Cancer Care Quality Program

Treatment Pathways

EFFECTIVE: NOVEMBER 12, 2018
LAST REVIEWED: AUGUST 21, 2018
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.
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Effective November 12, 2018
Cancer Care Quality Program

The goal of the Cancer Care Quality Program is to help provide access to quality and affordable cancer care. A key component of the Cancer Care Quality Program is Cancer Treatment Pathways (“Pathways”).

The 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. The Pathways developed for this Program are intended to support quality cancer care.

Selecting a Pathway depends upon a number of factors – the type of cancer, the stage of disease, and the biomarkers or specific genetic profile of the cancer. 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.

Pathways are not available for every medical condition but are intended to be applicable for 80%-90% of individuals with the most common types of cancer. Selecting the best cancer treatment depends upon a number of factors – the type of cancer, the stage, the biomarkers or specific genetic profile of the cancer, and unique aspects of each 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 for every specific situation. The treating oncologist will determine if, in his/her medical opinion, a 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 treatment for him or her.

It is important to note that we will review requested services in accordance with our medical policies and clinical guidelines. When a request is received from a provider that requires medical necessity review, whether it is a Pathway or non-pathway regimen it may be authorized if it is determined to be medically necessary pursuant to our medical policies and clinical guidelines.

Feedback to enhance the Cancer Care Quality Program, Pathways, and/or questions can be emailed to cancer.quality@anthem.com. Requests for the evidence summaries reviewed to develop individual Pathways can also be sent to the same email address.

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Effective November 12, 2018
# Bladder Cancer (Urothelial) Pathways

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

<table>
<thead>
<tr>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMV: cisplatin, methotrexate, and vinblastine 3 cycles&lt;sup&gt;4,5&lt;/sup&gt;</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar) and cisplatin 4 cycles&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG: bacillus calmette-guerin, intravesical&lt;sup&gt;20-24&lt;/sup&gt;</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar), intravesical (low-grade histology only)&lt;sup&gt;19&lt;/sup&gt; – Added effective 11/12/2018</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemcitabine (Gemzar) and cisplatin&lt;sup&gt;6,17,18&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemcitabine (Gemzar)&lt;sup&gt;9&lt;/sup&gt;</td>
</tr>
<tr>
<td>Paclitaxel&lt;sup&gt;14&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pembrolizumab (Keytruda)&lt;sup&gt;37&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

* 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

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Effective November 12, 2018
BLADDER CANCER (UROTHELIAL) REFERENCES

NCCN Practice Guidelines: Bladder Cancer Version 5.2018


These Guidelines are a work in progress that may be refined as often as new significant data becomes available.

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Effective November 12, 2018

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Effective November 12, 2018 7
Breast Cancer Pathways: Neoadjuvant

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

<table>
<thead>
<tr>
<th>Neoadjuvant Therapy</th>
<th>HER2 Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AC</strong> ➔ <strong>TH</strong>: doxorubicin (Adriamycin) and cyclophosphamide followed by paclitaxel and trastuzumab (Herceptin)[^1,14,23,24,26]</td>
<td></td>
</tr>
<tr>
<td><strong>TCH</strong>: docetaxel (Taxotere), carboplatin, and trastuzumab (Herceptin)[^25,49]</td>
<td></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><strong>TCH+P</strong>: docetaxel (Taxotere), carboplatin, trastuzumab (Herceptin)[^], and pertuzumab (Perjeta)[^50,51,54,55,57]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

[^]: Administration of trastuzumab (Herceptin) is limited to 1 year (maximum 18 cycles)

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Effective November 12, 2018
BREAST CANCER NEOADJUVANT REFERENCES

NCCN Clinical Practice Guidelines: Breast Cancer V1.2018


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Effective November 12, 2018

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Breast Cancer Pathways: Adjuvant

**Adjuvant Therapy | HER2 Negative**

ddAC → **weekly T**: dose dense doxorubicin (Adriamycin) and cyclophosphamide followed by weekly paclitaxel[^9,11,12,60]

**TC**: docetaxel (Taxotere) and cyclophosphamide[^10,19]

**Adjuvant Therapy | HER2 Positive**

**AC → TH**: doxorubicin (Adriamycin) and cyclophosphamide followed by paclitaxel and trastuzumab (Herceptin)[^23,26,58]

**TCH**: docetaxel (Taxotere), carboplatin, and trastuzumab (Herceptin)[^25,26,58]

**TH**: paclitaxel and trastuzumab (Herceptin)[^34,58] (Pathway for stage I, HER2 positive breast cancer only)

**Adjuvant Therapy | HER2 Negative | Hormone Receptor (ER/PR) Negative | Residual Disease following Neoadjuvant Therapy**

Capecitabine (Xeloda)[^56]

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[^56]: Adjuvant chemotherapy pathways do NOT apply to individuals with hormone-receptor positive, lymph node negative, OncotypeDX™ LOW risk score

[^23,26,58]: Administration of trastuzumab (Herceptin) is limited to 1 year (maximum 18 cycles)

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BREAST CANCER ADJUVANT REFERENCES

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37. Slamon DJ, Swain SM, Buyse M, et al. S1-03 Primary results from BETH, a phase 3 controlled study of adjuvant chemotherapy and trastuzumab in bevacizumab in patients with HER2-positive, node-negative or high risk node-negative breast cancer. Cancer Res. December 15, 2013; 73; S1-03. Abstract S1-03

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.
49. FDA Briefing Document for sBLA 125409/51, Pertuzumab (PERJETA®). Oncologic Drugs Advisory Committee Meeting, September 12, 2013.
51. Gianni, Luca, et al. 5-year analysis of neoadjuvant pertuzumab and trastuzumab in patients with locally advanced, inflammatory, or early-stage HER2-positive breast cancer (NeoSphere): a multicentre, open-label, phase 2 randomised trial. Lancet Oncol. 17.6 (2016): 791-800. PMID: 27179402
52. Schneeweiss A. Pertuzumab and trastuzumab plus standard neoadjuvant anthracycline-containing and anthracycline free chemotherapy regimens in patients with HER2-positive early breast cancer: Efficacy analysis of a phase II cardiac safety study (TRYPHAENA). SABCS 2016

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Effective November 12, 2018
# Breast Cancer Pathways: Advanced/Metastatic Disease

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

<table>
<thead>
<tr>
<th>Medication</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capecitabine (Xeloda)</td>
<td>4,24-26,28,60,65</td>
</tr>
<tr>
<td>Doxorubicin (Adriamycin)</td>
<td>4,5,9,65</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar)</td>
<td>14,60</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>18-20,65</td>
</tr>
<tr>
<td>Vinorelbine (Navelbine)</td>
<td>15-17,65</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Medication</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olaparib (Lynparza)</td>
<td>87</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Medication</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capecitabine (Xeloda) and trastuzumab (Herceptin)</td>
<td>40-43</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar) and trastuzumab (Herceptin)</td>
<td>44,45</td>
</tr>
<tr>
<td>Paclitaxel and trastuzumab (Herceptin)</td>
<td>35,36</td>
</tr>
<tr>
<td>Pertuzumab (Perjeta), trastuzumab (Herceptin), and docetaxel (Taxotere)</td>
<td>32,33,35</td>
</tr>
<tr>
<td>Pertuzumab (Perjeta), trastuzumab (Herceptin), and paclitaxel</td>
<td>34</td>
</tr>
<tr>
<td>Vinorelbine (Navelbine) and trastuzumab (Herceptin)</td>
<td>46,47</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Medication</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ado-trastuzumab emtansine (Kadcyla)</td>
<td>50,61,62</td>
</tr>
<tr>
<td>Capecitabine (Xeloda) and lapatinib (Tykerb)</td>
<td>51,52</td>
</tr>
<tr>
<td>Capecitabine (Xeloda) and trastuzumab (Herceptin)</td>
<td>40-43</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar) and trastuzumab (Herceptin)</td>
<td>44,45</td>
</tr>
<tr>
<td>Paclitaxel and trastuzumab (Herceptin)</td>
<td>35,36</td>
</tr>
<tr>
<td>Pertuzumab (Perjeta), trastuzumab (Herceptin), and docetaxel (Taxotere)</td>
<td>32,33,35,82</td>
</tr>
<tr>
<td>Pertuzumab (Perjeta), trastuzumab (Herceptin), and paclitaxel</td>
<td>34</td>
</tr>
<tr>
<td>Trastuzumab (Herceptin) and lapatinib (Tykerb)</td>
<td>49,50</td>
</tr>
<tr>
<td>Trastuzumab (Herceptin) monotherapy</td>
<td>37,48</td>
</tr>
<tr>
<td>Vinorelbine (Navelbine) and trastuzumab (Herceptin)</td>
<td>46,47</td>
</tr>
</tbody>
</table>

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Effective November 12, 2018
BREAST CANCER ADVANCED/METASTATIC REFERENCES

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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>Therapy</th>
<th>Reference(s)</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) high dose</td>
<td>5-7,22,26,33,42</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>Therapy</th>
<th>Reference(s)</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>4,20,21,39</td>
</tr>
<tr>
<td>Fulvestrant (Faslodex) high dose</td>
<td></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>Therapy</th>
<th>Reference(s)</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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35. Ellis MJ, Prahladan M, Green NL, Mari E, Robertson JFR. Abstract OT3-2-09: FALCON: A randomised, double-blind, multicentre, phase III study comparing fulvestrant 500 mg with anastrozole 1 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(10):OT3-2-09. http://cancerres.aacrjournals.org/content/73/24_Supplement/OT3-2-09


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Effective November 12, 2018
# Chronic Myelogenous Leukemia (CML) Pathways

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

- **Imatinib (Gleevec)**

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

- **Dasatinib (Sprycel)**
- **Imatinib (Gleevec)**
- **Nilotinib (Tasigna)**

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

- **Bosutinib (Bosulif)**
- **Dasatinib (Sprycel)**
- **Nilotinib (Tasigna)**
- **Ponatinib (Iclusig)**‡

## Third Line of Therapy (3rd Line)

- **Ponatinib (Iclusig)**

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* 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 November 12, 2018
CHRONIC MYELOGENOUS LEUKEMIA (CML) REFERENCES

NCCN Clinical Practice Guidelines: Chronic Myelogenous Leukemia V4.2018


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Effective November 12, 2018
Colorectal Cancer Pathways

**Adjuvant Therapy**

Capecitabine (Xeloda)\(^{52,69}\)

**CAPOX**: capecitabine (Xeloda) and oxaliplatin (limited to 3 months duration)\(^{69}\) - **Added effective 11/12/2018**

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

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

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

Capecitabine (Xeloda)\(^{27}\)

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

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

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

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

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

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

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

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

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

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

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

Pembrolizumab (Keytruda)\(^{91}\)

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

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

- **Adjuvant Pathways do not apply to stage II MSI-H (microsatellite instability-high) disease**
- **Limited to low-risk (T1-3, N1), stage III 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**

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Effective November 12, 2018
COLORECTAL CANCER REFERENCES


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Effective November 12, 2018
Gastric, Esophageal, and Gastroesophageal Junction Cancer (Adenocarcinoma) Pathways

### Primary Therapy | Resectable and Unresectable Disease

- Cisplatin and fluorouracil (5FU)\(^3,4\)
- Fluorouracil (5FU) and cisplatin with concurrent radiation therapy (RT)\(^36\)
- **FLOT**: Fluorouracil (5FU), leucovorin, oxaliplatin, and docetaxel (Taxotere)\(^47,48\)
- Paclitaxel and carboplatin with concurrent RT\(^5\)

### Post-Operative Treatment

- Fluorouracil (5FU) and leucovorin with concurrent RT\(^38\)

### Recurrent/Metastatic or Locally Advanced/Inoperable Disease | HER2 Negative | First Line of Therapy (1st Line)

- Cisplatin and fluorouracil (5FU)\(^15,19,21,26\)
- Fluorouracil (5FU) and irinotecan (Camptosar)\(^25,26\)
- **FLO/FOLFOX**: fluorouracil (5FU), leucovorin, and oxaliplatin\(^27\)
- **FLP**: fluorouracil (5FU), leucovorin, and cisplatin\(^27\)

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

- Cisplatin, fluorouracil (5FU), and trastuzumab (Herceptin)\(^15\)

### Recurrent/Metastatic or Locally Advanced/Inoperable Disease | Second Line of Therapy (2nd Line)

- Irinotecan (Camptosar)\(^24,29\)
- Paclitaxel\(^33\)

*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 November 12, 2018
GAstric, Esophageal, and Gastroesophageal Junction (Adenocarcinoma) Cancers References


References


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Effective November 12, 2018
(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 November 12, 2018
# Head and Neck Cancer Pathways

**Non-Nasopharyngeal (Squamous Cell Carcinoma) | Candidate for Local Therapy (M0) | Primary Systemic Therapy or Post-Operative Systemic Therapy**

- High dose cisplatin* with concurrent RT\(^3,10,37\)

**Non-Nasopharyngeal (Squamous Cell Carcinoma) | Metastatic and Recurrent Disease | First Line of Therapy (1st line)**

- Carboplatin, fluorouracil (5FU), and cetuximab (Erbitux)\(^14\)
- Cisplatin, fluorouracil (5FU), and cetuximab (Erbitux)\(^14\)

**Non-Nasopharyngeal (Squamous Cell Carcinoma) | Metastatic and Recurrent Disease | Second and Subsequent Lines of Therapy (2nd line+)**

- Nivolumab (Opdivo)\(^35\)
- Paclitaxel\(^23\)

**Nasopharynx | Candidate for Local Therapy (M0) | Primary Systemic Therapy**

- High dose cisplatin* with concurrent RT\(^13,37\)

**Nasopharynx | Metastatic and Recurrent Disease | First and Subsequent Lines of Therapy (1st Line+)**

- Carboplatin\(^21\)
- Cisplatin\(^20,22\)
- Cisplatin† and gemcitabine (Gemzar)\(^29,39\)
- Cisplatin† and paclitaxel\(^18,22,29\)
- Fluorouracil (5FU)\(^22\)
- Gemcitabine (Gemzar)\(^31\)
- Methotrexate\(^24,26\)
- Paclitaxel\(^23\)

* High dose cisplatin refers to dosing to achieve total dose of 200-300 mg/m\(^2\) of cisplatin over the course of the 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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**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 November 12, 2018
HEAD AND NECK CANCER REFERENCES

NCCN Clinical Practice Guidelines: Head and Neck Cancers V1.2018


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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

**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 November 12, 2018
HODGKIN LYMPHOMA REFERENCES

NCCN Clinical Practice Guidelines: Hodgkin Lymphoma V1.2018


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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)*</td>
<td>17,18</td>
</tr>
<tr>
<td>Nivolumab (Opdivo) and ipilimumab (Yervoy)*</td>
<td>46</td>
</tr>
<tr>
<td>Pazopanib (Votrient)</td>
<td>4,5,7</td>
</tr>
<tr>
<td>Sunitinib (Sutent)</td>
<td>1-3,37</td>
</tr>
<tr>
<td>Temsirolimus (Torisel)†</td>
<td>12,23</td>
</tr>
</tbody>
</table>

| Metastatic Disease | Second or Subsequent Lines of Therapy (2nd Line+) | Clear Cell Carcinoma |
|--------------------|-----------------------------------------------|
| Nivolumab (Opdivo) | 29,30,32 |

* Indicated only for tumors with a significant clear cell histology component

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Effective November 12, 2018
Effective November 12, 2018

KIDNEY CANCER (RENA CELL CARCINOMA) REFERENCES

NCCN Practice Guideline: Kidney Cancer V4.2018


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## Lung Cancer: Non-Small Cell Lung Cancer (NSCLC) Pathways

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

- **Cisplatin and etoposide (Toposar) with concurrent XRT**
- **Paclitaxel and carboplatin with concurrent XRT**

### Adjuvant Therapy

- **Carboplatin and paclitaxel**
- **Cisplatin and gemcitabine (Gemzar)**
- **Cisplatin and vinorelbine (Navelbine)**

### Metastatic Disease

- **Squamous**
  - **TPS > 50%**
  - **First Line of Therapy (1st Line)**
  - **ECOG PS: 0-2** – Added effective 11/12/2018
  - **Pembrolizumab (Keytruda)** – Added effective 11/12/2018

- **PD-L1 Expression <50%**
  - **First Line of Therapy (1st Line)**
  - **ECOG PS: 0-2** – Termed effective 11/12/2018

- **TPS < 50%**
  - **First Line of Therapy (1st Line)**
  - **ECOG PS: 0-2** – Added effective 11/12/2018

- **ALK and EGFR Negative | PD-L1 Positive**
  - **First Line of Therapy (1st Line)**
  - **ECOG PS: 0-2** – Termed effective 11/12/2018

- **Non-squamous | ALK/EGFR Negative (ROS1 Negative or Unknown) | PD-L1 Positive**
  - **First Line of Therapy (1st Line)**
  - **ECOG PS: 0-2** – Added Effective 11/12/2018

- **Non-Squamous**
  - **First Line of Therapy (1st Line)**
  - **ECOG PS: 0-2** – Added effective 11/12/2018

- **Squamous or Nonsquamous | Immunotherapy-Ineligible**
  - **First Line of Therapy (1st Line)**
  - **ECOG PS: 0-2** – Added effective 11/12/2018

### Notes

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Effective November 12, 2018
### Lung Cancer: Non-Small Cell Lung Cancer (NSCLC) Pathways (continued)

#### Metastatic Disease | Non-Squamous | Maintenance | ECOG PS: 0-2

- Continuation bevacizumab (Avastin)\(^{36,38}\)
- Continuation pemetrexed (Alimta)\(^{39,94}\)
- Pembrolizumab (Keytruda) and pemetrexed (Alimta) (if previously treated with carboplatin, pemetrexed, and pembrolizumab)\(^{113}\) – Added effective 11/12/2018
- Switch pemetrexed (Alimta)\(^{41,94}\)

#### Metastatic Disease | Second or Subsequent Lines of Therapy (2nd Line+) | ECOG PS: 0-2

- Atezolizumab (Tecentriq)\(^{104}\) – Termined effective 11/12/2018
- Atezolizumab (Tecentriq)\(^{104}\) (if no prior checkpoint inhibitors) – Added effective 11/12/2018
- Nivolumab (Opdivo)\(^{59,61,72,78}\) – Termined effective 11/12/2018
- Nivolumab (Opdivo)\(^{59,61,72,78}\) (if no prior checkpoint inhibitors) – Added effective 11/12/2018
- Pemetrexed (Alimta)\(^{43,44}\) (non-squamous histology) – Termined effective 11/12/2018
- Carboplatin\(^\dagger\) and paclitaxel\(^7,16,54\) – Added effective 11/12/2018
- Carboplatin\(^\dagger\) and gemcitabine (Gemzar) – Added effective 11/12/2018
- Carboplatin\(^\dagger\) and pemetrexed (Alimta) – Added effective 11/12/2018

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

- Alectinib (Alecensa)\(^{108}\)

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

- Osimertinib (Tagrisso)\(^{114}\)

#### Metastatic Disease | ALK or EGFR Positive | Second or Subsequent Lines of Therapy (2nd Line+) | ECOG PS: 0-2

- Carboplatin\(^\dagger\) and paclitaxel\(^7,16,54\)
- Carboplatin\(^\dagger\) and gemcitabine (Gemzar)\(^8,11,13,22,25\)
- Carboplatin\(^\dagger\) and pemetrexed (Alimta)\(^{17,18}\)

#### Metastatic Disease | EGFR Positive | ECOG PS: 3-4

- Erlotinib (Tarceva)\(^{42,48,50,51}\)

* Administered at a dose of 2 mg/kg (up to a maximum of 200 mg)

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

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Effective November 12, 2018
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 November 12, 2018
Lung Cancer: Small Cell Lung Cancer Pathways

**Limited Stage | Primary, Adjuvant, or First Line of Therapy (1\textsuperscript{st} Line)**
- Carboplatin and etoposide (Toposar) $\pm$ XRT\textsuperscript{3}
- Cisplatin and etoposide (Toposar) $\pm$ XRT\textsuperscript{1,2}

**Extensive Stage | First Line of Therapy (1\textsuperscript{st} Line)**
- Carboplatin and etoposide (Toposar)$^9$

**Second and Subsequent Lines of Therapy (2\textsuperscript{nd} Line+) | Relapse Greater than Six (6) Months**
- Carboplatin and etoposide (Toposar)$^9$

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LUNG CANCER: SMALL CELL LUNG CANCER REFERENCES


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Effective November 12, 2018
## Melanoma Pathways: Metastatic Melanoma

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<tr>
<th>Stage IIIB/IIIC (Resected)</th>
<th>Adjuvant Therapy</th>
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<tr>
<td>Nivolumab (Opdivo)\textsuperscript{59}</td>
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</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>First and Subsequent Lines of Therapy (1st Line+)</th>
<th>Any BRAF Status</th>
<th>ECOG PS: 0-2</th>
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</thead>
<tbody>
<tr>
<td>Pembrolizumab (Keytruda)\textsuperscript{35,45,55,56}</td>
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<tr>
<td>Nivolumab (Opdivo) and ipilimumab (Yervoy)\textsuperscript{85}</td>
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<tr>
<th>Metastatic Disease</th>
<th>First Line of Therapy (1st Line)</th>
<th>BRAF Mutated\textsuperscript{‡}</th>
<th>Symptomatic Disease</th>
<th>ECOG PS: 0-2</th>
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<tbody>
<tr>
<td>Vemurafenib (Zelboraf) and cobimetinib (Cotellic)\textsuperscript{26,40,42}</td>
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<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Second and Subsequent Lines of Therapy (2nd Line+)</th>
<th>BRAF Mutated\textsuperscript{†}</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vemurafenib (Zelboraf) and cobimetinib (Cotellic)\textsuperscript{26,40,42}</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Second and Subsequent Lines of Therapy (2nd Line+)</th>
<th>Any BRAF Status</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipilimumab (Yervoy)\textsuperscript{1,14,15,35,36}</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Administered at a dose of 2 mg/kg (up to a maximum of 200 mg)

† BRAF mutations include V600E and V600K mutations

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Effective November 12, 2018
MELANOMA: METASTATIC MELANOMA REFERENCES

NCCN Clinical Practice Guidelines: Melanoma V2.2018


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Effective November 12, 2018
# Myeloma Pathways: Multiple Myeloma

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

**VRD/VDR**: bortezomib (Velcade), lenalidomide (Revlimid), and dexamethasone

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

**CyBorD or VDC**: bortezomib (Velcade), cyclophosphamide, and dexamethasone

**R-dex**: lenalidomide (Revlimid) and low-dose dexamethasone

**VRD/VDR**: bortezomib (Velcade), lenalidomide (Revlimid), and dexamethasone

**VD**: bortezomib (Velcade) and dexamethasone

## Maintenance Therapy | Post-Transplant

Lenalidomide (Revlimid)

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

**CRd or KRd**: carfilzomib (Kyprolis), lenalidomide (Revlimid), and dexamethasone

**DRD**: daratumumab (Darzalex), lenalidomide (Revlimid), and dexamethasone

**DVD**: daratumumab (Darzalex), bortezomib (Velcade), and dexamethasone

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

Daratumumab (Darzalex)

Elotuzumab (Empliciti), lenalidomide (Revlimid), and dexamethasone

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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 November 12, 2018
MYELOMA: MULTIPLE MYELOMA REFERENCES

NCCN Clinical Practice Guidelines: Multiple Myeloma V3.2018


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Effective November 12, 2018
NHL: Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Pathways

<table>
<thead>
<tr>
<th>First Line of Therapy (1st Line)</th>
<th>With 17p Deletion or TP53 Mutation Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibrutinib (Imbruvica)</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>First Line of Therapy (1st Line)</th>
<th>Without 17p Deletion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BR</strong>: bendamustine (Bendeka, Treanda) and rituximab</td>
<td>13,15,39,51</td>
</tr>
<tr>
<td><strong>FCR</strong>: fludarabine (Fludara), cyclophosphamide, and rituximab*</td>
<td>1,2,39,51</td>
</tr>
<tr>
<td>Ibrutinib (Imbruvica)</td>
<td>28,37,46,47</td>
</tr>
<tr>
<td>Obinutuzumab (Gazyva) and chlorambucil (Leukeran)</td>
<td>16</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second and Subsequent Lines of Therapy (2nd Line+)</th>
<th>With 17p Deletion or TP53 Mutation Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibrutinib (Imbruvica)</td>
<td></td>
</tr>
<tr>
<td>Idelalisib (Zydelig)</td>
<td></td>
</tr>
<tr>
<td>Idelalisib (Zydelig) and rituximab*</td>
<td></td>
</tr>
<tr>
<td>Venetoclax (Venclexta) and rituximab</td>
<td><strong>Added effective 11/12/2018</strong></td>
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</table>

<table>
<thead>
<tr>
<th>Second and Subsequent Lines of Therapy (2nd Line+)</th>
<th>Without 17p Deletion</th>
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<tbody>
<tr>
<td><strong>BR</strong>: bendamustine (Bendeka, Treanda) and rituximab</td>
<td>13,15,42</td>
</tr>
<tr>
<td>Ibrutinib (Imbruvica)</td>
<td>28,37,46,47</td>
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<tr>
<td>Idelalisib (Zydelig)</td>
<td>43</td>
</tr>
<tr>
<td>Idelalisib (Zydelig) and rituximab</td>
<td>38</td>
</tr>
<tr>
<td>Venetoclax (Venclexta) and rituximab</td>
<td><strong>Added effective 11/12/2018</strong></td>
</tr>
</tbody>
</table>

Primary treatment for CLL should be initiated in accordance with the guidelines established by the Working Group on CLL

* 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)

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 November 12, 2018
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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56. Munir T, Howard DR, McParland L, et al. Results of the randomized phase IIb ADMIRE trial of FCR with or without mitoxantrone in previously untreated CLL. Leukemia. 2017-e-publication.PMID: 28216660.


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 November 12, 2018
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 (Toposar), 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 (Toposar), 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

*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 November 12, 2018
NHL: DIFFUSE LARGE B CELL LYMPHOMA REFERENCES


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# NHL: Follicular and Marginal Zone Lymphoma Pathways

## Gastric MALT (Mucosa-Associated Lymphoid Tissue) Lymphoma | Stage IE or IIE | *H. pylori* Positive

- Antibiotic therapy for *H. pylori* eradication

## Splenic Marginal Zone† or Gastric MALT Lymphoma | First Line of Therapy (1st Line)

- Rituximab

## Follicular (Grade I-IIIA) and Other Marginal Zone Lymphomas | First Line of Therapy (1st Line)

- **BR**: Bendamustine (Bendeka, Treanda) and rituximab
- **R-CHOP(21)**: Cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, and rituximab
- **R-CVP**: Cyclophosphamide, vincristine (Vincasar), prednisone, and rituximab
- Rituximab monotherapy

## Follicular and Other Marginal Zone Lymphomas | First Line of Therapy (1st Line) | Additional options for the elderly or infirm

- Chlorambucil (Leukeran)
- Chlorambucil (Leukeran) and rituximab
- Cyclophosphamide
- Cyclophosphamide and rituximab

## Follicular Lymphoma (Grade III) | First Line of Therapy (1st Line)

- **R-CHOP(21)**: Cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, and rituximab
- **R-CEOP**: Cyclophosphamide, etoposide (Toposar), vincristine (Vincasar), prednisone, and rituximab

*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.

† 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)
NHL: FOLLICULAR AND MARGINAL ZONE LYMPHOMA REFERENCES


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Effective November 12, 2018
Effective November 12, 2018

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## 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)\(^{42}\) – **Added effective 11/12/2018**
- **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 November 12, 2018
NHL: MANTLE CELL LYMPHOMA REFERENCES


References


13. Forstpointner 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: 15668470


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# Ovarian Cancer (Epithelial) Pathways

**Adjuvant Therapy | Stage IA/B (Grade 2 or 3) or IC (Grade 1-3)**

- Carboplatin and dose dense paclitaxel<sup>6-8</sup>
- Carboplatin and paclitaxel<sup>2,5,7</sup>

**Adjuvant or Primary Therapy | Stage II, III, IV**

- Carboplatin and paclitaxel<sup>6,8,45</sup> *(Administered weekly or every 3 weeks)*
- Intravenous (IV) paclitaxel and Intraperitoneal (IP) cisplatin and IP paclitaxel<sup>1,49</sup> *(Stage III only)*

**Recurrent Disease | First and Subsequent Lines of Therapy (1st Line+) | Platinum-Sensitive*<sup>+</sup>**

- Carboplatin<sup>8,9,12</sup>
- Carboplatin and gemcitabine (Gemzar)<sup>12,13</sup>
- Carboplatin and paclitaxel<sup>8,9,15</sup>
- Carboplatin and weekly paclitaxel

**Recurrent Disease | Maintenance Therapy | Platinum-Sensitive*<sup>+</sup>**

- Niraparib (Zejula)<sup>54</sup>
- Olaparib (Lynparza)<sup>55</sup> - Added effective 11/12/2018
- Rucaparib (Rubraca)<sup>60</sup> - Added effective 11/12/2018

**Recurrent Disease | Second and Subsequent Lines of Therapy (2nd Line+) | Platinum Resistant**

- Bevacizumab (Avastin) monotherapy<sup>42</sup>
- Docetaxel (Taxotere)<sup>17</sup>
- Gemcitabine (Gemzar)<sup>18,20</sup>
- Liposomal doxorubicin (Doxil or Lipodox)<sup>19-21</sup>
- Paclitaxel (weekly)<sup>22,23</sup>
- Paclitaxel and bevacizumab (Avastin)<sup>36,38</sup>
- Tamoxifen<sup>56</sup>
- Topotecan (Hycamtin)<sup>21,24</sup>
- Topotecan (Hycamtin) and bevacizumab (Avastin)<sup>36,37</sup>
- Vinorelbine (Navelbine)<sup>34,35</sup>

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

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Effective November 12, 2018
OVARIAN CANCER (EPITHELIAL) REFERENCES

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


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Effective November 12, 2018
Pancreatic Cancer (Adenocarcinoma) Pathways

### Adjuvant Therapy

- Capecitabine (Xeloda) and gemcitabine (Gemzar)\(^{36,40}\)
- **FULV**: fluorouracil (5FU) and leucovorin\(^{4,6,9}\)
- **mFOLFIRINOX**: fluorouracil (5FU), leucovorin, irinotecan (Camptosar), and oxaliplatin\(^{46}\)
- Gemcitabine (Gemzar)\(^{1,3-7}\)

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

- **FOLFIRINOX**: fluorouracil (5FU), leucovorin, irinotecan (Camptosar), and oxaliplatin\(^{5,21}\)
- Gemcitabine (Gemzar)\(^{5,15-21}\)
- Gemcitabine (Gemzar) and nab-paclitaxel (Abraxane)\(^{5,15,33}\)

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

- **OFF**: fluorouracil (5FU), leucovorin, and oxaliplatin\(^{32}\)
- Gemcitabine (Gemzar)\(^{21}\)

* Modified FOLFIRINOX: Bolus 5-FU not administered

**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 November 12, 2018
PANCREATIC CANCER (ADENOCARCINOMA) REFERENCES

NCCN Clinical Practice Guidelines: Pancreatic Adenocarcinoma V3.2017


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Effective November 12, 2018
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# 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)\(^39,41\)
- Docetaxel (Taxotere) (every 3 weeks) with Androgen Deprivation Therapy (ADT)\(^19\)
- Goserelin (Zoladex)\(^6\)
- Leuprolide (Eligard/Lupron)\(^6\)
- Triptorelin (Trelstar)\(^6\)

Bilateral orchietomy (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 orchietomy

‡ If neither abiraterone nor enzalutamide have been previously used

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

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Effective November 12, 2018
# Prostate Cancer (Adenocarcinoma) Pathways (continued)

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

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

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

- **Abiraterone (Zytiga)**<sup>‡</sup> and prednisone with continued ADT<sup>†,8,12,25-27</sup>
- **Cabazitaxel (Jevtana) with ADT**<sup>†,11</sup>
- **Docetaxel (Taxotere) (every 3 weeks) with continued ADT**<sup>†,§,9,10,19</sup>
- **Docetaxel (Taxotere) rechallenge with ADT**<sup>†,21,22</sup>
- **Goserelin (Zoladex) with bicalutamide (Casodex)**<sup>§,6,7</sup>
- **Leuprolide (Eligard/Lupron) with bicalutamide (Casodex)**<sup>§,6,7</sup>
- **Triptorelin (Trelstar) with bicalutamide (Casodex)**<sup>§,6,7</sup>
- **Continued ADT**<sup>†</sup> with supportive care ± dexamethasone<sup>13-16,24</sup>

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 (1st 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 November 12, 2018
PROSTATE CANCER (ADENOCARCINOMA) REFERENCES

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


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# Testicular (Germ Cell Tumors) Cancer Pathways

<table>
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<tr>
<th>Pathology</th>
<th>Stage</th>
<th>Risk</th>
<th>Therapy</th>
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<tbody>
<tr>
<td>**Seminoma</td>
<td>Stage II-IIIA</td>
<td>Primary Therapy**</td>
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<tr>
<td>BEP:</td>
<td>bleomycin, etoposide (Toposar), and cisplatin&lt;sup&gt;5&lt;/sup&gt;</td>
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<tr>
<td>EP:</td>
<td>etoposide (Toposar) and cisplatin&lt;sup&gt;4&lt;/sup&gt;</td>
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</tr>
<tr>
<td>**Seminoma</td>
<td>Stage IIIB-C</td>
<td>Good and Intermediate Risk</td>
<td>Metastatic Disease**</td>
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<tr>
<td>BEP:</td>
<td>bleomycin, etoposide (Toposar), and cisplatin&lt;sup&gt;5,6&lt;/sup&gt;</td>
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<tr>
<td>**Nonseminoma</td>
<td>Stage II-IIIA</td>
<td>Primary Therapy**</td>
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<td>BEP:</td>
<td>bleomycin, etoposide (Toposar), and cisplatin&lt;sup&gt;5,6&lt;/sup&gt;</td>
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<tr>
<td>EP:</td>
<td>etoposide (Toposar) and cisplatin&lt;sup&gt;4&lt;/sup&gt;</td>
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<tr>
<td>**Nonseminoma</td>
<td>Stage IIIB-C</td>
<td>Primary Therapy**</td>
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<td>BEP:</td>
<td>bleomycin, etoposide (Toposar), and cisplatin&lt;sup&gt;5,6&lt;/sup&gt;</td>
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<tr>
<td>**Nonseminoma</td>
<td>Adjuvant Therapy after RPLND†**</td>
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<tr>
<td>EP:</td>
<td>etoposide (Toposar) and cisplatin&lt;sup&gt;8,9,26&lt;/sup&gt;</td>
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</tbody>
</table>

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

† RPLND: Retroperitoneal lymph node dissection

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Effective November 12, 2018
TESTICULAR (GERM CELL TUMORS) CANCER REFERENCES


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Effective November 12, 2018
Uterine (Endometrial) Cancer Pathways

<table>
<thead>
<tr>
<th>Adjuvant Therapy</th>
<th>Stage III-IV or High Risk Histologies</th>
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<tr>
<td>Carboplatin and paclitaxel⁵,⁶</td>
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<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>
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</tr>
<tr>
<td>Cisplatin and doxorubicin (Adriamycin)²⁴,²⁵</td>
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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.
UTERINE (ENDOMETRIAL) CANCER REFERENCES


These Guidelines are a work in progress that may be refined as often as new significant data becomes available.

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