AIM Cancer 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**
- 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 (Venclextra) 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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AIM Cancer Treatment Pathways

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

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

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

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

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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

Gemcitabine (Gemzar) and cisplatin 4 cycles

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

**BCG**: bacillus calmette-guerin, intravesical

Gemcitabine (Gemzar), intravesical (low-grade histology only)

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

Gemcitabine (Gemzar) and cisplatin

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

Gemcitabine (Gemzar)

Paclitaxel

Pembrolizumab (Keytruda)†

* 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 November 18, 2019
BLADDER CANCER (UROTHELIAL) REFERENCES


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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\textsuperscript{8,11,12,39}
- **TC**: docetaxel (Taxotere) and cyclophosphamide\textsuperscript{10,43}

**Neoadjuvant Therapy | HER2 Positive**

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

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

- **TCH+P**: docetaxel (Taxotere), carboplatin, trastuzumab (Herceptin)*, and pertuzumab (Perjeta)*\textsuperscript{50,51,54,55,57}

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

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NCCN Clinical Practice Guidelines: Breast Cancer V4.2018

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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[^8,9,11,12,60]
- **TC**: docetaxel (Taxotere) and cyclophosphamide[^10,11]

### 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]

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* 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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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 patients with HER2-negative, node-positive 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.


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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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
- Paclitaxel28-20,65
- 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 paclitaxel34
- Vinorelbine (Navelbine) and trastuzumab (Herceptin)46,47

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

- Ado-trastuzumab emtansine (Kadcyla)50,61,62
- 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 paclitaxel34
- Trastuzumab (Herceptin) and lapatinib (Tykerb)19,50
- Trastuzumab (Herceptin) monotherapy37,48
- Vinorelbine (Navelbine) and trastuzumab (Herceptin)46,47

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Bio similarity is not a medical term.

Bio similar products are not considered "on pathway.

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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)

- Anastrozole (Arimidex)*1,6,7,10,11,22,33
- Anastrozole (Arimidex) and palbociclib (Ibrance)*K19,40,41
- Anastrozole (Arimidex) and ribociclib (Kisqali)*19,40,41
- Fulvestrant (Faslodex)* high dose5,7,22,26,33,42
- Fulvestrant (Faslodex) and ribociclib (Kisqali)*56
- Letrozole (Femara)*3,12,14,38
- Letrozole (Femara) and palbociclib (Ibrance)*19,40,41
- Letrozole (Femara) and ribociclib (Kisqali)*19,40,41,53
- Tamoxifen†12,26

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

- Anastrozole (Arimidex)*1,6,7,10,11,22,33
- Exemestane (Aromasin)*4,20,21,39
- Fulvestrant (Faslodex) high dose*
- Fulvestrant (Faslodex) and palbociclib (Ibrance)*‡40
- Letrozole (Femara)*3,12,14,38
- Tamoxifen†12,26

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

- Anastrozole (Arimidex) and trastuzumab (Herceptin)*46
- Letrozole (Femara) and trastuzumab (Herceptin)*49

* 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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BREAST CANCER ENDOCRINE THERAPY FOR ADVANCED/METASTATIC DISEASE REFERENCES

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35. Ellis MJ, Prlhalan 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 for premenopausal women with hormone receptor-positive locally advanced or metastatic breast cancer who have previously not been treated with any hormonal therapy. Cancer Res. 2013 Dec 15;73:OT3-2-09.

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Chronic Myelogenous Leukemia (CML) Pathways

<table>
<thead>
<tr>
<th>First Line of Therapy (1st Line)</th>
<th>Low Risk Disease</th>
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</thead>
<tbody>
<tr>
<td>Imatinib (Gleevec)</td>
<td>1,4,6,8,30,33,35</td>
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<table>
<thead>
<tr>
<th>First Line of Therapy (1st Line)</th>
<th>Intermediate or High Risk Disease*</th>
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<tr>
<td>Dasatinib (Sprycel)</td>
<td>1,2,30,37-39</td>
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<tr>
<td>Imatinib (Gleevec)</td>
<td>1,4,6,8,30,33,35</td>
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<tr>
<td>Nilotinib (Tasigna)</td>
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<table>
<thead>
<tr>
<th>Second Line of Therapy (2nd Line)</th>
<th>Following Treatment Failure, Suboptimal Response†, or Intolerance to 1st Line</th>
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<tbody>
<tr>
<td>Bosutinib (Bosulif)</td>
<td>23,33</td>
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<tr>
<td>Dasatinib (Sprycel)</td>
<td>1,2,9,10,12,36</td>
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<tr>
<td>Nilotinib (Tasigna)</td>
<td>16-18,31,32</td>
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<tr>
<td>Ponatinib (Iclusig)</td>
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<table>
<thead>
<tr>
<th>Third Line of Therapy (3rd Line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ponatinib (Iclusig)</td>
</tr>
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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 consult to determine whether proposed services will be covered.

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Colorectal Cancer Pathways

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

Capecitabine (Xeloda)\textsuperscript{52,69}

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

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

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

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

Capecitabine (Xeloda)\textsuperscript{27}

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

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

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

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

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

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

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

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

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

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

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

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

Pembrolizumab (Keytruda)\textsuperscript{§91}

Metastatic Disease | RAS Wild Type (WT) | Third or Subsequent Lines of Therapy (3\textsuperscript{rd} Line+) - Termed 11/18/2019

Panitumumab (Vectibix) monotherapy\textsuperscript{§13,61,56} – Termed 11/18/2019

* Limited to low-risk (T1-3, N1), stage III colon cancer only
† Exon 2 KRAS, non-exon 2 KRAS, and NRAS mutations; testing recommended for all patients with metastatic disease
‡ Limit to one line of therapy
§ Administered at a dose of 200 mg every 3 weeks per the FDA label OR 2 mg/kg (up to a maximum of 200 mg) every 3 weeks, as clinically appropriate

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
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: Pathways 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.


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73. Venook AP, Niedzwiecki D, Lenz H, et al. CALGB/SWOG 80405: Phase III trial of irinotecan/5-FU/leucovorin (FOLFOXIRI) versus oxaliplatin/5-FU/leucovorin (mFOLFOX6) with bevacizumab (BV) or cetuximab (CET) for patients (pts) with KRAS wild-type (wt) untreated metastatic adenocarcinoma of the colon or rectum (mCRC). J Clin Oncol. 32:5s, (2014; suppr abstr LBA3).


**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 December 18, 2019

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35


114. Atreya CE, Van Cutsem E, et al. Updated efficacy of the MEK inhibitor trametinib (T), BRAF inhibitor dabrafenib (D), and anti-EGFR antibody panitumumab (P) in patients (pts) with BRAF V600E mutated (BRAFm) metastatic colorectal cancer (mCRC). J Clin Oncol 2015 33:15_suppl, 103-103


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# 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\(^33\)

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* 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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Effective November 18, 2019
# Head and Neck Cancer Pathways

<table>
<thead>
<tr>
<th>Non-Nasopharyngeal (Squamous Cell Carcinoma)</th>
<th>Candidate for Local Therapy (M0)</th>
<th>Primary Systemic Therapy or Post-Operative Systemic Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose cisplatin* with concurrent RT(^3,10,37)</td>
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<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Non-Nasopharyngeal (Squamous Cell Carcinoma)</th>
<th>Metastatic and Recurrent Disease</th>
<th>Second and Subsequent Lines of Therapy (2(^{nd}) line+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab (Opdivo)(^{35})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paclitaxel(^{23})</td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Nasopharynx</th>
<th>Candidate for Local Therapy (M0)</th>
<th>Primary Systemic Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose cisplatin* with concurrent RT(^{13,37})</td>
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<td></td>
</tr>
<tr>
<td>Cisplatin and gemcitabine (Gemzar) followed by concurrent cisplatin/RT(^{45}) – Added 11/18/2019</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Nasopharynx</th>
<th>Metastatic and Recurrent Disease</th>
<th>First and Subsequent Lines of Therapy (1(^{st}) Line+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin(^{21})</td>
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<td></td>
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<tr>
<td>Cisplatin(^{20,22})</td>
<td></td>
<td></td>
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<tr>
<td>Cisplatin(^{†}) and gemcitabine (Gemzar)(^{29,39})</td>
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<td></td>
</tr>
<tr>
<td>Cisplatin(^{†}) and paclitaxel(^{18,22,29})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluorouracil (5FU)(^{22})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gemcitabine (Gemzar)(^{31})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methotrexate(^{24,26})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paclitaxel(^{23})</td>
<td></td>
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</tbody>
</table>

*Cisplatin dosed at 100 mg/m\(^2\) 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
HEAD AND NECK CANCER REFERENCES

NCCN Clinical Practice Guidelines: Head and Neck Cancers V3.2019


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Effective November 18, 2019


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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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Effective November 18, 2019
HODGKIN LYMPHOMA REFERENCES

NCCN Clinical Practice Guidelines: Hodgkin Lymphoma V1.2018


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Kidney Cancer (Renal Cell Carcinoma) Pathways

**Metastatic Disease | First Line of Therapy (1st Line) | Clear Cell Carcinoma**

- Nivolumab (Opdivo) and ipilimumab (Yervoy)\(^{18}\)
- Pembrolizumab (Keytruda) and axitinib (Inlyta)\(^{30}\)

**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 18, 2019
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# Lung Cancer: Non-Small Cell Lung Cancer (NSCLC) Pathways

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

Cisplatin and etoposide with concurrent XRT\(^{88,89}\)

Paclitaxel and carboplatin with concurrent XRT\(^{93}\)

## Adjuvant Therapy

Carboplatin and paclitaxel\(^{52}\)

Cisplatin and gemcitabine (Gemzar)

Cisplatin and vinorelbine (Navelbine)\(^{53}\)

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

Pembrolizumab (Keytruda)\(^ {125} \)

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

Pembrolizumab (Keytruda)*, carboplatin, and paclitaxel\(^ {126} \)

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

Pembrolizumab (Keytruda)*\(^ {102,125} \)

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

Carboplatin†, pemetrexed (Alimta), and pembrolizumab (Keytruda)*\(^ {124} \)

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

Carboplatin† and paclitaxel\(^ {7,16,54} \)

Carboplatin, paclitaxel, and bevacizumab (Avastin)\(^ {13,14,31} \) (NON-SQUAMOUS ONLY)

Cisplatin† and gemcitabine (Gemzar)\(^ {8,11,13,22-25} \)

Cisplatin† and pemetrexed (Alimta)\(^ {17,18} \) (NON-SQUAMOUS ONLY)

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

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

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

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Effective 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)
- Continuation pemetrexed (Alimta)
- Pembrolizumab (Keytruda) and pemetrexed (Alimta) *(if previously treated with carboplatin, pemetrexed, and pembrolizumab)*
- Switch pemetrexed (Alimta)

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

- Atezolizumab (Tecentriq) *(if no prior checkpoint inhibitors)*
- Nivolumab (Opdivo) *(if no prior checkpoint inhibitors)*
- Carboplatin* and paclitaxel
- Carboplatin* and gemcitabine (Gemzar)*
- Carboplatin* and pemetrexed (Alimta)*

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

- Alectinib (Alecensa)

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

- Osimertinib (Tagrisso)

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

- Carboplatin* and paclitaxel
- Cisplatin* and gemcitabine (Gemzar)
- Cisplatin* and pemetrexed (Alimta)

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

- Erlotinib (Tarceva)

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

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

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

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Effective November 18, 2019
LUNG CANCER: NON-SMALL CELL LUNG CANCER (NSCLC)

REFERENCES

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


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References


14. FDA review documents


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124. November 18, 2019


Lung Cancer: Small Cell Lung Cancer Pathways

<table>
<thead>
<tr>
<th>**Limited Stage</th>
<th>Primary, Adjuvant, or First Line of Therapy (1\textsuperscript{st} Line)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin and etoposide ± XRT\textsuperscript{3}</td>
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</tr>
<tr>
<td>Cisplatin and etoposide ± XRT\textsuperscript{1,2}</td>
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</tbody>
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<table>
<thead>
<tr>
<th>**Extensive Stage</th>
<th>First Line of Therapy (1\textsuperscript{st} Line)**</th>
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<tbody>
<tr>
<td>Carboplatin and etoposide\textsuperscript{9}</td>
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<tr>
<td>Atezolizumab (Tecentriq), carboplatin, and etoposide\textsuperscript{31}</td>
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<table>
<thead>
<tr>
<th>**Second and Subsequent Lines of Therapy (2\textsuperscript{nd} Line+)</th>
<th>Relapse Greater than Six (6) Months**</th>
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</thead>
<tbody>
<tr>
<td>Carboplatin and etoposide\textsuperscript{9}</td>
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Effective November 18, 2019
LUNG CANCER: SMALL CELL LUNG CANCER REFERENCES


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Effective November 18, 2019
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)⁵⁹</td>
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<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>
</tr>
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<tbody>
<tr>
<td>Nivolumab (Opdivo) and ipilimumab (Yervoy)⁶⁵</td>
<td></td>
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</tr>
<tr>
<td>Pembrolizumab (Keytruda)*⁴³,⁴⁵,⁵⁵,⁵⁶</td>
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<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>First Line of Therapy (1st Line)</th>
<th>BRAF Mutated†</th>
<th>Symptomatic Disease</th>
<th>ECOG PS: 0-2</th>
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<tbody>
<tr>
<td>Encorafenib (Braftovi) and binimetinib (Mektovi)⁶⁶</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†</th>
<th>ECOG PS: 0-2</th>
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<tbody>
<tr>
<td>Encorafenib (Braftovi) and binimetinib (Mektovi)⁶⁶</td>
<td></td>
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</tr>
</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)¹,¹⁴,¹⁵,³⁵,³⁶</td>
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</tbody>
</table>

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

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Effective November 18, 2019
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# Myeloma Pathways: Multiple Myeloma

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

**VRD/VDR**: bortezomib (Velcade), lenalidomide (Revlimid), and 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\(^*\)^\(^{113}\)

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

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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**

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

**First Line of Therapy (1st Line) | Without 17p Deletion or TP53 Mutation Present**

- **BR:** bendamustine (Bendeka, Treanda) and rituximab\(^{13,15,39,51}\) – **Termed 11/18/2019**
- **FCR:** fludarabine (Fludara), cyclophosphamide, and rituximab\(^{1,2,39,51}\) – **Termed 11/18/2019**
- Ibrutinib (Imbruvica)\(^{28,37,46,47}\)
- Obinutuzumab (Gazyva) and chlorambucil (Leukeran)\(^{16}\) – **Termed 11/18/2019**
- Venetoclax (Venclexta) and obinutuzumab (Gazyva)\(^{63}\) – **Added 11/18/2019**

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

- Duvelisib (Copiktra)\(^{80}\) – **Added 11/18/2019**
- Ibrutinib (Imbruvica)\(^{28,37,41,46,47}\)
- Idelalisib (Zydelig)\(^{43}\)
- Idelalisib (Zydelig) and rituximab\(^{38}\)
- Venetoclax (Venclexta) and rituximab\(^{59}\)

**Second and Subsequent Lines of Therapy (2nd Line+) | Without 17p Deletion or TP53 Mutation Present**

- Duvelisib (Copiktra)\(^{80}\) – **Added 11/18/2019**
- Ibrutinib (Imbruvica)\(^{28,37,41,46,47}\)
- Idelalisib (Zydelig)\(^{43}\)
- Idelalisib (Zydelig) and rituximab\(^{38}\)
- Venetoclax (Venclexta) and rituximab\(^{59}\)

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

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

**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
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
NHL: Diffuse Large B-Cell Lymphoma Pathways

First Line of Therapy (1st Line)

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

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

**R-CEOP:** cyclophosphamide, etoposide, vincristine (Vincasar), prednisone, and rituximab

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

**R-GDP:** gemcitabine (Gemzar), dexamethasone, cisplatin, and rituximab

**R-GDP:** gemcitabine (Gemzar), dexamethasone, carboplatin, and rituximab

**R-ICE:** ifosfamide (Ifex), carboplatin, etoposide, and rituximab

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

**BR:** bendamustine (Bendeka, Treanda) and Rituximab

**R-GDP:** gemcitabine (Gemzar), dexamethasone, cisplatin, and rituximab

**R-GDP:** gemcitabine (Gemzar), dexamethasone, carboplatin, and rituximab

**R-GemOx:** gemcitabine (Gemzar), oxaliplatin, and rituximab

*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: 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

<table>
<thead>
<tr>
<th>First Line of Therapy (1st Line)</th>
<th>ASCT Candidates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alternating R-CHOP/R-DHAP</strong>: cyclophosphamide (Cytoxan), doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, rituximab* alternating with dexamethasone, cisplatin, cytarabine (Ara-C), and rituximab*4,5,28,30,31</td>
<td></td>
</tr>
<tr>
<td><strong>Nordic Regimen</strong>: dose intensifed rituximab*, cyclophosphamide, vincristine (Vincasar), doxorubicin (Adriamycin), prednisone alternating with rituximab* and high dose cytarabine (Ara-C)3</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>First Line of Therapy (1st Line)</th>
<th>Not an ASCT Candidate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BR</strong>: bendamustine (Bendeka, Treanda) and rituximab*9,10</td>
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<table>
<thead>
<tr>
<th>Second and Subsequent Lines of Therapy (2nd Line+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acalabrutinib (Calquence)42</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>
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<tr>
<td>Lenalidomide (Revlimid)20-23</td>
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</tbody>
</table>

*Rituximab may be administered as Rituxan or Rituxan Hyge. When Rituxan Hyge is chosen, treatment with SC rituximab (Rituxan Hyge) 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
Carboplatin and paclitaxel

Neoadjuvant, Adjuvant, or Primary Therapy | Stage II, III, IV
Carboplatin and paclitaxel (Administered weekly or every 3 weeks)
Intravenous (IV) paclitaxel and Intraperitoneal (IP) cisplatin and IP paclitaxel (Stage III only)

Recurrent Disease | First and Subsequent Lines of Therapy (1st Line+) | Platinum-Sensitive*
Carboplatin
Carboplatin and gemcitabine (Gemzar)
Carboplatin and paclitaxel
Carboplatin and weekly paclitaxel

Recurrent Disease | Maintenance Therapy | Platinum-Sensitive*
Niraparib (Zejula)
Olaparib (Lynparza)
Rucaparib (Rubraca)

Recurrent Disease | Second and Subsequent Lines of Therapy (2nd Line+) | Platinum Resistant
Bevacizumab (Avastin) monotherapy
Docetaxel (Taxotere)
Gemcitabine (Gemzar)
Liposomal doxorubicin (Doxil or Lipodox)
Paclitaxel (weekly)
Paclitaxel and bevacizumab (Avastin)
Tamoxifen
Topotecan (Hycamtin)
Topotecan (Hycamtin) and bevacizumab (Avastin)
Vinorelbine (Navelbine)

* 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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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


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


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Pancreatic Cancer (Adenocarcinoma) Pathways

**Adjuvant Therapy**

- 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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Neoptolemos J, Palmer D, Ghanesh P, et al. ESPAC-4: A multicenter, international, open-label randomized controlled phase III trial of adjuvant combination chemotherapy of gemcitabine (GEM) and capicitabine (CAP) versus monotherapy gemcitabine in patients with resected pancreatic ductal adenocarcinoma* J Clin Oncol 34, 2016 (supplement) Abstract LBA4006


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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)\(^‡\)\(^39,41\)
- Apalutamide (Erleada) with Androgen Deprivation Therapy (ADT)\(^63\) - Added 11/18/2019
- Docetaxel (Taxotere) (every 3 weeks) with Androgen Deprivation Therapy (ADT)\(^19\)
- Enzalutamide (Xtandi) with Androgen Deprivation Therapy (ADT)\(^64\) - Added 11/18/2019
- Goserelin (Zoladex)\(^6\)
- Leuprolide (Eligard/Lupron)\(^6\)
- Triptorelin (Trelstar)\(^6\)

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

* May be coadministered with bicalutamide (Casodex) or flutamide (Eulexin) for up to 30-60 days in patients who are at risk of developing symptoms associated with testosterone flare
† 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 (1\(^{st}\) Line) setting

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Prostate Cancer (Adenocarcinoma)
Pathways (continued)

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

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

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

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

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§ 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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Testicular (Germ Cell Tumors) Cancer Pathways

**Seminoma | Stage II-IIIA | Primary Therapy**

**BEP**: bleomycin, etoposide, and cisplatin

**EP**: etoposide and cisplatin

**Seminoma | Stage IIIB-C | Good and Intermediate Risk | Metastatic Disease**

**BEP**: bleomycin, etoposide, and cisplatin

**Nonseminoma | Stage II-IIIA | Primary Therapy**

**BEP**: bleomycin, etoposide, and cisplatin

**EP**: etoposide and cisplatin

**Nonseminoma | Stage IIIB-C | Primary Therapy**

**BEP**: bleomycin, etoposide, and cisplatin

**Nonseminoma | Adjuvant Therapy after RPLND†**

**EP**: etoposide and cisplatin

* 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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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 paclitaxel[^6]</td>
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</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 paclitaxel[^5,27-29]</td>
<td></td>
</tr>
<tr>
<td>Cisplatin and doxorubicin (Adriamycin)[^24,25]</td>
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</tbody>
</table>

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UTERINE (ENDOMETRIAL) CANCER REFERENCES


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