AIM Cancer Treatment Pathways

EFFECTIVE AUGUST 12, 2019
LAST REVIEWED MAY 28, 2019
Review and updates during 2nd quarter 2019

Kidney Cancer (Renal Cell Carcinoma)

- Pembrolizumab (Keytruda) and axitinib (Inlyta) combination regimen added as a pathway option in the following clinical scenario: ‘Metastatic Disease | First Line of Therapy (1st Line) | Clear Cell Carcinoma’
- The following regimens have been removed as a pathway option from the clinical scenario: ‘Metastatic Disease | First Line of Therapy (1st Line)’
  - High dose intravenous (IV) interleukin-2 (IL2, Proleukin)
  - Pazopanib (Votrient)
  - Sunitinib (Sutent)
  - Temsirolimus (Torisel)

Metastatic Melanoma

- Encorafenib (Braftovi) and binimetinib (Mektovi) combination regimen added as a pathway option AND vemurafenib (Zelboraf) and cobimetinib (Cotellic) removed as a pathway option from the following clinical scenarios:
  - ‘Metastatic Disease | First Line of Therapy (1st Line) | BRAF Mutated | Symptomatic Disease | ECOG PS 0-2’
  - ‘Metastatic Disease | Second and Subsequent Lines of Therapy (2nd Line +) | BRAF Mutated | Symptomatic Disease | ECOG PS 0-2’

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AIM Cancer Treatment Pathways

The goal of the medical oncology programs administered by AIM on behalf of our clients is to help provide access to quality and affordable cancer care. AIM Cancer Treatment Pathways are a key component of each program.

AIM Pathways are developed using a rigorous process of evidence-based medicine. Pathways differ from clinical practice guidelines in that the objective of a Pathway is to identify a subset of regimens supported by clinical evidence and practice guidelines with the goal of further reducing unwarranted variation in care and cost. Pathways are selected based on: clinical benefit (efficacy), safety/side effects (especially those leading to hospitalizations & impacting quality of life), strength of national guideline recommendations, and cost of regimens. Dosage and drug schedules (i.e. the interval between doses) may be considered in the selection of Pathway regimens. AIM Pathways are intended to support the use of quality cancer care.

Pathways are not available for every medical condition, but are intended to be applicable for individuals with the most common cancer types. Within each cancer type, separate Pathways are usually available for early stage and advanced cancer, sub-types of cancer (e.g. HER2 positive) and different lines of therapy. When selecting the best cancer treatment for a patient a treating oncologist should consider the type of cancer, the stage, the biomarkers or specific genetic profile of the cancer, and unique aspects the individual’s medical condition. Given the complexity of cancer and all of the unique individual circumstances, it would not be possible to have a Pathway option available for every specific situation. The treating oncologist will determine if, in his/her medical opinion, an AIM Pathway treatment regimen is the best option for a patient or whether, given his or her unique circumstances, another treatment regimen will be a better choice.

It is important to note that, for some health plans, we will review requested services in accordance with client medical policies and clinical guidelines. If a request is received from a provider that is not an AIM Pathway regimen, it may be reviewed and may be authorized if it is determined to be medically necessary pursuant to medical policies and clinical guidelines.

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Effective August 12, 2019
# Bladder Cancer (Urothelial) Pathways

## Neoadjuvant Therapy | Clinical Stage II, III, or IV Without Evidence of Metastases (cT2, cT3, cT4a, cT4b, M0)

**CMV**: cisplatin, methotrexate, and vinblastine 3 cycles\(^4,5\)

Gemcitabine (Gemzar) and cisplatin 4 cycles\(^2\)

## Adjuvant Therapy | Stage 0 (Ta, Tis) or Stage I | After TURBT\(^*\) or Following Resection of Recurrent or Persistent Disease

**BCG**: bacillus calmette-guerin, intravesical\(^20-24\)

Gemcitabine (Gemzar), intravesical **(low-grade histology only)**\(^19\)

## Metastatic Disease | First Line of Therapy (1st Line)

Gemcitabine (Gemzar) and cisplatin\(^6,17,18\)

## Metastatic Disease | Second Line of Therapy (2nd Line)

Gemcitabine (Gemzar)\(^9\)

Paclitaxel\(^14\)

Pembrolizumab (Keytruda)\(^2,37\)

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* TURBT: Transurethral resection of bladder tumor

† In the setting of recurrent/metastatic disease, a substitution of carboplatin for cisplatin will be considered a pathway option

‡ Administered at a dose of 200 mg every 3 weeks per the FDA label OR 2 mg/kg (up to a maximum of 200 mg) every 3 weeks, as clinically appropriate

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Effective August 12, 2019
BLADDER CANCER (UROTHELIAL) REFERENCES

NCCN Practice Guidelines: Bladder Cancer Version 5.2018


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Breast Cancer Pathways: Neoadjuvant

<table>
<thead>
<tr>
<th>Neoadjuvant Therapy</th>
<th>HER2 Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>ddAC → weekly T:</td>
<td>dose dense doxorubicin (Adriamycin) and cyclophosphamide followed by weekly paclitaxel[^8,^11,^12,^39]</td>
</tr>
<tr>
<td>TC:</td>
<td>docetaxel (Taxotere) and cyclophosphamide[^10,^43]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Neoadjuvant Therapy</th>
<th>HER2 Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC → TH:</td>
<td>doxorubicin (Adriamycin) and cyclophosphamide followed by paclitaxel and trastuzumab (Herceptin)*[^1,^14,^23,^24,^26]</td>
</tr>
<tr>
<td>TCH:</td>
<td>docetaxel (Taxotere), carboplatin, and trastuzumab (Herceptin)*[^25,^49]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Neoadjuvant Therapy</th>
<th>HER2 Positive</th>
<th>Hormone Receptor (ER/PR) Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCH+P:</td>
<td>doxoraxel (Taxotere), carboplatin, trastuzumab (Herceptin)<em>, and pertuzumab (Perjeta)</em>[^50,^51,^54,^55,^57]</td>
<td></td>
</tr>
</tbody>
</table>

* Administration of trastuzumab (Herceptin) is limited to 1 year (maximum 18 cycles)

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Effective August 12, 2019
NCCN Clinical Practice Guidelines: Breast Cancer V4.2018

References


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Effective August 12, 2019


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54. FDA Briefing Document for sBLA 125409/51, Pertuzumab (PERJETA®). Oncologic Drugs Advisory Committee Meeting, September 12, 2013.


Breast Cancer Pathways: Adjuvant

<table>
<thead>
<tr>
<th>Adjuvant Therapy</th>
<th>HER2 Negative*</th>
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<tbody>
<tr>
<td>ddAC → weekly T: dose dense doxorubicin (Adriamycin) and cyclophosphamide followed by weekly paclitaxel⁸,⁹,¹¹,¹²,⁶⁰</td>
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<td>TC: docetaxel (Taxotere) and cyclophosphamide¹⁰,¹⁹</td>
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<table>
<thead>
<tr>
<th>Adjuvant Therapy</th>
<th>HER2 Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC → TH: doxorubicin (Adriamycin) and cyclophosphamide followed by paclitaxel and trastuzumab (Herceptin)†²³,²⁶,⁵⁸</td>
<td></td>
</tr>
<tr>
<td>TCH: docetaxel (Taxotere), carboplatin, and trastuzumab (Herceptin)†²⁵,²⁶,⁵⁸</td>
<td></td>
</tr>
<tr>
<td>TH: paclitaxel and trastuzumab (Herceptin)†³⁴,⁵⁸ (Pathway for stage I, HER2 positive breast cancer only)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adjuvant Therapy</th>
<th>HER2 Negative</th>
<th>Hormone Receptor (ER/PR) Negative</th>
<th>Residual Disease following Neoadjuvant Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capecitabine (Xeloda)⁵⁶</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Adjuvant Therapy</th>
<th>HER2 Positive</th>
<th>Residual Disease following Neoadjuvant Therapy</th>
<th>- Added effective 5/13/2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trastuzumab emtansine (Kadcyla)⁶³ – Added effective 5/13/2019</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

* Adjuvant chemotherapy pathways do NOT apply to individuals with hormone-receptor positive, lymph node negative, OncotypeDX™ LOW risk score
† Administration of trastuzumab (Herceptin) is limited to 1 year (maximum 18 cycles)

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Effective August 12, 2019
BREAST CANCER ADJUVANT REFERENCES

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# Breast Cancer Pathways: Advanced/Metastatic Disease

## Advanced/Metastatic Disease | HER2 Negative | First and Subsequent Lines of Therapy (1st Line+)

- Capecitabine (Xeloda)\(^4,4.24-26,28,60,65\)
- Doxorubicin (Adriamycin)\(^4,5,9,65\)
- Gemcitabine (Gemzar)\(^14,60\)
- Paclitaxel\(^28-20,65\)
- Vinorelbine (Navelbine)\(^15-17,65\)

## Advanced/Metastatic Disease | HER2 Negative | Deleterious Germline BRCA Mutation | First and Subsequent Lines of Therapy (1st Line+)

- Olaparib (Lynparza)\(^87\)

## Advanced/Metastatic Disease | HER2 Positive | First Line of Therapy (1st Line)

- Capecitabine (Xeloda) and trastuzumab (Herceptin)\(^40,43\)
- Gemcitabine (Gemzar) and trastuzumab (Herceptin)\(^44,45\)
- Paclitaxel and trastuzumab (Herceptin)\(^35,36\)
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and docetaxel (Taxotere)\(^32,33,35\)
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and paclitaxel\(^34\)
- Vinorelbine (Navelbine) and trastuzumab (Herceptin)\(^46,47\)

## Advanced/Metastatic Disease | HER2 Positive | Second and Subsequent Lines of Therapy (2nd Line+)

- Ado-trastuzumab emtansine (Kadcyla)\(^59,61,62\)
- Capecitabine (Xeloda) and lapatinib (Tykerb)\(^51,52\)
- Capecitabine (Xeloda) and trastuzumab (Herceptin)\(^40,43\)
- Gemcitabine (Gemzar) and trastuzumab (Herceptin)\(^44,45\)
- Paclitaxel and trastuzumab (Herceptin)\(^35,36\)
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and docetaxel (Taxotere)\(^32,33,35,82\)
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and paclitaxel\(^34\)
- Trastuzumab (Herceptin) and lapatinib (Tykerb)\(^49,50\)
- Trastuzumab (Herceptin) monotherapy\(^37,48\)
- Vinorelbine (Navelbine) and trastuzumab (Herceptin)\(^46,47\)

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Effective August 12, 2019
Breast Cancer Pathways: Endocrine Therapy for Advanced/Metastatic Disease

### Advanced/Metastatic Disease | Hormone Receptor Positive | First Line of Therapy (1st Line)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole (Arimidex)</td>
<td>*1,6,7,10,11,22,33</td>
</tr>
<tr>
<td>Anastrozole (Arimidex) and palbociclib (Ibrance)</td>
<td>*19,40,41</td>
</tr>
<tr>
<td>Anastrozole (Arimidex) and ribociclib (Kisqali)</td>
<td>*19,40,41</td>
</tr>
<tr>
<td>Fulvestrant (Faslodex)</td>
<td>* high dose*5,7,22,26,33,42</td>
</tr>
<tr>
<td>Fulvestrant (Faslodex) and ribociclib (Kisqali)</td>
<td>*58 - Added effective 5/13/2019</td>
</tr>
<tr>
<td>Letrozole (Femara)</td>
<td>*3,12,14,38</td>
</tr>
<tr>
<td>Letrozole (Femara) and palbociclib (Ibrance)</td>
<td>*19,40,41</td>
</tr>
<tr>
<td>Letrozole (Femara) and ribociclib (Kisqali)</td>
<td>*19,40,41,53</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>†12,26</td>
</tr>
</tbody>
</table>

### Advanced/Metastatic Disease | Hormone Receptor Positive | Second and Subsequent Lines of Therapy (2nd Line+)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole (Arimidex)</td>
<td>*1,6,7,10,11,22,33</td>
</tr>
<tr>
<td>Exemestane (Aromasin)</td>
<td>*14,20,21,39</td>
</tr>
<tr>
<td>Fulvestrant (Faslodex)</td>
<td>high dose*</td>
</tr>
<tr>
<td>Fulvestrant (Faslodex) and palbociclib (Ibrance)</td>
<td>*‡40</td>
</tr>
<tr>
<td>Letrozole (Femara)</td>
<td>*3,12,14,38</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>†12,26</td>
</tr>
</tbody>
</table>

### Advanced/Metastatic Disease | Hormone Receptor Positive | HER2 Positive | First and Subsequent Lines of Therapy (1st Line+)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole (Arimidex) and trastuzumab (Herceptin)</td>
<td>*46</td>
</tr>
<tr>
<td>Letrozole (Femara) and trastuzumab (Herceptin)</td>
<td>*49</td>
</tr>
</tbody>
</table>

* With ovarian suppression for premenopausal individuals. Ovarian suppression utilizes LHRH agonists given as monthly injections. 3-month depot dosing does not reliably suppress estrogen levels.
† Tamoxifen is considered pathway for premenopausal individuals with or without ovarian suppression.
‡ Palbociclib regimens are not considered pathway when continued in the second line setting if the patient has received an available CDK4/6 inhibitor regimen in the first line setting.

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Effective August 12, 2019
NCCN Clinical Practice Guidelines: Breast Cancer V4.2018

Effective August 12, 2019

References


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35. Ellis MJ, Prahlandan M, Green NL, Mari E, Robertson JFR. Abstract OT3-2-09: FALCON: A randomised, double-blind, multicentre, phase III study comparing fulvestrant 500 mg for postmenopausal women with hormone receptor-positive locally advanced or metastatic breast cancer who have not previously been treated with any hormonal therapy. Cancer Res. 2013 Dec 15;73:OT3-2-09. http://cancerscience.aacrjournals.org/content/73/24_Supplement/OT3-2-09


44. Cristofanilli M, Bondarenko I, Ro J, et al. [P41301] PALOMA3: Phase 3 trial of fulvestrant with or without palbociclib in pre and postmenopausal women with hormone receptor positive, HER2negative metastatic breast cancer that progressed on prior endocrine therapy—confirmed efficacy and safety. San Antonio Breast Cancer Symposium. December 11, 2015. Abstract P4-13-01

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47. Kornblum NS, Klein P, et al. PrECOG 0102: A randomized, double-blind, phase II trial of fulvestrant plus everolimus or placebo in postmenopausal women with hormone receptor (HR)-positive, HER2-negative metastatic breast cancer (MBC) resistant to aromatase inhibitor (AI) therapy. San Antonio Breast Cancer Symposium; San Antonio TX2016. SABCS Abstract S1-02


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### Chronic Myelogenous Leukemia (CML) Pathways

**First Line of Therapy (1st Line) | Low Risk Disease**

- Imatinib (Gleevec)\(^1\)-4,6,8,30,33-35

**First Line of Therapy (1st Line) | Intermediate or High Risk Disease\(^*\)**

- Dasatinib (Sprycel)\(^1\),2,30,37-39
- Imatinib (Gleevec)\(^1\)-4,6,8,30,33-35
- Nilotinib (Tasigna)\(^6\)-8,31,32

**Second Line of Therapy (2nd Line) | Following Treatment Failure, Suboptimal Response\(^†\), or Intolerance to 1st Line**

- Bosutinib (Bosulif)\(^23,33\)
- Dasatinib (Sprycel)\(^1\),2,9,10,12,36
- Nilotinib (Tasigna)\(^16\)-18,31,32
- Ponatinib (Iclusig)\(^26\)

**Third Line of Therapy (3rd Line)**

- Ponatinib (Iclusig)\(^26\)

\(^*\) For patients with intermediate or high risk disease based on Sokal or Hasford score:
- Sokal: Intermediate Risk=0.8-1.2; High Risk>1.2
- Hasford: Intermediate Risk=781-1480; High Risk>1480

\(^†\) Defined as lack of complete hematologic response or BCR-ABL1 transcripts > 10% (IS) or lack of partial cytogenetic response on bone marrow cytogenetics.

\(^‡\) Pathway option for second line therapy only after failure, suboptimal response, or intolerance of a second generation TKI has been used in the first line setting, or T315I mutation has been identified.

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Effective August 12, 2019
CHRONIC MYELOGENOUS LEUKEMIA (CML) REFERENCES

NCCN Clinical Practice Guidelines: Chronic Myelogenous Leukemia V1.2019


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Colorectal Cancer Pathways

Adjuvant Therapy*

Capecitabine (Xeloda)\textsuperscript{52,69}

**CAPOX**: capecitabine (Xeloda) and oxaliplatin (limited to 3 months duration)\textsuperscript{94}

**FOLFOX**: fluorouracil (5-FU), leucovorin, and oxaliplatin\textsuperscript{7,8,50,51,60,69}

**FULV**: fluorouracil (5FU) and leucovorin\textsuperscript{1,4,7,49,52,69}

Metastatic Disease | RAS Wild Type (WT) or Mutant (MT)‡ | First or Second Lines of Therapy (1\textsuperscript{st} or 2\textsuperscript{nd} Line)

Capecitabine (Xeloda)\textsuperscript{27}

**FOLFIRI**: fluorouracil (5FU), leucovorin, and irinotecan (Camptosar)\textsuperscript{18,23,30,32,34}

**FOLFIRI + bevacizumab**: fluorouracil (5FU), leucovorin, and irinotecan (Camptosar) with bevacizumab (Avastin)\textsuperscript{21,23,31,36,44,45,58}

**FOLFOX**: fluorouracil (5FU), leucovorin, and oxaliplatin\textsuperscript{24,26,28,30,34}

**FOLFOX + bevacizumab**: fluorouracil (5FU), leucovorin, oxaliplatin, with bevacizumab (Avastin)\textsuperscript{25,26,28,33,44,45,70}

**FOLFIRI + bevacizumab**: fluorouracil (5FU), leucovorin, oxaliplatin, and irinotecan (Camptosar) with bevacizumab (Avastin)\textsuperscript{25,26,28,33,44,45,70}

**FULV**: fluorouracil (5FU) and leucovorin\textsuperscript{22,27,35}

**FULV**: fluorouracil (5FU) and leucovorin with bevacizumab (Avastin)\textsuperscript{22,25,35}

Metastatic Disease | RAS Wild Type (WT) | First or Second Lines of Therapy (1\textsuperscript{st} or 2\textsuperscript{nd} Line)

**FOLFIRI + panitumumab**: fluorouracil (5FU), leucovorin, and irinotecan (Camptosar) with panitumumab (Vectibix)\textsuperscript{11,62}

**FOLFOX + panitumumab**: fluorouracil (5-FU), leucovorin, and oxaliplatin with panitumumab (Vectibix)\textsuperscript{12,53,59}

Irinotecan (Camptosar) and panitumumab (Vectibix)\textsuperscript{47}

Metastatic Disease | MSI-H or dMMR | Second Line of Therapy (2\textsuperscript{nd} Line)

Pembrolizumab (Keytruda)\textsuperscript{191}

Metastatic Disease | RAS Wild Type (WT) | Third or Subsequent Lines of Therapy (3\textsuperscript{rd} Line+)

Panitumumab (Vectibix) monotherapy\textsuperscript{13,61,56}

* Adjuvant Pathways do not apply to stage II MSI-H (microsatellite instability-high) disease
† Limited to low-risk (T1-3, N1), stage III colon cancer only
‡ Exon 2 KRAS, non-exon 2 KRAS, and NRAS mutations; testing recommended for all patients with metastatic disease
§ Limit to one line of therapy
|| Administered at a dose of 200 mg every 3 weeks per the FDA label OR 2 mg/kg (up to a maximum of 200 mg) every 3 weeks, as clinically appropriate

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Effective August 12, 2019
COLORECTAL CANCER REFERENCES


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Gruenberger T, Bridgewater JA, Chau I, et al. Randomized, phase II study of bevacizumab with mFOLFOX6 or FOLFOXIRI in patients with initially unresectable liver metastases from colorectal cancer: resectability and safety in OLIVIA. J Clin Oncol. 2013;31(15s):A3619 Abstract 3619


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Gastric, Esophageal, and Gastroesophageal Junction Cancer (Adenocarcinoma) Pathways

<table>
<thead>
<tr>
<th>**Primary Therapy</th>
<th>Resectable and Unresectable Disease**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin and fluorouracil (5FU)³,⁴</td>
<td></td>
</tr>
<tr>
<td>Fluorouracil (5FU) and cisplatin with concurrent radiation therapy (RT)³⁶</td>
<td></td>
</tr>
<tr>
<td><strong>FLOT:</strong> Fluorouracil (5FU), leucovorin, oxaliplatin, and docetaxel (Taxotere)⁴⁷,⁴⁸</td>
<td></td>
</tr>
<tr>
<td>Paclitaxel and carboplatin with concurrent RT⁵</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Post-Operative Treatment</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluorouracil (5FU) and leucovorin with concurrent RT³⁸</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>**Recurrent/Metastatic or Locally Advanced/Inoperable Disease</th>
<th>HER2 Negative</th>
<th>First Line of Therapy (1ˢᵗ Line)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin and fluorouracil (5FU)¹⁵,¹⁹,²¹,²⁶</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluorouracil (5FU) and irinotecan (Camptosar)²⁵,²⁶</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>FLO/FOLFOX:</strong> fluorouracil (5FU), leucovorin, and oxaliplatin²⁷</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>FLP:</strong> fluorouracil (5FU), leucovorin, and cisplatin²⁷</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>**Recurrent/Metastatic or Locally Advanced/Inoperable Disease</th>
<th>HER2 Positive</th>
<th>First Line of Therapy (1ˢᵗ Line)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin, fluorouracil (5FU), and trastuzumab (Herceptin)¹⁵</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>**Recurrent/Metastatic or Locally Advanced/Inoperable Disease</th>
<th>Second Line of Therapy (2ⁿᵈ Line)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irinotecan (Camptosar)²⁴,²⁹</td>
<td></td>
</tr>
<tr>
<td>Paclitaxel²³</td>
<td></td>
</tr>
</tbody>
</table>

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(FLOT4-AIO): results from the phase 2 part of a multicentre, open-label, randomised phase 2/3 trial. Lancet Oncol. 2016;17(12):1697-708. PMID 27776843


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Effective August 12, 2019
# Head and Neck Cancer Pathways

<table>
<thead>
<tr>
<th>Non-Nasopharyngeal (Squamous Cell Carcinoma)</th>
<th>Candidate for Local Therapy (M0)</th>
<th>Primary Systemic Therapy or Post-Operative Systemic Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose cisplatin* with concurrent RT3,10,37</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Non-Nasopharyngeal (Squamous Cell Carcinoma)</th>
<th>Metastatic and Recurrent Disease</th>
<th>First Line of Therapy (1st line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin, fluorouracil (5FU), and cetuximab (Erbitux)14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisplatin, fluorouracil (5FU), and cetuximab (Erbitux)14</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Non-Nasopharyngeal (Squamous Cell Carcinoma)</th>
<th>Metastatic and Recurrent Disease</th>
<th>Second and Subsequent Lines of Therapy (2nd line+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab (Opdivo)35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paclitaxel23</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nasopharynx</th>
<th>Candidate for Local Therapy (M0)</th>
<th>Primary Systemic Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose cisplatin* with concurrent RT13,37</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nasopharynx</th>
<th>Metastatic and Recurrent Disease</th>
<th>First and Subsequent Lines of Therapy (1st Line+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisplatin20,22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisplatin† and gemcitabine (Gemzar)29,39</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisplatin† and paclitaxel18,22,29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluorouracil (5FU)22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gemcitabine (Gemzar)31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methotrexate24,26</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paclitaxel23</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Cisplatin dosed at 100 mg/m² every three weeks over the course of radiotherapy. There are several different appropriate cisplatin schedules that may be used.

† Substitution of carboplatin for cisplatin, and vice-versa, is acceptable for metastatic disease

---

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Effective August 12, 2019
HEAD AND NECK CANCER REFERENCES

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Effective August 12, 2019
Hodgkin Lymphoma Pathways

**Classical Hodgkin Lymphoma | Early Stage (Stage I-IIA, Favorable and Unfavorable Risk)**

**ABVD**: doxorubicin (Adriamycin), bleomycin, vinblastine, and dacarbazine (DTIC) ± ISRT*1-5,30,35,36

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**Classical Hodgkin Lymphoma | Advanced Stage (Stage IIB, III, and IV)**

**ABVD**: doxorubicin (Adriamycin), bleomycin, vinblastine, and dacarbazine (DTIC) ± ISRT*7-10,32

* ISRT – Involved site radiation therapy

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Effective August 12, 2019
HODGKIN LYMPHOMA REFERENCES

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Effective August 12, 2019
## Kidney Cancer (Renal Cell Carcinoma) Pathways

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>First Line of Therapy (1st Line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose intravenous (IV) interleukin-2 (IL2, Proleukin)*[^17,18]</td>
<td>TERMED Effective 8/12/2019</td>
</tr>
<tr>
<td>Pazopanib (Votrient)[^4,5,7]</td>
<td>TERMED Effective 8/12/2019</td>
</tr>
<tr>
<td>Sunitinib (Sutent)[^1-3,37]</td>
<td>TERMED Effective 8/12/2019</td>
</tr>
<tr>
<td>Temsirolimus (Torisel)[^12,23]</td>
<td>TERMED Effective 8/12/2019</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>First Line of Therapy (1st Line)</th>
<th>Clear Cell Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab (Opdivo) and ipilimumab (Yervoy)[^18]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pembrolizumab (Keytruda) and axitinib (Inlyta)[^50]</td>
<td>ADDED Effective 8/12/2019</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Second or Subsequent Lines of Therapy (2nd Line+)</th>
<th>Clear Cell Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab (Opdivo)[^29,30,32]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Indicated only for tumors with a significant clear cell histology component
KIDNEY CANCER (RENAL CELL CARCINOMA) REFERENCES

NCCN Practice Guideline: Kidney Cancer V3.2019


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Effective August 12, 2019
Lung Cancer: Non-Small Cell Lung Cancer (NSCLC) Pathways

**Neoadjuvant/Preoperative/Induction Therapy or Adjuvant/Definitive Therapy**

Cisplatin and etoposide with concurrent XRT<sup>88,89</sup>

Paclitaxel and carboplatin with concurrent XRT<sup>93</sup>

**Adjuvant Therapy**

Carboplatin and paclitaxel<sup>52</sup>

Cisplatin and gemcitabine (Gemzar)

Cisplatin and vinorelbine (Navelbine)<sup>53</sup>

**Metastatic Disease | Squamous | ALK/EGFR Negative (ROS Negative or Unknown) | TPS > 50% | First Line of Therapy (1st Line) | ECOG PS: 0-2**

Pembrolizumab (Keytruda)<sup>125</sup>

**Metastatic Disease | Squamous | TPS < 50% | First Line of Therapy (1st Line) | ECOG PS: 0-2**

Pembrolizumab (Keytruda)*, carboplatin, and paclitaxel<sup>126</sup>

**Metastatic Disease | Nonsquamous | ALK/EGFR Negative (ROS1 Negative or Unknown) | TPS ≥ 50% | First Line of Therapy (1st Line) | ECOG PS: 0-2**

Pembrolizumab (Keytruda)<sup>102,125</sup>

**Metastatic Disease | Nonsquamous | ALK/EGFR Negative (ROS1 Negative or Unknown) | TPS < 50% | First Line of Therapy (1st Line) | ECOG PS: 0-2**

Carboplatin†, pemetrexed (Alimta), and pembrolizumab (Keytruda)<sup>124</sup>

**Metastatic Disease | Squamous or Nonsquamous | Immunotherapy-Ineligible | First Line of Therapy (1st Line) | ECOG PS: 0-2**

Carboplatin† and paclitaxel<sup>17,16,54</sup>

Carboplatin, paclitaxel, and bevacizumab (Avastin)<sup>13,14,31</sup> (NON-SQUAMOUS ONLY)

Cisplatin† and gemcitabine (Gemzar)<sup>8,11,13,22-25</sup>

Cisplatin† and pemetrexed (Alimta)<sup>17,18</sup> (NON-SQUAMOUS ONLY)

* Administered at a dose of 200 mg every 3 weeks per the FDA label OR 2 mg/kg (up to a maximum of 200 mg) every 3 weeks, as clinically appropriate

† In the setting of recurrent/metastatic NSCLC, a substitution of cisplatin for carboplatin (or vice-versa) will be considered a pathway option.

‡ Eligible only if immunotherapy alone was administered as first line treatment. Ineligible if chemotherapy was used in the first line setting.

---

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Effective August 12, 2019
Lung Cancer: Non-Small Cell Lung Cancer (NSCLC) Pathways (continued)

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Non-Squamous</th>
<th>Maintenance</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Continued bevacizumab (Avastin)$^{36,38}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Continuation pemetrexed (Alimta)$^{39,94}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pembrolizumab (Keytruda)* and pemetrexed (Alimta) (if previously treated with carboplatin†, pemetrexed, and pembrolizumab)$^{513}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Switch pemetrexed (Alimta)$^{41,94}$</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Second or Subsequent Lines of Therapy (2nd Line+)</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atezolizumab (Tecentriq)$^{104}$ (if no prior checkpoint inhibitors)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nivolumab (Opdivo)$^{59,61,72,78}$ (if no prior checkpoint inhibitors)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carboplatin† and paclitaxel$^{7,16,54}$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carboplatin† and gemcitabine (Gemzar)‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carboplatin† and pemetrexed (Alimta)†</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>ALK Positive</th>
<th>First Line of Therapy (1st Line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alectinib (Alecensa)$^{108}$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>EGFR Positive</th>
<th>First Line of Therapy (1st Line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osimertinib (Tagrisso)$^{114}$</td>
<td></td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>ALK or EGFR Positive</th>
<th>Second or Subsequent Lines of Therapy (2nd Line+)</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin† and paclitaxel$^{7,16,54}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisplatin† and gemcitabine (Gemzar)$^{8,11,13,22,25}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisplatin† and pemetrexed (Alimta)$^{17,18}$</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>EGFR Positive</th>
<th>ECOG PS: 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erlotinib (Tarceva)$^{42,48,50,51}$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Administered at a dose of 200 mg every 3 weeks per the FDA label OR 2 mg/kg (up to a maximum of 200 mg) every 3 weeks, as clinically appropriate
† In the setting of recurrent/metastatic NSCLC, a substitution of cisplatin for carboplatin (or vice-versa) will be considered a pathway option.
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LUNG CANCER: NON-SMALL CELL LUNG CANCER (NSCLC) REFERENCES

NCCN Clinical Practice Guidelines: Non-Small Cell Lung Cancer V6.2018


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References

14. FDA review documents

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Effective August 12, 2019
## Lung Cancer: Small Cell Lung Cancer Pathways

<table>
<thead>
<tr>
<th>Limited Stage</th>
<th>Primary, Adjuvant, or First Line of Therapy (1st Line)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Carboplatin and etoposide ± XRT³</td>
</tr>
<tr>
<td></td>
<td>Cisplatin and etoposide ± XRT¹,₂</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Extensive Stage</th>
<th>First Line of Therapy (1st Line)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Carboplatin and etoposide⁹</td>
</tr>
<tr>
<td></td>
<td>Atezolizumab (Tecentriq), carboplatin, and etoposide³¹</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second and Subsequent Lines of Therapy (2nd Line+)</th>
<th>Relapse Greater than Six (6) Months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Carboplatin and etoposide⁹</td>
</tr>
</tbody>
</table>

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Effective August 12, 2019
LUNG CANCER: SMALL CELL LUNG CANCER REFERENCES


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# Melanoma Pathways: Metastatic Melanoma

<table>
<thead>
<tr>
<th>Stage III B/IIIC (Resected)</th>
<th>Adjuvant Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab (Opdivo)&lt;sup&gt;59&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>First and Subsequent Lines of Therapy (1&lt;sup&gt;st&lt;/sup&gt; Line+)</th>
<th>Any BRAF Status</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab (Opdivo) and ipilimumab (Yervoy)&lt;sup&gt;65&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>First Line of Therapy (1&lt;sup&gt;st&lt;/sup&gt; Line)</th>
<th>BRAF Mutated&lt;sup&gt;†&lt;/sup&gt;</th>
<th>Symptomatic Disease</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vemurafenib (Zelboraf) and cobimetinib (Cotellic)&lt;sup&gt;26,40,42&lt;/sup&gt;</td>
<td>TERMED Effective 8/12/2019</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Encorafenib (Braftovi) and binimetinib (Mektovi)&lt;sup&gt;66&lt;/sup&gt;</td>
<td>ADDED Effective 8/12/2019</td>
<td></td>
<td></td>
<td></td>
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<thead>
<tr>
<th>Metastatic Disease</th>
<th>Second and Subsequent Lines of Therapy (2&lt;sup&gt;nd&lt;/sup&gt; Line+)</th>
<th>BRAF Mutated&lt;sup&gt;†&lt;/sup&gt;</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vemurafenib (Zelboraf) and cobimetinib (Cotellic)&lt;sup&gt;26,40,42&lt;/sup&gt;</td>
<td>TERMED Effective 8/12/2019</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Encorafenib (Braftovi) and binimetinib (Mektovi)&lt;sup&gt;66&lt;/sup&gt;</td>
<td>ADDED Effective 8/12/2019</td>
<td></td>
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</tbody>
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<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Second and Subsequent Lines of Therapy (2&lt;sup&gt;nd&lt;/sup&gt; Line+)</th>
<th>Any BRAF Status</th>
<th>ECOG PS: 0-2</th>
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<tbody>
<tr>
<td>Ipilimumab (Yervoy)&lt;sup&gt;1,14,15,35,36&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Administered at a dose of 200 mg every 3 weeks per the FDA label OR 2 mg/kg (up to a maximum of 200 mg) every 3 weeks, as clinically appropriate
† BRAF mutations include V600E and V600K mutations

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**Note:** Pathways are independent of specific health plan medical policy coverage criteria. Health plan medical policy/clinical guidelines should be consulted to determine whether proposed services will be covered.

Effective August 12, 2019
MELANOMA: METASTATIC MELANOMA REFERENCES

NCCN Clinical Practice Guidelines: Melanoma V2.2019

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References


11 Carvajal RD1, Antonescu CR, Wolchok JD, et al. KIT as a therapeutic target in metastatic melanoma. JAMA. 2011 Jun 8;305(22):2327-34. PMID: 21642685


Note: Pathways are independent of specific health plan medical policy coverage criteria. Health plan medical policy/clinical guidelines should be consulted to determine whether proposed services will be covered.

Effective August 12, 2019


34 NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Melanoma (BRIM melanoma). ASCO Meeting Abstracts. 2015;33:Abstract 9020. Abstract 9020


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Effective August 12, 2019

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# Myeloma Pathways: Multiple Myeloma

## Primary/First Line of Therapy (1st Line) | Transplant Candidates

**VRD/VDR**: bortezomib (Velcade), lenalidomide (Revlimid), and dexamethasone¹⁰,¹²,⁷⁹

## Primary/First Line of Therapy (1st Line) | Non-Transplant Candidates

- **CyBorD or VDC**: bortezomib (Velcade), cyclophosphamide, and dexamethasone⁹,¹⁰,⁸⁴
- **R-dex**: lenalidomide (Revlimid) and low-dose dexamethasone¹⁰,¹¹,¹³,⁷³
- **VRD/VDR**: bortezomib (Velcade), lenalidomide (Revlimid), and dexamethasone¹⁰,¹²,⁷⁹
- **VD**: bortezomib (Velcade) and dexamethasone¹³,¹²,²⁴,⁸⁹

## Maintenance Therapy | Post-Transplant

- Lenalidomide (Revlimid)²⁶,²⁷,⁸³,⁹²

## Relapsed Disease | Second and Subsequent Lines of Therapy (2nd Line+)

- **CRd or KRd**: carfilzomib (Kyprolis), lenalidomide (Revlimid), and dexamethasone⁸²
- **DRD**: daratumumab (Darzalex), lenalidomide (Revlimid), and dexamethasone¹⁰⁰
- **DVD**: daratumumab (Darzalex), bortezomib (Velcade), and dexamethasone¹⁰³

## Relapsed Disease | Third and Subsequent Lines of Therapy (3rd Line+)

- Daratumumab (Darzalex)³⁹⁵
- Elotuzumab (Empliciti), lenalidomide (Revlimid), and dexamethasone⁹⁷
- Elotuzumab (Empliciti), pomalidomide (Pomalyst), and dexamethasone*¹¹³ — Added Effective 5/13/2019

* Eligible only if patient has received prior therapy with lenalidomide and proteasome inhibitor

Note: Pathways are independent of specific health plan medical policy coverage criteria. Health plan medical policy/clinical guidelines should be consulted to determine whether proposed services will be covered.

Effective August 12, 2019
MYELOMA: MULTIPLE MYELOMA REFERENCES

NCCN Clinical Practice Guidelines: Multiple Myeloma V2.2019


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References


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42. Anderson KC, Jagannath S, Jakubowiak A, et al. Phase II study of lenalidomide (Len), bortezomib (Bz), and dexamethasone (Dex) in patients (pts) with relapsed or relapsed and refractory multiple myeloma (MM). J Clin Oncol. 2008; 26(15S):A8545 Abstract 8545


55. Richardson PG, Siegel DS, Gj, et al. Randomized open-label phase 1/2 study of pomalidomide (POM) alone or in combination with low-dose dexamethasone (LoDex) in patients with relapsed and refractory multiple myeloma who have received prior treatment that includes lenalidomide (LEN) and bortezomib (BORT): Phase 2 results. [Abstract 634]. Blood. 2011. Accessed. Abstract 634


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Effective August 12, 2019
NHL: Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Pathways

**First Line of Therapy (1st Line) | With 17p Deletion or TP53 Mutation Present**

Ibrutinib (Imbruvica)\(^{28,37,41,46,47}\)

**First Line of Therapy (1st Line) | Without 17p Deletion**

**BR:** bendamustine (Bendeka, Treanda) and rituximab\(^{13,15,39,51}\)

**FCR:** fludarabine (Fludara), cyclophosphamide, and rituximab\(^*^{1,2,39,51}\)

Ibrutinib (Imbruvica)\(^{29,37,46,47}\)

Obinutuzumab (Gazyva) and chlorambucil (Leukeran)\(^{16}\)

**Second and Subsequent Lines of Therapy (2nd Line+) | With 17p Deletion or TP53 Mutation Present**

Ibrutinib (Imbruvica)\(^{28,37,41,46,47}\)

Idelalisib (Zydelig)\(^{43}\)

Idelalisib (Zydelig) and rituximab\(^*^{38}\)

Venetoclax (Venclexta) and rituximab\(^{59}\)

**Second and Subsequent Lines of Therapy (2nd Line+) | Without 17p Deletion**

Ibrutinib (Imbruvica)\(^{28,37,41,46,47}\)

Idelalisib (Zydelig)\(^{43}\)

Idelalisib (Zydelig) and rituximab\(^{38}\)

Venetoclax (Venclexta) and rituximab\(^{59}\)

Primary treatment for CLL should be initiated in accordance with the guidelines established by the Working Group on CLL\(^{58}\)

\(^*\) Rituximab may be administered as Rituxan or Rituxan Hycela. When Rituxan Hycela is chosen, treatment with SC rituximab (Rituxan Hycela) should only be initiated after patients have received at least one full dose of IV rituximab (Rituxan)

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Effective August 12, 2019
NHL: CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) / SMALL LYMPHOCYTIC LYMPHOMA (SLL) REFERENCES

NCCN Practice Guidelines: Chronic Lymphocytic Leukemia / Small Lymphocytic Lymphoma V5.2018


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Effective August 12, 2019
# NHL: Diffuse Large B-Cell Lymphoma Pathways

## First Line of Therapy (1st Line)

**R-CHOP (21):** cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, and rituximab*1,4,52,53

## First Line of Therapy (1st Line) | Contraindication to Anthracycline

**R-CEOP:** cyclophosphamide, etoposide, vincristine (Vincasar), prednisone, and rituximab*13,14,40,41,52,53

## Second and Subsequent Lines of Therapy (2nd Line+) | Transplant Candidates

**R-GDP:** gemcitabine (Gemzar), dexamethasone, cisplatin, and rituximab*23,24,43,52,53  
**R-GDP:** gemcitabine (Gemzar), dexamethasone, carboplatin, and rituximab*23,24,43,52,53  
**R-ICE:** ifosfamide (Ifex), carboplatin, etoposide, and rituximab*18,19,29,52,53

## Second and Subsequent Lines of Therapy (2nd Line+) | Non-Transplant Candidates

**BR:** bendamustine (Bendeka, Treanda) and Rituximab*32,33,52,53  
**R-GDP:** gemcitabine (Gemzar), dexamethasone, cisplatin, and rituximab*23,24,52,53  
**R-GDP:** gemcitabine (Gemzar), dexamethasone, carboplatin, and rituximab*23,24,52,53  
**R-GemOx:** gemcitabine (Gemzar), oxaliplatin, and rituximab*25,27,52,53

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*Rituximab may be administered as Rituxan or Rituxan Hycela. When Rituxan Hycela is chosen, treatment with SC rituximab (Rituxan Hycela) should only be initiated after patients have received at least one full dose of IV rituximab (Rituxan)*

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Effective August 12, 2019
NHL: DIFFUSE LARGE B CELL LYMPHOMA REFERENCES


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Effective August 12, 2019
## NHL: Follicular and Marginal Zone Lymphoma Pathways

<table>
<thead>
<tr>
<th>Gastric MALT (Mucosa-Associated Lymphoid Tissue) Lymphoma</th>
<th>Stage IE or IIE</th>
<th><em>H. pylori</em> Positive*†*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic therapy† for <em>H. pylori</em> eradication†33,34</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Splenic Marginal Zone† or Gastric MALT Lymphoma</th>
<th>First Line of Therapy (1st Line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituximab‡ monotherapy27-29,52,53</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Follicular (Grade I-IIIA) and Other Marginal Zone Lymphomas</th>
<th>First Line of Therapy (1st Line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BR: Bendamustine (Bendeka, Treanda) and rituximab§5,6,52,53</td>
<td></td>
</tr>
<tr>
<td>R-CHOP(21): Cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, and rituximab§1-3,5,52,53</td>
<td></td>
</tr>
<tr>
<td>R-CVP: Cyclophosphamide, vincristine (Vincasar), prednisone, and rituximab§1,4,52,53</td>
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</tr>
<tr>
<td>Rituximab§ monotherapy7,17,52,53</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Follicular and Other Marginal Zone Lymphomas</th>
<th>First Line of Therapy (1st Line)</th>
<th>Additional options for the elderly or infirm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorambucil (Leukeran)10</td>
<td></td>
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</tr>
<tr>
<td>Chlorambucil (Leukeran) and rituximab§10,11,52,53</td>
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<td></td>
</tr>
<tr>
<td>Cyclophosphamide11-13</td>
<td></td>
<td></td>
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<tr>
<td>Cyclophosphamide and rituximab§52,53</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Follicular Lymphoma (Grade III)</th>
<th>First Line of Therapy (1st Line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-CHOP(21): Cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, and rituximab§1-5,52,53</td>
<td></td>
</tr>
<tr>
<td>R-CEOP: Cyclophosphamide, etoposide, vincristine (Vincasar), prednisone, and rituximab§13,35-37,52,53</td>
<td></td>
</tr>
</tbody>
</table>

* Gastric MALT with translocation 11;18 (t11;18) (q21;q21) predicts a lower response rate to anti-*H. pylori* treatment. Radiation therapy or other local intervention may be indicated.
† Only generic antibiotics are considered pathway options for *H. pylori* eradication
‡ Splenectomy is also a recommended option for splenic marginal zone lymphoma (NCCN 2A)
§ Rituximab may be administered as Rituxan or Rituxan Hycela. When Rituxan Hycela is chosen, treatment with SC rituximab (Rituxan Hycela) should only be initiated after patients have received at least one full dose of IV rituximab (Rituxan)

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Effective August 12, 2019
NHL: FOLLICULAR AND MARGINAL ZONE LYMPHOMA REFERENCES


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Effective August 12, 2019

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Effective August 12, 2019 79
# NHL: Mantle Cell Lymphoma Pathways

## First Line of Therapy (1st Line) | ASCT Candidates

- **Alternating R-CHOP/R-DHAP**: cyclophosphamide (Cytoxan), doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, rituximab* alternating with dexamethasone, cisplatin, cytarabine (Ara-C), and rituximab*4,5,28,30,31

- **Nordic Regimen**: dose intensified rituximab*, cyclophosphamide, vincristine (Vincasar), doxorubicin (Adriamycin), prednisone alternating with rituximab* and high dose cytarabine (Ara-C)3

## First Line of Therapy (1st Line) | Not an ASCT Candidate

- **BR**: bendamustine (Bendeka, Treanda) and rituximab*9,10

## Second and Subsequent Lines of Therapy (2nd Line+)

- Acalabrutinib (Calquence)42
- **BR**: bendamustine (Bendeka, Treanda) and rituximab*
- Bortezomib (Velcade)17
- Ibrutinib (Imbruvica)19,20
- Lenalidomide (Revlimid)20-23

*Rituximab may be administered as Rituxan or Rituxan Hycela. When Rituxan Hycela is chosen, treatment with SC rituximab (Rituxan Hycela) should only be initiated after patients have received at least one full dose of IV rituximab (Rituxan)

---

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Effective August 12, 2019
NHL: MANTLE CELL LYMPHOMA REFERENCES


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References

13. Forristpointer R, Dreyling M, German Low-Grade Lymphoma Study Group, et al. The addition of rituximab to a combination of fludarabine, cyclophosphamide, mitoxantrone (FCM) significantly increases the response rate and prolongs survival as compared with FCM alone in patients with relapsed and refractory follicular and mantle cell lymphomas: results of a prospective randomized study of the German Low-Grade Lymphoma Study Group. Blood. 2004 Nov 15;104(10):3064-3071. PMID: 15284112

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Effective August 12, 2019
# Ovarian Cancer (Epithelial) Pathways

## Adjuvant Therapy | Stage IA/B (Grade 2 or 3) or IC (Grade 1-3)
- Carboplatin and dose dense paclitaxel[^6-8]
- Carboplatin and paclitaxel[^2,5,7]

## Adjuvant or Primary Therapy | Stage II, III, IV
- Carboplatin and paclitaxel[^6,8,45] (*Administered weekly or every 3 weeks*)
- Intravenous (IV) paclitaxel and Intraperitoneal (IP) cisplatin and IP paclitaxel[^1,49] (*Stage III only*)

## Recurrent Disease | First and Subsequent Lines of Therapy (1st Line+) | Platinum-Sensitive*
- Carboplatin[^8,9,12]
- Carboplatin and gemcitabine (Gemzar)[^12,13]
- Carboplatin and paclitaxel[^8,9,15]
- Carboplatin and weekly paclitaxel

## Recurrent Disease | Maintenance Therapy | Platinum-Sensitive*
- Niraparib (Zejula)[^54]
- Olaparib (Lynparza)[^55]
- Rucaparib (Rubraca)[^60]

## Recurrent Disease | Second and Subsequent Lines of Therapy (2nd Line+) | Platinum Resistant
- Bevacizumab (Avastin) monotherapy[^42]
- Docetaxel (Taxotere)[^17]
- Gemcitabine (Gemzar)[^18,20]
- Liposomal doxorubicin (Doxil or Lipodox)[^19-21]
- Paclitaxel (weekly)[^22,23]
- Paclitaxel and bevacizumab (Avastin)[^36-38]
- Tamoxifen[^56]
- Topotecan (Hycamtin)[^21,24]
- Topotecan (Hycamtin) and bevacizumab (Avastin)[^36,37]
- Vinorelbine (Navelbine)[^34,35]

* Platinum sensitive disease is defined as recurrence of greater than 6 months after prior platinum-based therapy

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*Note: Pathways are independent of specific health plan medical policy coverage criteria. Health plan medical policy/clinical guidelines should be consulted to determine whether proposed services will be covered.*

Effective August 12, 2019
OVARIAN CANCER (EPITHELIAL) REFERENCES

NCCN Clinical Practice Guidelines: Ovarian Cancer, Including Fallopian Tube Cancer and Primary Peritoneal Cancer V2.2018


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38. O'Malley DM, Richardson DL, Rheuma PS, et al. Addition of bevacizumab to weekly paclitaxel significantly improves progression-free survival in heavily pretreated recurrent epithelial ovarian cancer. Gynecol Oncol. 2011 May 1;121(2):269-72. PMID: 21315428


41. Tillmanns TD, Lowe MP, Walker MS, Stepanski EJ, and Schwartzberg LS. Phase II clinical trial of bevacizumab with albumin-bound paclitaxel in patients with recurrent, platinum-resistant primary epithelial ovarian or primary peritoneal carcinoma. Gynecol Oncol. 2013 Feb;128(2):221-8. PMID: 22960352


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## Pancreatic Cancer (Adenocarcinoma) Pathways

### Adjuvant Therapy

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<th>Therapy</th>
</tr>
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<tbody>
<tr>
<td>Capecitabine (Xeloda) and gemcitabine (Gemzar)³⁶,⁴⁰</td>
</tr>
<tr>
<td><strong>FULV</strong>: fluorouracil (5FU) and leucovorin⁴,⁶,⁹</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar)¹,³-⁷</td>
</tr>
<tr>
<td><strong>mFOLFIRINOX</strong>: fluorouracil (5FU), leucovorin, irinotecan (Camptosar), and oxaliplatin⁴⁶</td>
</tr>
</tbody>
</table>

### Locally Advanced/Unresectable and Metastatic Disease | First Line of Therapy (1st Line) | ECOG PS: 0-2

<table>
<thead>
<tr>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FOLFIRINOX</strong>: fluorouracil (5FU), leucovorin, irinotecan (Camptosar), and oxaliplatin⁵,²¹</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar)⁵,¹⁵-²¹</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar) and nab-paclitaxel (Abraxane)⁵,¹⁵,³³</td>
</tr>
</tbody>
</table>

### Locally Advanced/Unresectable and Metastatic Disease | Second Line of Therapy (2nd Line) | ECOG PS: 0-2

<table>
<thead>
<tr>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemcitabine (Gemzar)²¹</td>
</tr>
</tbody>
</table>

* Modified FOLFIRINOX: Bolus 5-FU not administered

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**Effective August 12, 2019**
PANCREATIC CANCER (ADENOCARCINOMA) REFERENCES

NCCN Clinical Practice Guidelines: Pancreatic Adenocarcinoma V2.2018


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Effective August 12, 2019
# Prostate Cancer (Adenocarcinoma) Pathways

## Adjuvant Therapy | Post-Prostatectomy | Lymph Node Positive (LN+)

- Goserelin (Zoladex)\(^1,2\)
- Leuprolide (Eligard/Lupron)\(^1,2\)
- Triptorelin (Trelstar)\(^1,2\)

## Intermediate Risk | Primary Treatment with Radiotherapy (RT)

- Goserelin (Zoladex)\(^3,5\)
- Leuprolide (Eligard/Lupron)\(^3,5\)
- Triptorelin (Trelstar)\(^3,5\)

## High Risk (T3a or Gleason 8-10), Very High Risk (T3b-T4), and Locally Advanced Prostate Cancer (LN+) | Primary Treatment with Radiotherapy (RT)

- Goserelin (Zoladex)\(^4\)
- Goserelin (Zoladex)* with abiraterone (Zytiga)\(^4,1\)
- Leuprolide (Eligard/Lupron)*\(^4\)
- Leuprolide (Eligard/Lupron)* with abiraterone (Zytiga)\(^4,1\)
- Triptorelin (Trelstar)*\(^4\)
- Triptorelin (Trelstar) with abiraterone (Zytiga)*\(^4,1\)

## Recurrent and Metastatic Disease | Hormone Sensitive

- Abiraterone (Zytiga) and prednisone with Androgen Deprivation Therapy (ADT)\(^3,9,4,1\)
- Docetaxel (Taxotere) (every 3 weeks) with Androgen Deprivation Therapy (ADT)\(^1,9\)
- Goserelin (Zoladex)\(^6\)
- Leuprolide (Eligard/Lupron)\(^6\)
- Triptorelin (Trelstar)\(^6\)

---

Bilateral orchiectomy (surgical castration) is an equally effective alternative to medical castration

* May be coadministered with bicalutamide (Casodex) or flutamide (Eulexin) for up to 30-60 days in patients who are at risk of developing symptoms associated with testosterone flare

† ADT pathway options, when given as listed above: goserelin (Zoladex), leuprolide (Eligard/Lupron), triptorelin (Trelstar) or history of orchiectomy

‡ If neither abiraterone nor enzalutamide have been previously used

§ If not previously used in the first line (\(^1\)st Line) setting

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**Note:** Pathways are independent of specific health plan medical policy coverage criteria. Health plan medical policy/clinical guidelines should be consulted to determine whether proposed services will be covered.

Effective August 12, 2019
Pathway options, when given as listed above: goserelin (Zoladex), leuprolide (Eligard/Lupron), triptorelin (Trelstar), or history of orchiectomy

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Continuous ADT† with supportive care ± dexamethasone13-16,24

Prostate Cancer (Adenocarcinoma) Pathways (continued)

Recurrence and Metastatic Disease | Hormone Resistant | First Line of Therapy (1st Line)

- Abiraterone (Zytiga) and prednisone with continued ADT†8,12,25-27
- Docetaxel (Taxotere) (every 3 weeks) with continued ADT†9,10,19
- Enzalutamide (Xtandi) with continued ADT†
- Goserelin (Zoladex) with bicalutamide (Casodex)6,7
- Leuprolide (Eligard/Lupron) with bicalutamide (Casodex)6,7
- Triptorelin (Trelstar) with bicalutamide (Casodex)6,7

Recurrence and Metastatic Disease | Hormone Resistant | Second and Subsequent Lines of Therapy (2nd Line+)

- Abiraterone (Zytiga)‡ and prednisone with continued ADT†8,12,25-27
- Cabazitaxel (Jevtana) with ADT†11
- Docetaxel (Taxotere) (every 3 weeks) with continued ADT†§8,10,19
- Docetaxel (Taxotere) rechallenge with ADT†21,22
- Goserelin (Zoladex) with bicalutamide (Casodex)§6,7
- Leuprolide (Eligard/Lupron) with bicalutamide (Casodex)§6,7
- Triptorelin (Trelstar) with bicalutamide (Casodex)§6,7
- Continued ADT† with supportive care ± dexamethasone13-16,24

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PROSTATE CANCER (ADENOCARCINOMA) REFERENCES

NCCN Clinical Practice Guidelines: Prostate Cancer. Version 3. 2018


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Testicular (Germ Cell Tumors) Cancer Pathways

<table>
<thead>
<tr>
<th>Seminoma</th>
<th>Stage II-III</th>
<th>Primary Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BEP:</strong> bleomycin, etoposide, and cisplatin(^5)</td>
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<td></td>
</tr>
<tr>
<td><strong>EP:</strong> etoposide and cisplatin(^4)</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Seminoma</th>
<th>Stage IIIB-C</th>
<th>Good and Intermediate Risk</th>
<th>Metastatic Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BEP:</strong> bleomycin, etoposide, and cisplatin(^5,6)</td>
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</table>

<table>
<thead>
<tr>
<th>Nonseminoma</th>
<th>Stage II-III</th>
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<td><strong>BEP:</strong> bleomycin, etoposide, and cisplatin(^5,6)</td>
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</table>

<table>
<thead>
<tr>
<th>Nonseminoma</th>
<th>Adjuvant Therapy after RPLND(^\dagger)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EP:</strong> etoposide and cisplatin(^8,9,26)</td>
<td></td>
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</tbody>
</table>

\(^*\) BEP is typically given for 3 cycles in good risk seminoma, and 4 cycles in intermediate risk

\(^\dagger\) RPLND: Retroperitoneal lymph node dissection

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TESTICULAR (GERM CELL TUMORS) CANCER REFERENCES


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Effective August 12, 2019
# Uterine (Endometrial) Cancer Pathways

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<thead>
<tr>
<th>**Adjuvant Therapy</th>
<th>Stage III-IV or High Risk Histologies**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin and paclitaxel⁵,⁶</td>
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</table>

<table>
<thead>
<tr>
<th>**Recurrent/Metastatic</th>
<th>First and Subsequent Lines of Therapy (1st Line+)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin and paclitaxel⁵,²⁷-²⁹</td>
<td></td>
</tr>
<tr>
<td>Cisplatin and doxorubicin (Adriamycin)²⁴,²⁵</td>
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</tbody>
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UTERINE (ENDOMETRIAL) CANCER REFERENCES


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