Cancer Care Quality Program

Treatment Pathways

EFFECTIVE NOVEMBER 18, 2019
LAST REVIEWED AUGUST 27, 2019
Review and updates during 3rd quarter 2019

Colorectal Cancer
- ‘Metastatic Disease | RAS Wild Type (WT) | Third or Subsequent Lines of Therapy (3rd Line+)’ clinical scenario and associated panitumumab (Vectibix) monotherapy option removed from pathway

Gastric, Esophageal, and Gastroesophageal
- Footnote added to paclitaxel and carboplatin with concurrent RT combination regimen to limit to esophageal and GE junction cancers ONLY

Head and Neck
- Footnote added to paclitaxel and carboplatin with concurrent RT combination regimen to limit to esophageal and GE junction cancers ONLY
- Induction cisplatin and gemcitabine (Gemzar) followed by cisplatin/RT added as a pathway option in the following clinical scenario: ‘Nasopharynx | Candidate for Local Therapy (M0) | Primary Systemic Therapy’

NHL: Chronic Lymphocytic Leukemia (CLL)/ Small Lymphocytic Lymphoma (SLL)
- The following regimens removed as a pathway option from clinical scenario: ‘First Line of Therapy (1st Line) | Without 17p Deletion’
  - Fludarabine (Fludara), cyclophosphamide, and rituximab (FCR)
  - Bendamustine (Bendeka, Treanda) and rituximab (BR)
- Obinutuzumab (Gazyva) and chlorambucil (Leukeran) combination regimen replaced with venetoclax (Venclexa) and obinutuzumab (Gazyva) as a pathway option in the following clinical scenario: ‘First Line of Therapy (1st Line) | Without 17p Deletion’
- Duvelisib (Copiktra) added as a pathway option in the following clinical scenarios:
  - ‘Second and Subsequent Lines of Therapy (2nd Line+) | With 17p Deletion or TP53 Mutation Present’
  - ‘Second and Subsequent Lines of Therapy (2nd Line+) | Without 17p deletion’

Prostate Cancer (Adenocarcinoma)
- Asterisk added to abiraterone (Zytiga) containing regimens to allow for regional, lymph node positive disease ONLY in the following clinical scenario: ‘High Risk (T3a or Gleason 8-10), Very High Risk (T3b-T4), and Locally Advanced Prostate Cancer (LN+) | Primary Treatment with Radiotherapy (RT)’
- Enzalutamide (Xtandi) + ADT and apalutamide (Erleada) + ADT added as pathway options to the following clinical scenario: ‘Recurrent and Metastatic Disease | Hormone Sensitive’
- Footnote added to ALL abiraterone (Zytiga) containing regimens to clarify that abiraterone (Zytiga) should NOT be used concurrently with Radium 223

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**TABLE OF CONTENTS**

- Cancer Care Quality Program 4
- Bladder Cancer (Urothelial) Pathways 5
- Breast Cancer Pathways: Neoadjuvant 9
- Breast Cancer Pathways: Adjuvant 13
- Breast Cancer Pathways: Advanced/Metastatic Disease 17
- Breast Cancer Pathways: Endocrine Therapy for Advanced/Metastatic Disease 23
- Chronic Myelogenous Leukemia (CML) Pathways 27
- Colorectal Cancer Pathways 31
- Gastric, Esophageal, and Gastroesophageal Junction Cancer (Adenocarcinoma) Pathways 37
- Head and Neck Cancer Pathways 41
- Hodgkin Lymphoma Pathways 44
- Kidney Cancer (Renal Cell Carcinoma) Pathways 47
- Lung Cancer: Non-Small Cell Lung Cancer (NSCLC) Pathways 50
- Lung Cancer: Small Cell Lung Cancer Pathways 57
- Melanoma Pathways: Metastatic Melanoma 60
- Myeloma Pathways: Multiple Myeloma 65
- NHL: Chronic Lymphocytic Leukemia (CLL)/ Small Lymphocytic Lymphoma (SLL) Pathways 71
- NHL: Diffuse Large B-Cell Lymphoma Pathways 76
- NHL: Follicular and Marginal Zone Lymphoma Pathways 80
- NHL: Mantle Cell Lymphoma Pathways 84
- Ovarian Cancer (Epithelial) Pathways 88
- Pancreatic Cancer (Adenocarcinoma) Pathways 93
- Prostate Cancer (Adenocarcinoma) Pathways 96
- Testicular (Germ Cell Tumors) Cancer Pathways 102
- Uterine (Endometrial) Cancer Pathways 105

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Effective November 18, 2019 3
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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# 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\(^5,17,18\)

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

- Gemcitabine (Gemzar)\(^9\)
- Paclitaxel\(^14\)
- Pembrolizumab (Keytruda)\(^‡37\)

* 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 reimbursement for biosimilar products may be impacted by health plan specific formularies, medical policy and preferred products consulted to determine whether proposed services will be covered.  

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# Breast Cancer Pathways: Neoadjuvant

## Neoadjuvant Therapy | HER2 Negative

- **ddAC → weekly T**: dose dense doxorubicin (Adriamycin) and cyclophosphamide followed by weekly paclitaxel[^8,11,12,39]
- **TC**: docetaxel (Taxotere) and cyclophosphamide[^10,43]

## Neoadjuvant Therapy | HER2 Positive

- **AC → TH**: doxorubicin (Adriamycin) and cyclophosphamide followed by paclitaxel and trastuzumab (Herceptin)[^1,14,23,24,26]
- **TCH**: docetaxel (Taxotere), carboplatin, and trastuzumab (Herceptin)[^25,49]

## Neoadjuvant Therapy | HER2 Positive | Hormone Receptor (ER/PR) Negative

- **TCH+P**: docetaxel (Taxotere), carboplatin, trastuzumab (Herceptin)[^50,51,54,55,57], and pertuzumab (Perjeta)[^50,51,54,55,57]

[^8]: Administration of trastuzumab (Herceptin) is limited to 1 year (maximum 18 cycles)

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Effective November 18, 2019
Effective reimbursement for biosimilar products may be impacted by health plan specific formularies, medical policy and preferred products. Pathway

BREAST CANCER NEOADJUVANT REFERENCES

NCCN Clinical Practice Guidelines: Breast Cancer V4.2018


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


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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[^8,9,11,12,60]
- **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]

**Adjuvant Therapy | HER2 Positive | Residual Disease following Neoadjuvant Therapy**

- Trastuzumab emtansine (Kadcyla)^[63]

* 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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References

16. Martín M, Villar A, Solé-Calvo A, et al. Doxorubicin in combination with fluorouracil and cyclophosphamide (i.e. FAC regimen, day 1, 21) versus methotrexate in combination with fluorouracil and cyclophosphamide (i.e. CMF regimen, day 1, 21) as adjuvant chemotherapy for operable breast cancer: a study by the GEICAM group. Ann Oncol. 2003 Jun;14(6):833-842.

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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 + 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.


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


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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)\(^4,24-26,28,60,65\)
- 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)\(^19,50\)
- Trastuzumab (Herceptin) monotherapy\(^37,48\)
- Vinorelbine (Navelbine) and trastuzumab (Herceptin)\(^46,47\)

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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>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole (Arimidex)*1,6,7,10,11,22,33</td>
</tr>
<tr>
<td>Anastrozole (Arimidex) and palbociclib (Ibrance)*19,40,41</td>
</tr>
<tr>
<td>Anastrozole (Arimidex) and ribociclib (Kisqali)*19,40,41</td>
</tr>
<tr>
<td>Fulvestrant (Faslodex)* high dose5,7,22,26,33,42</td>
</tr>
<tr>
<td>Fulvestrant (Faslodex) and ribociclib (Kisqali)*56</td>
</tr>
<tr>
<td>Letrozole (Femara)*3,12,14,38</td>
</tr>
<tr>
<td>Letrozole (Femara) and palbociclib (Ibrance)*19,40,41</td>
</tr>
<tr>
<td>Letrozole (Femara) and ribociclib (Kisqali)*19,40,41,53</td>
</tr>
<tr>
<td>Tamoxifen†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>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole (Arimidex)*1,6,7,10,11,22,33</td>
</tr>
<tr>
<td>Exemestane (Aromasin)*4,20,21,39</td>
</tr>
<tr>
<td>Fulvestrant (Faslodex) high dose*</td>
</tr>
<tr>
<td>Fulvestrant (Faslodex) and palbociclib (Ibrance)*‡41</td>
</tr>
<tr>
<td>Letrozole (Femara)*3,12,14,38</td>
</tr>
<tr>
<td>Tamoxifen†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>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole (Arimidex) and trastuzumab (Herceptin)*46</td>
</tr>
<tr>
<td>Letrozole (Femara) and trastuzumab (Herceptin)*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 November 18, 2019
**BREAST CANCER ENDOCRINE THERAPY FOR ADVANCED/METASTATIC DISEASE REFERENCES**

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Effective November 18, 2019
Chronic Myelogenous Leukemia (CML) Pathways

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imatinib (Gleevec)</td>
<td>1,4,6,8,30,33,35</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dasatinib (Sprycel)</td>
<td>1,2,30,37-39</td>
</tr>
<tr>
<td>Imatinib (Gleevec)</td>
<td>1,4,6,8,30,33,35</td>
</tr>
<tr>
<td>Nilotinib (Tasigna)</td>
<td>6,8,31,32</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bosutinib (Bosulif)</td>
<td>23,33</td>
</tr>
<tr>
<td>Dasatinib (Sprycel)</td>
<td>1,2,9,10,12,36</td>
</tr>
<tr>
<td>Nilotinib (Tasigna)</td>
<td>16-18,31,32</td>
</tr>
<tr>
<td>Ponatinib (Iclusig)‡</td>
<td>26</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ponatinib (Iclusig)‡</td>
<td>26</td>
</tr>
</tbody>
</table>

* 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 18, 2019
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## Colorectal Cancer Pathways

### Adjuvant Therapy | Microsatellite Instability – Low (MSI-L)

- **Capecitabine (Xeloda)**

**CAPOX**: capecitabine (Xeloda) and oxaliplatin (limited to 3 months duration)\(^*\)\(^4\)

**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)\(^\dagger\) | 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)\(^25,26,28,33,44,45,70\)

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

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

**FULV + bevacizumab**: 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+) – Termined 11/18/2019

- **Panitumumab (Vectibix) monotherapy**\(^11,62,66\) – Termined 11/18/2019

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\(*\) Limited to low-risk (T1-3, N1), stage III colon cancer only

\(\dagger\) Exon 2 KRAS, non-exon 2 KRAS, and NRAS mutations; testing recommended for all patients with metastatic disease

\(\ddagger\) Limit to one line of therapy

\(\S\) 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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COLORECTAL CANCER REFERENCES


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Effective November 18, 2019
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>Pacitaxel and carboplatin with concurrent RT^5</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Post-Operative Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluorouracil (5FU) and leucovorin with concurrent RT^38</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 oxaliplatin^27</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>FLP</strong>: fluorouracil (5FU), leucovorin, and cisplatin^27</td>
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</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>
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<td></td>
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</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>Pacitaxel^33</td>
<td></td>
</tr>
</tbody>
</table>

* Limited to esophageal and gastroesophageal junction cancers only

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Effective November 18, 2019
GASTRIC, ESOPHAGEAL, AND GASTROESOPHAGEAL JUNCTION (ADENOCARCINOMA) CANCERS REFERENCES


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32. Ilson DH, Waldleig RG, Leichman LP, et al. Paclitaxel given by a weekly 1-


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Effective November 18, 2019
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 RT3,10,37

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
- Paclitaxel23

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

- High dose cisplatin* with concurrent RT13,37

- Cisplatin and gemcitabine (Gemzar) followed by concurrent cisplatin/RT45 – Added 11/18/2019

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

- Carboplatin21
- Cisplatin20,22
- Cisplatin† and gemcitabine (Gemzar)29,39
- Cisplatin† and paclitaxel18,22,29
- Fluorouracil (5FU)22
- Gemcitabine (Gemzar)31
- Methotrexate24,26
- Paclitaxel23

*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 November 18, 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 |

**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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HODGKIN LYMPHOMA REFERENCES

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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>
<th>Clear Cell Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab (Opdivo)</td>
<td>and ipilimumab (Yervoy)</td>
<td></td>
</tr>
<tr>
<td>Pembrolizumab (Keytruda) and axitinib (Inlyta)</td>
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</tbody>
</table>

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

* Indicated only for tumors with a significant clear cell histology component
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Lung Cancer: Non-Small Cell Lung Cancer (NSCLC) Pathways

<table>
<thead>
<tr>
<th>Neoadjuvant/Preoperative/Induction Therapy or Adjuvant/Definitive Therapy</th>
</tr>
</thead>
</table>
| Cisplatin and etoposide with concurrent XRT<sup>88,89</sup>  
Paclitaxel and carboplatin with concurrent XRT<sup>93</sup> |

<table>
<thead>
<tr>
<th>Adjuvant Therapy</th>
</tr>
</thead>
</table>
| Carboplatin and paclitaxel<sup>52</sup>  
Cisplatin and gemcitabine (Gemzar)  
Cisplatin and vinorelbine (Navelbine)<sup>53</sup> |

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Squamous</th>
<th>ALK/EGFR Negative (ROS Negative or Unknown)</th>
<th>TPS &gt; 50%</th>
<th>First Line of Therapy (1st Line)</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembrolizumab (Keytruda)&lt;sup&gt;125&lt;/sup&gt;</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Squamous</th>
<th>TPS &lt; 50%</th>
<th>First Line of Therapy (1st Line)</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembrolizumab (Keytruda)*, carboplatin, and paclitaxel&lt;sup&gt;126&lt;/sup&gt;</td>
<td></td>
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</tbody>
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<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Nonsquamous</th>
<th>ALK/EGFR Negative (ROS1 Negative or Unknown)</th>
<th>TPS &gt; 50%</th>
<th>First Line of Therapy (1st Line)</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembrolizumab (Keytruda)*&lt;sup&gt;102,125&lt;/sup&gt;</td>
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<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Nonsquamous</th>
<th>ALK/EGFR Negative (ROS1 Negative or Unknown)</th>
<th>TPS &lt; 50%</th>
<th>First Line of Therapy (1st Line)</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin&lt;sup&gt;†&lt;/sup&gt;, pemetrexed (Alimta), and pembrolizumab (Keytruda)*&lt;sup&gt;124&lt;/sup&gt;</td>
<td></td>
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<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Squamous or Nonsquamous</th>
<th>Immunotherapy-Ineligible</th>
<th>First Line of Therapy (1st Line)</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
</table>
| Carboplatin<sup>†</sup> and paclitaxel<sup>17-16,54</sup>  
Carboplatin, paclitaxel, and bevacizumab (Avastin)<sup>13,14,31</sup> (NON-SQUAMOUS ONLY)  
Cisplatin<sup>†</sup> and gemcitabine (Gemzar)<sup>8,11,13,22-25</sup>  
Cisplatin<sup>†</sup> 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.

**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. Biosimilars of reference products listed are considered “on pathway.” However, reimbursement for biosimilar products may be impacted by health plan specific formularies, medical policy and preferred product rules.

Effective November 18, 2019
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\(^\dagger\), pemetrexed, and pembrolizumab)\(^{51,13}\)
- Switch pemetrexed (Alimta)\(^{41,94}\)

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

- Atezolizumab (Tecentriq)\(^{104}\) (if no prior checkpoint inhibitors)
- Nivolumab (Opdivo)\(^{59,61,72,78}\) (if no prior checkpoint inhibitors)
- Carboplatin\(^\dagger\) and paclitaxel\(^\dagger\)\(^{7,16,54}\)
- Carboplatin\(^\dagger\) and gemcitabine (Gemzar)\(^\dagger\)
- Carboplatin\(^\dagger\) and pemetrexed (Alimta)\(^\dagger\)

### Metastatic Disease | ALK Positive | First Line of Therapy (1\(^{st}\) Line)

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

### Metastatic Disease | EGFR Positive | First Line of Therapy (1\(^{st}\) Line)

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

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

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

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

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

* Administered at a dose of 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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NCCN Clinical Practice Guidelines: Non-Small Cell Lung Cancer V6.2018


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References

14. FDA review documents

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Lung Cancer: Small Cell Lung Cancer Pathways

**Limited Stage | Primary, Adjuvant, or First Line of Therapy (1st Line)**

- Carboplatin and etoposide ± XRT\(^3\)
- Cisplatin and etoposide ± XRT\(^1,2\)

**Extensive Stage | First Line of Therapy (1st Line)**

- Carboplatin and etoposide\(^9\)
- Atezolizumab (Tecentriq), carboplatin, and etoposide\(^31\)

**Second and Subsequent Lines of Therapy (2nd Line+) | Relapse Greater than Six (6) Months**

- Carboplatin and etoposide\(^9\)

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Effective November 18, 2019
LUNG CANCER: SMALL CELL LUNG CANCER REFERENCES


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Melanoma Pathways: Metastatic Melanoma

**Stage IIB/IIIC (Resected) | Adjuvant Therapy**

Nivolumab (Opdivo)\(^59\)

**Metastatic Disease | First and Subsequent Lines of Therapy (1\(^{st}\) Line+) | Any BRAF Status | ECOG PS: 0-2**

Nivolumab (Opdivo) and ipilimumab (Yervoy)\(^65\)

Pembrolizumab (Keytruda)\(^{35,45,55,56}\)

**Metastatic Disease | First Line of Therapy (1\(^{st}\) Line) | BRAF Mutated\(^\dagger\) | Symptomatic Disease | ECOG PS: 0-2**

Encorafenib (Braftovi) and binimetinib (Mektovi)\(^66\)

**Metastatic Disease | Second and Subsequent Lines of Therapy (2\(^{nd}\) Line+) | BRAF Mutated\(^\dagger\) | ECOG PS: 0-2**

Encorafenib (Braftovi) and binimetinib (Mektovi)\(^66\)

**Metastatic Disease | Second and Subsequent Lines of Therapy (2\(^{nd}\) Line+) | Any BRAF Status | ECOG PS: 0-2**

Ipilimumab (Yervoy)\(^{1,14,15,35,36}\)

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* 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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MELANOMA: METASTATIC MELANOMA REFERENCES

NCCN Clinical Practice Guidelines: Melanoma V2.2019


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November 18, 2019
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Effective November 18, 2019
Myeloma Pathways: Multiple Myeloma

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

VRD/VDR: bortezomib (Velcade), lenalidomide (Revlimid), and dexamethasone\(^{10,12,79}\)

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

CyBorD or VDC: bortezomib (Velcade), cyclophosphamide, and dexamethasone\(^{9,10,84}\)

R-dex: lenalidomide (Revlimid) and low-dose dexamethasone\(^{10,11,13,73}\)

VRD/VDR: bortezomib (Velcade), lenalidomide (Revlimid), and dexamethasone\(^{50,12,79}\)

VD: bortezomib (Velcade) and dexamethasone\(^{1,3,12,24,89}\)

**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 dexamethasone\(^{82}\)

DRD: daratumumab (Darzalex), lenalidomide (Revlimid), and dexamethasone\(^{100}\)

DVD: daratumumab (Darzalex), bortezomib (Velcade), and dexamethasone\(^{103}\)

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

Daratumumab (Darzalex)\(^{95}\)

Elotuzumab (Empliciti), lenalidomide (Revlimid), and dexamethasone\(^{97}\)

Elotuzumab (Empliciti), pomalidomide (Pomalyst), and dexamethasone\(^{*113}\)

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

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Effective November 18, 2019
MYELOMA: MULTIPLE MYELOMA REFERENCES

NCCN Clinical Practice Guidelines: Multiple Myeloma V2.2019


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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


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Effective November 18, 2019
### NHL: Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Pathways

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

<table>
<thead>
<tr>
<th>Medication</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibrutinib (Imbruvica)</td>
<td></td>
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</tbody>
</table>

#### First Line of Therapy (1st Line) | Without 17p Deletion or TP53 Mutation Present - clarification added 11/18/2019

<table>
<thead>
<tr>
<th>Medication</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BR</strong>: bendamustine (Bendeka, Treanda) and rituximab</td>
<td>Termed 11/18/2019</td>
</tr>
<tr>
<td><strong>FCR</strong>: fludarabine (Fludara), cyclophosphamide, and rituximab</td>
<td>Termed 11/18/2019</td>
</tr>
<tr>
<td>Ibrutinib (Imbruvica)</td>
<td></td>
</tr>
<tr>
<td>Obinutuzumab (Gazyva) and chlorambucil (Leukeran)</td>
<td>Termed 11/18/2019</td>
</tr>
<tr>
<td>Venetoclax (Venclexta) and obinutuzumab (Gazyva)</td>
<td>Added 11/18/2019</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Medication</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duvelisib (Copiktra)</td>
<td>Added 11/18/2019</td>
</tr>
<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></td>
</tr>
</tbody>
</table>

#### Second and Subsequent Lines of Therapy (2nd Line+) | Without 17p Deletion or TP53 Mutation Present - clarification added 11/18/2019

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</tr>
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<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></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).

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**Effective November 18, 2019**
NHL: CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) / SMALL LYMPHOCYTIC LYMPHOMA (SLL) REFERENCES

NCCN Practice Guidelines: Chronic Lymphocytic Leukemia / Small Lymphocytic Lymphoma V5.2019


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Effective November 18, 2019


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


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Effective November 18, 2019
Pathway

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NHL: Diffuse Large B-Cell Lymphoma Pathways

<table>
<thead>
<tr>
<th>First Line of Therapy (1st Line)</th>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>R-CHOP (21):</strong> cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, and rituximab*1,4,52,53</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>First Line of Therapy (1st Line)</th>
<th>Contraindication to Anthracyline</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>R-CEOP:</strong> cyclophosphamide, etoposide, vincristine (Vincasar), prednisone, and rituximab*13,14,40,41,52,53</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second and Subsequent Lines of Therapy (2nd Line+)</th>
<th>Transplant Candidates</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>R-GDP:</strong> gemcitabine (Gemzar), dexamethasone, cisplatin, and rituximab*23,24,43,52,53</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>R-GDP:</strong> gemcitabine (Gemzar), dexamethasone, carboplatin, and rituximab*23,24,43,52,53</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>R-ICE:</strong> ifosfamide (Ifex), carboplatin, etoposide, and rituximab*18,19,29,52,53</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second and Subsequent Lines of Therapy (2nd Line+)</th>
<th>Non-Transplant Candidates</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BR:</strong> bendamustine (Bendeka, Treanda) and Rituximab*32,33,52,53</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>R-GDP:</strong> gemcitabine (Gemzar), dexamethasone, cisplatin, and rituximab*23,24,52,53</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>R-GDP:</strong> gemcitabine (Gemzar), dexamethasone, carboplatin, and rituximab*23,24,52,53</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>R-GemOx:</strong> gemcitabine (Gemzar), oxaliplatin, and rituximab*25,27,52,53</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Effective November 18, 2019
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 eradication33,34

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

Rituximab§ monotherapy27,29,52,53

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

BR: Bendamustine (Bendeka, Treanda) and rituximab§5,6,52,53

R-CHOP(21): Cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, and rituximab§1-3,5,52,53

R-CVP: Cyclophosphamide, vincristine (Vincasar), prednisone, and rituximab§1,4,52,53

Rituximab§ monotherapy7,17,52,53

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

Chlorambucil (Leukeran)10

Chlorambucil (Leukeran) and rituximab§10,11,52,53

Cyclophosphamide11-13

Cyclophosphamide and rituximab§52,53

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

R-CHOP(21): Cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, and rituximab§1-5,52,53

R-CEOP: Cyclophosphamide, etoposide, vincristine (Vincasar), prednisone, and rituximab§13,35,37,52,53

* 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 November 18, 2019
NHL: FOLLICULAR AND MARGINAL ZONE LYMPHOMA REFERENCES


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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+)

<table>
<thead>
<tr>
<th>Drug</th>
</tr>
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<tbody>
<tr>
<td>Acalabrutinib (Calquence)</td>
</tr>
<tr>
<td>BR: bendamustine (Bendeka, Treanda) and rituximab*</td>
</tr>
<tr>
<td>Bortezomib (Velcade)17</td>
</tr>
<tr>
<td>Ibrutinib (Imbruvica)19,20</td>
</tr>
<tr>
<td>Lenalidomide (Revlimid)20,23</td>
</tr>
</tbody>
</table>

* 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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NHL: MANTLE CELL LYMPHOMA REFERENCES


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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: 15284112

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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>

**Neoadjuvant, 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*"**

- 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*"**

- Niraparib (Zejula)<sup>54</sup>
- Olaparib (Lynparza)<sup>55</sup>
- Rucaparib (Rubraca)<sup>60</sup>

**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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OVARIAN CANCER (EPITHELIAL) REFERENCES

NCCN Clinical Practice Guidelines: Ovarian Cancer, Including Fallopian Tube Cancer and Primary Peritoneal Cancer V1.2019


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38. O'Malley DM, Richardson DL, Rheaume 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


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86. Barber EL, Zsiros E, et al. The combination of intravenous bevacizumab and metronomic oral cyclophosphamide is an effective regimen for platinum-resistant recurrent ovarian cancer. J Gynecol Oncol. 2013 Jul;24(3):258-64. PMID:23875076


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Effective November 18, 2019
Pancreatic Cancer (Adenocarcinoma) Pathways

### Adjuvant Therapy

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

### 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

- Gemcitabine (Gemzar)\(^{21}\)

* Modified FOLFIRINOX: Bolus 5-FU not administered

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PANCREATIC CANCER (ADENOCARCINOMA) REFERENCES

NCCN Clinical Practice Guidelines: Pancreatic Adenocarcinoma V2.2018


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Effective November 18, 2019
Prostate Cancer (Adenocarcinoma) Pathways

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

- Goserelin (Zoladex)
- Leuprolide ( Eligard/Lupron)
- Triptorelin (Trelstar)

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

- Goserelin (Zoladex)
- Leuprolide ( Eligard/Lupron)
- Triptorelin (Trelstar)

### 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)
- Goserelin (Zoladex) with abiraterone (Zytiga)
- Leuprolide ( Eligard/Lupron)
- Leuprolide ( Eligard/Lupron) with abiraterone (Zytiga)
- Triptorelin (Trelstar)
- Triptorelin (Trelstar) with abiraterone (Zytiga)

### Recurrent and Metastatic Disease | Hormone Sensitive

- Abiraterone (Zytiga) and prednisone with Androgen Deprivation Therapy (ADT)
- Apalutamide (Erleada) with Androgen Deprivation Therapy (ADT)
- Docetaxel (Taxotere) (every 3 weeks) with Androgen Deprivation Therapy (ADT)
- Enzalutamide (Xtandi) with Androgen Deprivation Therapy (ADT)
- Goserelin (Zoladex)
- Leuprolide ( Eligard/Lupron)
- Triptorelin (Trelstar)

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
- For regional, lymph node positive disease ONLY
- Should not be used concurrently with Radium 223
- 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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Effective November 18, 2019
Prostate Cancer (Adenocarcinoma) Pathways (continued)

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

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Abiraterone (Zytiga) and prednisone with continued ADT</td>
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<tr>
<td>Docetaxel (Taxotere) (every 3 weeks) with continued ADT</td>
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<tr>
<td>Enzalutamide (Xtandi) with continued ADT</td>
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<tr>
<td>Goserelin (Zoladex) with bicalutamide (Casodex)</td>
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<tr>
<td>Leuprolide (Eligard/Lupron) with bicalutamide (Casodex)</td>
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<tr>
<td>Triptorelin (Trelstar) with bicalutamide (Casodex)</td>
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### Recurrent and Metastatic Disease | Hormone Resistant | Second and Subsequent Lines of Therapy (2nd Line+)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Abiraterone (Zytiga) and prednisone with continued ADT</td>
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<tr>
<td>Cabazitaxel (Jevtana) with ADT</td>
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</tr>
<tr>
<td>Docetaxel (Taxotere) (every 3 weeks) with continued ADT</td>
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<tr>
<td>Docetaxel (Taxotere) rechallenge with ADT</td>
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<tr>
<td>Goserelin (Zoladex) with bicalutamide (Casodex)</td>
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<tr>
<td>Leuprolide (Eligard/Lupron) with bicalutamide (Casodex)</td>
<td></td>
</tr>
<tr>
<td>Triptorelin (Trelstar) with bicalutamide (Casodex)</td>
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<tr>
<td>Continued ADT with supportive care ± dexamethasone</td>
<td></td>
</tr>
</tbody>
</table>

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.
- For regional, lymph node positive disease ONLY
- Should not be used concurrently with Radium 223
- 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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PROSTATE CANCER (ADENOCARCINOMA) REFERENCES


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Effective reimbursement for biosimilar products may be impacted by health plan specific formularies, medical policy and preferred products. Note: Pathway 49.


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# Testicular (Germ Cell Tumors) Cancer Pathways

**Seminoma | Stage II-III A | Primary Therapy**
- **BEP:** bleomycin, etoposide, and cisplatin[^5]
- **EP:** etoposide and cisplatin[^4]

**Seminoma | Stage IIIB-C | Good and Intermediate Risk | Metastatic Disease**
- **BEP:** bleomycin, etoposide, and cisplatin[^5,6]

**Nonseminoma | Stage II-III A | Primary Therapy**
- **BEP:** bleomycin, etoposide, and cisplatin[^5,6]
- **EP:** etoposide and cisplatin[^4]

**Nonseminoma | Stage IIIB-C | Primary Therapy**
- **BEP:** bleomycin, etoposide, and cisplatin[^5,6]

**Nonseminoma | Adjuvant Therapy after RPLND†**
- **EP:** etoposide and cisplatin[^8,9,26]

[^5]: BEP is typically given for 3 cycles in good risk seminoma, and 4 cycles in intermediate risk
[^6]: RPLND: Retroperitoneal lymph node dissection

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[^5]: BEP is typically given for 3 cycles in good risk seminoma, and 4 cycles in intermediate risk
[^6]: RPLND: Retroperitoneal lymph node dissection

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**Effective November 18, 2019**

102
Effective reimbursement for biosimilar products may be impacted by health plan specific formularies, medical policy and preferred products consulted to determine whether proposed services will be covered. Note: Pathway 5

TESTICULAR (GERM CELL TUMORS) CANCER REFERENCES


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Uterine (Endometrial) Cancer Pathways

<table>
<thead>
<tr>
<th>Adjuvant Therapy</th>
<th>Stage III-IV or High Risk Histologies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin and paclitaxel⁶,⁶</td>
<td></td>
</tr>
</tbody>
</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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UTERINE (ENDOMETRIAL) CANCER REFERENCES


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