2b</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T2c–d</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3b–c</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T3d</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4b–c</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIC</td>
<td>T4d–e</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>Any N</td>
<td>M1a–c</td>
</tr>
</tbody>
</table>

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FIGURE 1: CLASSIFICATION OF CILIARY BODY AND CHOROID UVEAL MELANOMA BASED ON THICKNESS AND DIAMETER

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# Discussion

## NCCN Categories of Evidence and Consensus

**Category 1:** Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

**Category 2A:** Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

**Category 2B:** Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

**Category 3:** Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

All recommendations are category 2A unless otherwise noted.