Cancer Care Quality Program

Treatment Pathways

EFFECTIVE: NOVEMBER 1, 2017
LAST REVIEWED AUGUST 29, 2017

UPDATES FOR 3rd QUARTER 2017

UPDATES TO EXISTING CANCER TREATMENT PATHWAYS

- Bladder Cancer (Urothelial)
  - Changed Neoadjuvant Therapy | Clinical Stage II, III, or Stage IV without evidence of metastases (cT2, cT3, cT4) to Neoadjuvant Therapy | Clinical Stage II, III, IV without evidence of metastases (cT2, cT3, cT4, M0)
  - Added ‘3 cycles’ to CMV: cisplatin, methotrexate, and vinblastine | Neoadjuvant Therapy | Clinical Stage II, III, IV without evidence of metastases (cT2, cT3, cT4, M0)
  - Removed ddMVAC: dose dense methotrexate, vinblastine, doxorubicin (Adryanycin), and cisplatin | Neoadjuvant Therapy | Clinical Stage II, III, IV without evidence of metastases (cT2, cT3, cT4, M0)
  - Added “4 cycles” to gemcitabine (Gemzar) and cisplatin | Neoadjuvant Therapy | Clinical Stage II, III, IV without evidence of metastases (cT2, cT3, cT4, M0)
  - Removed mitomycin C intravesical | Adjuvant Therapy | Stage I or II after TURBT* or following resection of recurrent or persistent disease
• Colorectal Cancer:
  - Added "†" in the setting of recurrent/metastatic disease, a substitution of carbo for cisplatin will be considered a pathway option for gemcitabine (Gemzar) and cisplatin | Metastatic Disease | First line therapy (1st line)
  - Added Metastatic Disease | Second line therapy (2nd line)
  - Added gemcitabine (Gemzar) | Metastatic Disease | Second line therapy (2nd line)
  - Added paclitaxel | Metastatic Disease | Second line therapy (2nd line)
  - Added pembrolizumab (Keytruda) Metastatic Disease | Second line therapy (2nd line)
  - Added FOLFIRI + bevacizumab: fluorouracil (5-FU), leucovorin, and oxaliplatin | Metastatic disease | RAS Wild Type (WT) or Mutant (MT) † | First or second lines of therapy (1st line or 2nd line)
  - Added FOLFOX: fluorouracil (5-FU), leucovorin, and oxaliplatin | Metastatic disease | RAS Wild Type (WT) or Mutant (MT) † | First or second lines of therapy (1st line or 2nd line)
  - Added clarification for FOLFOX + bevacizumab: fluorouracil (5-FU), leucovorin, and oxaliplatin | Metastatic disease | RAS Wild Type (WT) or Mutant (MT) † | First or second lines of therapy (1st line or 2nd line)
  - Added clarification for FOLFOXIRI + bevacizumab: fluorouracil (5-FU), leucovorin, and oxaliplatin | Metastatic disease | RAS Wild Type (WT) or Mutant (MT) † | First or second lines of therapy (1st line or 2nd line)
  - Removed Modified FOLFOX-6: fluorouracil (5-FU), leucovorin, and oxaliplatin | Metastatic disease | RAS Wild Type (WT) or Mutant (MT) † | First or second lines of therapy (1st line or 2nd line)
  - Changed Metastatic disease | RAS WT or MT | Third and subsequent lines of therapy (3rd line +)
  - Removed Trifluridine + tipiracil (Lonsurf) | Metastatic disease | RAS WT or MT | Third and subsequent lines of therapy (3rd line +)
  - Added clarification for FOLFIRI + panitumumab: fluorouracil (5-FU), leucovorin, and oxaliplatin with panitumumab (Vectibix) | Metastatic disease | RAS wild type (WT) | First or Second lines of therapy (1st or 2nd line)
  - Added FOLFOX: fluorouracil (5-FU), leucovorin, and oxaliplatin with panitumumab (Vectibix) | Metastatic disease | RAS wild type (WT) | First or second lines of therapy (1st line or 2nd line)
  - Removed Modified FOLFOX-6: fluorouracil (5-FU), leucovorin, and oxaliplatin with bevacizumab (Avastin) | Metastatic disease | RAS Wild Type (WT) or Mutant (MT) † | First or second lines of therapy (1st line or 2nd line)
  - Changed Metastatic disease | RAS WT | Second lines of therapy (2nd line) to Metastatic disease | RAS wild type (WT) | First or Second lines of therapy (1st or 2nd line)
  - Added Metastatic disease | MSI-H or dMMR | Second line therapy (2nd line)
  - Added pembrolizumab (Keytruda) | Metastatic disease | MSI-H or dMMR | Second line therapy (2nd line)
  - Added clarification metastatic disease | RAS "wild type" (WT) | Third and subsequent lines of therapy (3rd line +)
  - Removed irinotecan (Camptosar) and panitumumab ( Vectibix) | Metastatic disease | RAS WT or MT | Third and subsequent lines of therapy (3rd line +)
  - Added Metastatic disease | MSI-H or dMMR | Second line therapy (2nd line)
  - Added pembrolizumab (Keytruda) | Metastatic disease | MSI-H or dMMR | Second line therapy (2nd line)
  - Added clarication for FOLFIRI + panitumumab† | Metastatic disease | RAS wild type (WT) | First or Second lines of therapy (1st or 2nd line)

• NHL: Chronic Lymphocytic Leukemia (CLL) / Small Lymphocytic Lymphoma (SLL)
  - Changed First Line Therapy (1st line) | Without 17p Deletion or Unspecified to First Line Therapy (1st line) | Without 17p Deletion
  - Added BR: bendamustine (Bendeka, Treanda) and rituximab (Rituxan) | First Line Therapy (1st line) | Without 17p Deletion
  - Removed obinutuzumab (Gazyva) and chlorambucil (Keukeran) | First Line Therapy (1st line) | Without 17p Deletion
  - Added Obinutuzumab (Gazyva) (Monotherapy) | First Line Therapy (1st line) | Without 17p Deletion
  - Changed Second and subsequent line therapy (2nd line +) | Without 17p Deletion or Unspecified to Second and subsequent line therapy (2nd line +) | Without 17p Deletion
  - Removed ASCT Candidate
  - Added footnotes: indications to initiate treatment may include (not limited to):

• NHL: Mantle Cell Lymphoma
  - Changed First line of therapy (1st line) | Ineligible for transplant (not ASCT candidate) to First line of therapy (1st line) | Not ASCT Candidate
  - Removed FCMR: fludarabine (Fludara), cyclophosphamide, mitoxantone (Nevantrone), and rituximab (Rituxan)
  - Removed ** from lenalidomide (Revlimid) | Second and subsequent lines of therapy (2nd line +)
  - Removed FCR: fludarabine (Fludara), cyclophosphamide, and rituximab (Rituxan) | Second and subsequent line therapy (2nd line +) | Without 17p Deletion
  - Added note “Stage III only” for IV paclitaxel and intraperitoneal (IP) cisplatin + IP paclitaxel | Adjuvant or Primary Therapy | Stage II, III, IV
  - Added carboplatin | Recurrent Disease | First or subsequent line of therapy (1st Line +) platinum-sensitive†
  - Updated Cancer (Adenocarcinoma)
- Added goserelin* (Zoladex) with abiraterone (Zytiga) | High Risk (T3a or Gleason 8-10), Very High Risk (T3b-T4), and Locally Advanced Prostate Cancer (LN+) | Primary treatment with radiation therapy
- Removed histrelin* (Vantas) | High Risk (T3a or Gleason 8-10), Very High Risk (T3b-T4), and Locally Advanced Prostate Cancer (LN+) | Primary treatment with radiation therapy
- Added leuprolide* (Eligard/Lupron) with abiraterone (Zytiga) | High Risk (T3a or Gleason 8-10), Very High Risk (T3b-T4), and Locally Advanced Prostate Cancer (LN+) | Primary treatment with radiation therapy
- Added triptorelin* (Trelstar) with abiraterone (Zytiga) | High Risk (T3a or Gleason 8-10), Very High Risk (T3b-T4), and Locally Advanced Prostate Cancer (LN+) | Primary treatment with radiation therapy
- Added abiraterone (Zytiga) and prednisone with Androgen Deprivation Therapy (ADT) | Recurrent and Metastatic disease | Hormone Sensitive
- Removed ** from goserelin (Zoladex) | Recurrent and Metastatic disease | Hormone Sensitive
- Removed histrelin (Vantas) | Recurrent and Metastatic disease | Hormone Sensitive
- Removed ** from leuprolide (Eligard/Lupron) | Recurrent and Metastatic disease | Hormone Sensitive
- Removed ** from triptorelin (Trelstar) | Recurrent and Metastatic disease | Hormone Sensitive
- Updated footnote
- Changed Recurrent and Metastatic Disease | Hormone Resistant | First and subsequent lines of therapy (1st line +) to Recurrent and Metastatic Disease | Hormone Resistant | First line of therapy (1st line)
- Added clarification *and prednisone* to abiraterone | Recurrent and Metastatic Disease | Hormone Resistant | First line of therapy (1st line)
- Removed degarelix (Firmagon) with bicalutamide (Casodex) | Recurrent and Metastatic Disease | Hormone Resistant | First line of therapy (1st line)
- Added enzalutamide (Xtandi) | Recurrent and Metastatic Disease | Hormone Resistant | First line of therapy (1st line)
- Added enzalutamide (Xtandi) with goserelin (Zoladex) | Recurrent and Metastatic Disease | Hormone Resistant | First line of therapy (1st line)
- Added enzalutamide (Xtandi) with leuprolide (Eligard/Lupron) | Recurrent and Metastatic Disease | Hormone Resistant | First line of therapy (1st line)
- Added enzalutamide (Xtandi) with triptorelin (Trelstar) | Recurrent and Metastatic Disease | Hormone Resistant | First line of therapy (1st line)
- Added abiraterone (Zytiga)** and prednisone with continue ADT**† | Recurrent and Metastatic Disease | Hormone Resistant | Second and subsequent lines of therapy (2nd line+)
- Added docetaxel** (Taxotere) (every 3 weeks) with continue ADT**‡ | Recurrent and Metastatic Disease | Hormone Resistant | Second and subsequent lines of therapy (2nd line+)
- Removed enzalutamide (Xtandi)** with ADT | Recurrent and Metastatic Disease | Hormone Resistant | Second and subsequent lines of therapy (2nd line+)
- Added goserelin (Zoladex) with bicalutamide (Casodex) ‡ | Recurrent and Metastatic Disease | Hormone Resistant | Second and subsequent lines of therapy (2nd line+)
- Added leuprolide (Eligard/Lupron) with bicalutamide (Casodex) ‡ | Recurrent and Metastatic Disease | Hormone Resistant | Second and subsequent lines of therapy (2nd line+)
- Updated footnotes
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.

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.
# 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 cycles⁴,⁵

- **ddMVAC:** dose dense methotrexate, vinblastine, doxorubicin (Adriamycin), and cisplatin¹,³,¹⁶,¹⁹ No Longer Effective 11/1/2017

  Gemcitabine (Gemzar) and cisplatin 4 cycles²

**Adjuvant Therapy | Stage I or II after TURBT* or following resection of recurrent or persistent disease**

- **BCG:** bacillus calmette-guerin, intravesical²⁰-²⁴

  Mitomycin C intravesical²⁰-²⁴ No Longer Effective 11/1/2017

**Metastatic Disease | First line therapy (1st line)**

- Gemcitabine (Gemzar) and cisplatin†⁶,¹⁷,¹⁸

**Metastatic Disease | Second line therapy (2nd line) (Added Effective 11/1/2017)**

- Gemcitabine (Gemzar)⁹ (Added Effective 11/1/2017)

- Paclitaxel¹⁴ (Added Effective 11/1/2017)

- Pembrolizumab (Keytruda)³⁷ (Added Effective 11/1/2017)

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* TURBT: Transurethral Resection of Bladder Tumor

† In the setting of recurrent/metastatic disease, a substitution of carboplatin for cisplatin will be considered a Pathway option
Breast Cancer Pathways: Neoadjuvant

**Neoadjuvant Therapy | HER2 Negative**

- **AC** to **weekly T**: doxorubicin (Adriamycin) and cyclophosphamide (every 3 weeks) followed by weekly paclitaxel

- **ddAC** to **weekly T**: dose dense doxorubicin (Adriamycin) and cyclophosphamide followed by weekly paclitaxel

- **TC**: docetaxel (Taxotere) and cyclophosphamide

**Neoadjuvant Therapy | HER2 Positive**

- **AC→TH**: doxorubicin (Adriamycin) and cyclophosphamide followed by paclitaxel and trastuzumab (Herceptin)

- **TCH**: docetaxel (Taxotere), carboplatin, and trastuzumab (Herceptin)

**Neoadjuvant Therapy | HER2 Positive | Hormone receptor (ER/PR) negative**

- **TCH+P**: docetaxel (Taxotere), carboplatin, trastuzumab (Herceptin), and pertuzumab (Perjeta)
Breast Cancer Pathways: Adjuvant

**Adjuvant Therapy | HER2 Negative**

**AC → weekly T:** doxorubicin (Adriamycin) and cyclophosphamide (every 3 weeks) followed by weekly paclitaxel\(^1,3\)

**ddAC → weekly T:** dose dense doxorubicin (Adriamycin) and cyclophosphamide followed by weekly paclitaxel\(^5,7\)

**TC:** docetaxel (Taxotere) and cyclophosphamide\(^3,4\)

**Adjuvant Therapy | HER2 Positive**

**AC→TH:** doxorubicin (Adriamycin) and cyclophosphamide followed by paclitaxel and trastuzumab (Herceptin)\(^7,10,12\)

**TCH:** docetaxel (Taxotere), carboplatin, and trastuzumab (Herceptin)\(^11\)

**TH:** paclitaxel and trastuzumab (Herceptin)\(^33\) (*Pathway for stage I HER2 Positive breast cancer only*)

*Adjuvant chemotherapy pathways do NOT apply to individuals with Hormone-Receptor positive, lymph node negative, OncotypeDX™ LOW risk score*
## Breast Cancer Pathways: Advanced/Metastatic Disease

### Metastatic disease | HER2 Negative | First and subsequent lines of therapy (1st line +)

<table>
<thead>
<tr>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capecitabine (Xeloda)(^{13,27-30})</td>
</tr>
<tr>
<td>Doxorubicin (Adriamycin)(^{13-18})</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar)(^{20})</td>
</tr>
<tr>
<td>Paclitaxel(^{13,16, 24-26})</td>
</tr>
<tr>
<td>Vinorelbine (Navelbine)(^{21-23})</td>
</tr>
</tbody>
</table>

### Metastatic disease | HER2 Positive | First line of therapy (1\(^{st}\) line)

<table>
<thead>
<tr>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capecitabine (Xeloda) and trastuzumab (Herceptin)(^{13,36-39})</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar) and Trastuzumab (Herceptin)(^{40,41})</td>
</tr>
<tr>
<td>Paclitaxel and trastuzumab (Herceptin)</td>
</tr>
<tr>
<td>Pertuzumab (Perjeta), trastuzumab (Herceptin), and docetaxel (Taxotere)(^{12,33-35})</td>
</tr>
<tr>
<td>Pertuzumab (Perjeta), trastuzumab (Herceptin), and paclitaxel(^{34})</td>
</tr>
<tr>
<td>Vinorelbine (Navelbine) and trastuzumab (Herceptin)(^{36,42,43})</td>
</tr>
</tbody>
</table>

### Metastatic disease | HER2 Positive | Second and subsequent lines of therapy (2nd line +)

<table>
<thead>
<tr>
<th>Therapy</th>
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</thead>
<tbody>
<tr>
<td>Ado-trastuzumab emtansine (Kadcyla)(^{50})</td>
</tr>
<tr>
<td>Capecitabine (Xeloda) and lapatinib (Tykerb)(^{44,45})</td>
</tr>
<tr>
<td>Capecitabine (Xeloda) and trastuzumab (Herceptin)(^{20,36-39})</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar) and trastuzumab (Herceptin)(^{40,42})</td>
</tr>
<tr>
<td>Paclitaxel and trastuzumab (Herceptin)</td>
</tr>
<tr>
<td>Pertuzumab (Perjeta), trastuzumab (Herceptin), and docetaxel (Taxotere)</td>
</tr>
<tr>
<td>Pertuzumab (Perjeta), trastuzumab (Herceptin), and paclitaxel</td>
</tr>
<tr>
<td>Trastuzumab (Herceptin) and lapatinib (Tykerb)(^{48})</td>
</tr>
<tr>
<td>Trastuzumab (Herceptin) monotherapy(^{25,46,47})</td>
</tr>
<tr>
<td>Vinorelbine (Navelbine) and trastuzumab (Herceptin)(^{32,43})</td>
</tr>
</tbody>
</table>
Breast Cancer Pathways:
Endocrine Therapy for Recurrent or Metastatic Disease

<table>
<thead>
<tr>
<th>First line therapy (1st line)</th>
<th>Recurrent or Metastatic Disease</th>
<th>Hormone receptor positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole (Arimidex)*1,6,7,10,11,22,33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fulvestrant, (Faslodex) high dose*5,7,22,26,33,42</td>
<td></td>
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<tr>
<td>Letrozole (Femara)*3,12-14,38</td>
<td></td>
<td></td>
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<tr>
<td>Letrozole (Femara) and palbociclib (Ibrance)*40</td>
<td></td>
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<tr>
<td>Tamoxifen**12,26</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Second and subsequent lines of therapy (2nd line +)</th>
<th>Recurrent or Metastatic Disease</th>
<th>Hormone receptor positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole (Arimidex)*1,6,7,10,11,22,33</td>
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<tr>
<td>Exemestane (Aromasin)*4,20,21,39</td>
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</tr>
<tr>
<td>Fulvestrant (Faslodex) high dose*</td>
<td></td>
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</tr>
<tr>
<td>Fulvestrant (Faslodex) and palbociclib (Ibrance)*40</td>
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</table>

<table>
<thead>
<tr>
<th>First and subsequent lines of therapy (1st line +)</th>
<th>Recurrent or Metastatic Disease</th>
<th>Hormone receptor positive</th>
<th>HER2 positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole (Arimidex) and trastuzumab (Herceptin)*46</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Letrozole (Femara) and trastuzumab (Herceptin)*49</td>
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</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.
Chronic Myelogenous Leukemia (CML) Pathways

**First Line Therapy (1st line)**

<table>
<thead>
<tr>
<th>Drug</th>
<th>For intermediate or high risk disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dasatinib* (Sprycel)</td>
<td></td>
</tr>
<tr>
<td>Imatinib (Gleevec)</td>
<td></td>
</tr>
<tr>
<td>Nilotinib* (Tasigna)</td>
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</tbody>
</table>

**Second Line Therapy (2nd line)** Following treatment failure, suboptimal response†, or intolerance to first line therapy

<table>
<thead>
<tr>
<th>Drug</th>
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<tbody>
<tr>
<td>Bosutinib (Bosulif)</td>
<td></td>
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<tr>
<td>Dasatinib (Sprycel)</td>
<td></td>
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<tr>
<td>Nilotinib (Tasigna)</td>
<td></td>
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<tr>
<td>Ponatinib‡ (Iclusig)</td>
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</table>

**Third line of therapy (3rd line)**

<table>
<thead>
<tr>
<th>Drug</th>
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<tbody>
<tr>
<td>Ponatinib</td>
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</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.
Colorectal Cancer Pathways

**Adjuvant Therapy**

Capcitabine (Xeloda)\(^52,69\)

**FLOX**: fluorouracil (5-FU), leucovorin, and oxaliplatin\(^5,8,49,69\) No Longer Effective 11/1/2017

**FOLFOX**: fluorouracil (5-FU), leucovorin, and oxaliplatin \(^7,8,50,51,60,69\) (Added Effective 11/1/2017)

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

**Modified FOLFOX-6**: fluorouracil (5-FU), leucovorin, and oxaliplatin \(^7,8,51,60,69\) No Longer Effective 11/1/2017

**Metastatic disease | RAS Wild Type (WT) or Mutant (MT) † | First or second lines of therapy (1st or 2nd line)**

Capcitabine (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 \(^24,26,28,30,34\) (Added Effective 11/1/2017)

**FOLFOX** + bevacizumab; fluorouracil (5FU), leucovorin, oxaliplatin, with bevacizumab (Avastin)\(^25,26,28,33,44,45,70\) (Added Effective 11/1/2017)

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

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

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

**Modified FOLFOX-6**: fluorouracil (5FU), leucovorin, and oxaliplatin\(^24,26,28,30,34\) No Longer Effective 11/1/2017

**Modified FOLFOX-6**: fluorouracil (5FU), leucovorin, and oxaliplatin with bevacizumab (Avastin)\(^25,26,28,33,44,45,70\) No Longer Effective 11/1/2017

**Metastatic disease | RAS wild type (WT) | First or second lines of therapy (1st or 2nd line) (Added Effective 11/1/2017)**

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

**FOLFOX-6**: fluorouracil (5FU), leucovorin, and oxaliplatin with panitumumab (Vectibix)\(^12,53,59\) No Longer Effective 11/1/2017

**FOLFOX** + panitumumab: fluorouracil (5-FU), leucovorin, and oxaliplatin with panitumumab (Vectibix)\(^12,53,59\) (Added Effective 11/1/2017)

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

**Metastatic disease | RAS WT or MT‡ | Third and subsequent lines of therapy (3rd line +) No Longer Effective 11/1/2017**

Trifluridine + tipiracil (Lonsurf)\(^85\) No Longer Effective 11/1/2017

**Metastatic disease | MSI-H or dMMR | Second line therapy (2nd line) (Added Effective 11/1/2017)**

Pembrolizumab (Keytruda)\(^91\) (Added Effective 11/1/2017)

**Metastatic disease | RAS wild type (WT) | Third and subsequent lines of therapy (3rd line +)**

Irinotecan (Camptosar) and panitumumab (Vectibix)\(^47\) No Longer Effective 11/1/2017

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

* Adjuvant Pathways do not apply to stage II MSI-H (microsatellite instability-high) disease.
† Exon 2 KRAS, non-exon 2 KRAS, and NRAS mutations; testing recommended for all patients with metastatic disease.
‡ Limit to one line of therapy
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)\(^35\)
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 (1\(^{st}\) 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 (1\(^{st}\) line)**

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

**Recurrent/metastatic or locally advanced/inoperable disease | Second line of therapy (2\(^{nd}\) line)**

Irinotecan (Camptosar)\(^24,29\)
Paclitaxel\(^33\)
# Head and Neck Cancer Pathways

<table>
<thead>
<tr>
<th>Hypopharynx and larynx: candidate for local therapy (M0)</th>
<th>Primary systemic therapy &amp; concurrent radiation therapy (RT)</th>
</tr>
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<tr>
<td>High dose cisplatin* with concurrent RT³</td>
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<th>Hypopharynx and larynx: candidate for local therapy (M0)</th>
<th>Post-operative systemic therapy &amp; concurrent radiation therapy (RT)</th>
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<tr>
<td>High dose cisplatin* with concurrent RT¹⁰</td>
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<tr>
<th>Lip, oral cavity, oropharynx, ethmoid sinus, maxillary sinus, occult primary: candidate for local therapy (M0)</th>
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<table>
<thead>
<tr>
<th>Nasopharynx: candidate for local therapy (M0)</th>
<th>Primary systemic therapy &amp; concurrent radiation therapy (RT) followed by adjuvant therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose cisplatin* with concurrent RT following by cisplatin and fluorouracil (5FU)¹³</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nasopharynx</th>
<th>Metastatic and recurrent disease</th>
<th>First Line and subsequent lines of therapy</th>
<th>Performance Status 0,1,2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin† and fluorouracil (5FU)¹⁴,¹⁸,²⁴,²⁹</td>
<td>Cisplatin† and gemcitabine (Gemzar)²⁹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisplatin† and paclitaxel¹⁸,²²</td>
<td>Cisplatin OR carboplatin (single agent)²⁰,²²</td>
<td></td>
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</tr>
<tr>
<td>Cisplatin OR carboplatin (single agent)²⁰,²²</td>
<td>Gemcitabine (Gemzar)³¹</td>
<td></td>
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</tr>
<tr>
<td>Methotrexate²⁴,²⁶</td>
<td>Paclitaxel²³</td>
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</table>

<table>
<thead>
<tr>
<th>Non-Nasopharyngeal (Squamous cell)</th>
<th>Metastatic and recurrent disease</th>
<th>First Line</th>
<th>Performance Status 0,1,2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin, fluorouracil (5FU), and cetuximab (Erbitux)¹⁴</td>
<td>Cisplatin, fluorouracil (5FU), and cetuximab (Erbitux)¹⁴</td>
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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Non-nasopharyngeal (Squamous cell)</th>
<th>Metastatic and recurrent disease</th>
<th>Second Line and Subsequent lines of therapy</th>
<th>Performance Status 0,1,2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluorouracil (5FU)²²</td>
<td>Methotrexate²⁴,²⁶</td>
<td>Nivolumab (Opdivo)³⁵</td>
<td>Paclitaxel²³</td>
</tr>
</tbody>
</table>

* “High dose cisplatin” refers to dosing to achieve total dose of 200-300 mg/m² of cisplatin over the course of the radiotherapy. There are several different appropriate cisplatin schedules that may be used.
† Substitution of carboplatin for cisplatin, and vice-versa, is acceptable for metastatic disease
Hodgkin’s Lymphoma Pathways

Classical Hodgkin | Early or Late Stage | with or without Radiation Therapy (RT)

**ABVD:** doxorubicin (Adriamycin), bleomycin, vinblastine, and dacarbazine (DTIC)\(^1\)\(^{-10,30,32}\)
## Kidney Cancer Pathways

**Metastatic | First line therapy (1st line) | Clear Cell and Non-clear Cell**

- Pazopanib (Votrient)\(^4\)\(^-\)\(^7\)
- Sunitinib (Sutent)\(^1\)\(^-\)\(^3\)
- Temsirolimus (Torisel)\(^1\)\(^2\)

**Metastatic | Second line therapy (2nd line) | Clear Cell**

- Axitinib (Inlyta)\(^2\)\(^2\)
- Cabozantinib (Cabometytx)\(^2\)\(^8\),\(^3\)\(^0\),\(^3\)\(^1\)
- Nivolumab (Opdivo)\(^2\)\(^9\),\(^3\)\(^0\),\(^3\)\(^2\)
- Sorafenib (Nexavar)\(^2\)\(^2\),\(^2\)\(^4\)
# Lung Cancer: Non-Small Cell Pathways

## Adjuvant Therapy
- Cisplatin and vinorelbine (Navelbine)\(^{53,54}\)
- Gemcitabine (Gemzar) and cisplatin
- Paclitaxel and carboplatin\(^{52}\)

## Primary Therapy for Locally Advanced / Unresectable | Stage III
- Paclitaxel (every 3 weeks) and carboplatin with XRT\(^{92}\)

## Metastatic disease | ALK Positive or ROS1 Positive | First line (1\(^{st}\) line)
- Crizotinib (Xalkori)\(^{1,58}\)

## Metastatic disease | EGFR Positive | First line (1\(^{st}\) line)
- Afatinib (Gilotrif)\(^{6}\)
- Erlotinib (Tarceva)\(^{41,42,73,87}\)

## Metastatic disease | Non-squamous | ECOG PS: 0, 1, 2 | First line (1\(^{st}\) line)
- Carboplatin* and paclitaxel\(^{7-16,54}\)
- Cisplatin * and gemcitabine (Gemzar)\(^{8,11,13,22-25}\)
- Cisplatin * and pemetrexed (Alimta)\(^{17,18}\)
- Paclitaxel, carboplatin, and bevacizumab (Avastin)\(^{13,14,30,31}\)

## Metastatic disease | Squamous | ECOG PS: 0, 1, 2 | First line (1\(^{st}\) line)
- Carboplatin* and paclitaxel\(^{7-16}\)
- Cisplatin * and gemcitabine (Gemzar)\(^{8,11,13,17,23,75}\)

## Metastatic disease | PD-L1 Positive | First line (1st line)
- Pembrolizumab (Keytruda)\(^{102}\)

## Metastatic disease | Non-squamous | ECOG PS: 0, 1, 2 | Maintenance
- Continuation bevacizumab (Avastin)\(^{36-38}\)
- Continuation pemetrexed (Alimta)\(^{39}\)
- Switch pemetrexed (Alimta)\(^{41}\)

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

\(\dagger\) In the setting of recurrent/metastatic NSCLC, a substitution of carboplatin for cisplatin (or vice-versa) will be considered a Pathway option.
Lung Cancer: Non-Small Cell Pathways (Continued)

<table>
<thead>
<tr>
<th>Metastatic disease</th>
<th>ALK Positive or EGFR Positive</th>
<th>ECOG PS: 0, 1, 2</th>
<th>Second line (2nd line) after targeted 1st line therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td>Carboplatin* and paclitaxel</td>
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<tr>
<td></td>
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<td></td>
<td>Cisplatin* and gemcitabine (Gemzar)†³³</td>
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<td></td>
<td></td>
<td></td>
<td>Cisplatin* and pemetrexed (Alimta)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic disease</th>
<th>EGFR T790M mutation</th>
<th>Second line (2nd line) after targeted 1st line therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Osimertinib (Tagrisso)†³⁶,⁵⁰</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic disease</th>
<th>Non-squamous</th>
<th>ECOG PS: 0, 1, 2</th>
<th>Second line (2nd line)</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Docetaxel (Taxotere)⁴³-⁴⁷,⁵⁵</td>
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<td></td>
<td></td>
<td></td>
<td>Nivolumab (Opdivo)⁷²</td>
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<td>Pemetrexed (Alimta)³¹,³²</td>
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<td></td>
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<td>Nivolumab (Opdivo)⁵⁹,⁶¹</td>
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* In the setting of recurrent/metastatic NSCLC, a substitution of carboplatin for cisplatin (or vice-versa) will be considered a Pathway option
† For patients with EGFR T790M mutation
Lung Cancer: Small Cell Lung Cancer Pathways

**Limited Stage | Primary, Adjuvant, or First Line Therapy (1st line)**
- Carboplatin and etoposide (Toposar) ± XRT³
- Cisplatin and etoposide (Toposar) ± XRT¹,²

**Extensive Stage | First line of therapy (1st line)**
- Carboplatin and etoposide (Toposar)⁹

**Second and subsequent lines of therapy (2nd line +) | Relapse greater than 6 months**
- Carboplatin and etoposide (Toposar)⁹
# Melanoma Pathways

<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: 0,1,2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembrolizumab (Keytruda)*35,45,55,56</td>
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</tbody>
</table>

| Metastatic disease | First line of therapy (1st line) | BRAF mutated † | Symptomatic disease | ECOG PS: 0,1,2 |
|--------------------|----------------------------------|----------------|--------------------|
| Vemurafenib (Zelboraf) and cobimetinib (Cotellic)26,40-42 |

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Second and subsequent lines of therapy (2nd line +)</th>
<th>BRAF mutated †</th>
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<th>Any BRAF status</th>
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<tbody>
<tr>
<td>Ipilimumab (Yervoy)1,14,15,35,36</td>
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</table>

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

† BRAF mutations include V600E and V600K mutations.
Myeloma Pathways

Primary/First line of therapy (1st line) | Transplant candidates

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

Primary/First Line of therapy (1st line) | Ineligible for transplant

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

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

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

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

Maintenance therapy | Post-transplant

Lenalidomide (Revlimid)

Relapsed Disease | Second and subsequent lines of therapy (2nd line +)

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

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

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

Relapsed Disease | Third and subsequent lines of therapy (3rd line +)

Daratumumab (Darzalex)

Elotuzumab (Empliciti), lenalidomide (Revlimid), and dexamethasone
# NHL: Chronic Lymphocytic Leukemia (CLL) / Small Lymphocytic Lymphoma (SLL) Pathways

### First Line of Therapy (1st line) | With 17p Deletion

- Ibrutinib (Imbruvica)

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

- **BR:** bendamustine (Bendeka, Treanda) and rituximab (Rituxan) *(Added Effective 11/1/2017)*
- **FCR:** fludarabine (Fludara), cyclophosphamide, and rituximab (Rituxan)
- Ibrutinib (Imbruvica)
- Obinutuzumab (Gazyva) and chlorambucil (Leukeran) *(No Longer Effective 11/1/2017)*
- Obinutuzumab (Gazyva) (Monotherapy) *(Added Effective 11/1/2017)*

### Second and subsequent lines of therapy (2nd line +) | With 17p Deletion

- Ibrutinib (Imbruvica)
- Idelalisib (Zydelig)
- Idelalisib (Zydelig) and rituximab (Rituxan)

### Second and subsequent lines of therapy (2nd line +) | Without 17p Deletion

- **BR:** bendamustine (Bendeka, Treanda) and rituximab (Rituxan)
- **FCR:** fludarabine (Fludara), cyclophosphamide, and rituximab (Rituxan) *(No Longer Effective 11/1/2017)*
- Ibrutinib (Imbruvica)
- Idelalisib (Zydelig)
- Idelalisib (Zydelig) and rituximab (Rituxan)

### Indications to initiate treatment may include (not limited to):

1. WBC elevation above 200-300 x 10⁹
2. Signs of leukostasis
3. Lymphocyte doubling time of less than 6 months
4. In low or intermediate risk disease:
   a. Significant disease-related symptoms such as severe fatigue, weight loss, night sweats, otherwise unexplained fever
   b. Signs of end-organ damage
   c. Significant or progressive bulky disease, such as massive splenomegaly (≥6 cm below the costal margin) or massive lymphadenopathy (>10 cm in longest diameter)
   d. Clinically significant progressive or symptomatic anemia or thrombocytopenia
   i. Not caused by autoimmune etiology, unless poor response to conventional immunosuppressive therapy
5. High risk disease, particularly with progressive cytopenias
NHL: Diffuse Large B-Cell Lymphoma Pathways

First line of therapy (1st line)

**R-CHOP (21):** cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, and rituximab (Rituxan)\(^1,4\)

First line of therapy (1st line) | Contraindication to anthracycline

**R-CEOP:** cyclophosphamide, etoposide (Toposar), vincristine (Vincasar), prednisone, and rituximab (Rituxan)\(^13,14,40,41\)

Second and subsequent line of therapy (2nd line +) | Transplant candidates

**R-GDP:** gemcitabine (Gemzar), dexamethasone, cisplatin, and rituximab (Rituxan) OR gemcitabine (Gemzar), dexamethasone, carboplatin, and rituximab (Rituxan)\(^23,24,43\)

**R-ICE:** ifosfamide (Ifex), carboplatin, etoposide (Toposar), and rituximab (Rituxan)\(^18,19,29\)

Second and subsequent line of therapy (2nd line +) | Non-Transplant candidates

**BR:** bendamustine (Bendeka, Treanda) and rituximab (Rituxan)\(^32,33\)

**R-GDP:** gemcitabine (Gemzar), dexamethasone, cisplatin, and rituximab (Rituxan) OR gemcitabine (Gemzar), dexamethasone, carboplatin, and rituximab (Rituxan)\(^23,24\)

**R-GemOx:** gemcitabine (Gemzar), oxaliplatin, and rituximab (Rituxan)\(^25,27\)

Rituximab (Rituxan) monotherapy reserved for frail patients or elderly patients
NHL: Follicular Lymphoma and Marginal Zone Lymphoma Pathways

**Gastric MALT (Mucosa-associated Lymphoid Tissue) Lymphoma: Stage IIE or IIE, *H. pylori* positive**

Antibiotic therapy for *H. pylori* eradication

**Splenic Marginal Zone Lymphoma † OR Gastric MALT Lymphoma: First line of therapy (1st line)**

Rituximab (Rituxan) monotherapy

**Follicular (Grade I-IIIA) Lymphoma and other Marginal Zone Lymphomas | First line of therapy (1st line)**

**BR:** bendamustine (Bendeka, Treanda) and rituximab (Rituxan)

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

**R-CVP:** cyclophosphamide, vincristine (Vincasar), prednisone, and rituximab (Rituxan)

Rituximab (Rituxan) monotherapy

**Follicular (Grade I-IIIA) Lymphoma and other Marginal Zone Lymphomas | First line of therapy (1st line) | Additional options for the elderly or infirm**

Chlorambucil (Leukeran)

Chlorambucil (Leukeran) and rituximab (Rituxan)

Cyclophosphamide

Cyclophosphamide and rituximab (Rituxan)

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

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

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

* Gastric MALT with translocation 11;18 (t11;18) (q21;q21) predicts a lower response rate to anti-*H.pylori* treatment. Radiation therapy or other local intervention may be indicated.

† Splenectomy is also a recommended option for Splenic Marginal Zone Lymphoma (NCCN 2A).
NHL: Mantle Cell Lymphoma Pathways

**First line of therapy (1st line) | ASCT Candidates**

**Alternating R-CHOP/R-DHAP:** cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, rituximab (Rituxan), alternating with dexamethasone, cisplatin, cytarabine (Ara-C), and rituximab (Rituxan)\(^4.5.28.30.31\)

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

**First line of therapy (1st line) | Not ASCT Candidates**

**BR:** bendamustine (Bendeka, Treanda) and rituximab (Rituxan)\(^9.10\)

**Second and subsequent lines of therapy (2nd line +)**

**BR:** bendamustine (Bendeka, Treanda) and rituximab (Rituxan)

**Bortezomib (Velcade)\(^17\)**

**FCMR:** fludarabine (Fludara), cyclophosphamide, mitoxantrone (Novantrone), and rituximab (Rituxan)\(^13\) No Longer Effective 11/1/2017

**Ibrutinib (Imbruvica)\(^19.20\)**

**Lenalidomide (Revlend)\(^20.23\)**
# Ovarian Cancer Pathways

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

## Adjuvant or Primary Therapy | Stage II, III, IV
- Carboplatin* and paclitaxel\(^1-4,7\) **No Longer Effective 11/1/2017**
- Carboplatin and dose dense (weekly) paclitaxel\(^6,8,45\)
- Intravenous (IV) paclitaxel and Intraperitoneal (IP) cisplatin and IP paclitaxel\(^1,49\) *(Stage III only)*

## Recurrent Disease | First and subsequent line of therapy (1st line +) | Platinum-sensitive*
- Carboplatin\(^8,9,12\) *(Added Effective 11/1/2017)*
- Carboplatin and gemcitabine (Gemzar)\(^12,13\)
- Carboplatin and paclitaxel\(^8,9,15\)
- Carboplatin and weekly paclitaxel
- Cisplatin and gemcitabine (Gemzar)\(^16\) **No Longer Effective 11/1/2017**

## Recurrent Disease | Maintenance Therapy | Platinum-sensitive (Added Effective 11/1/2017)
- Niraparib (Zejula)\(^54\) *(Added Effective 11/1/2017)*

## Recurrent Disease | Second or subsequent lines of therapy (2nd line +) | Platinum resistant
- Bevacizumab (Avastin) monotherapy\(^42\)
- Docetaxel (Taxotere)\(^17\)
- Gemcitabine (Gemzar)\(^19-20\)
- Liposomal doxorubicin (Doxil or Lipodox)\(^19,20,21\)
- Paclitaxel (weekly)\(^22,23\)
- Paclitaxel and bevacizumab (Avastin)\(^36-38\)
- Tamoxifen\(^66\) *(Added Effective 11/1/2017)*
- Topotecan (Hycamtin)\(^21,24\)
- Topotecan (Hycamtin) and bevacizumab (Avastin)\(^36,37\)
- Vinorelbine (Navelbine)\(^34-35\)

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* Platinum sensitive disease is defined as recurrence of greater than 6 months after prior platinum-based therapy
Pancreatic Cancer (Adenocarcinoma)
Pathways

**Adjuvant Therapy**

Capecitabine (Xeloda) and gemcitabine (Gemzar)\textsuperscript{36, 40}

**FULV:** fluorouracil (5FU) and leucovorin\textsuperscript{4,6,9}

Gemcitabine (Gemzar)\textsuperscript{1,3-7}

<table>
<thead>
<tr>
<th>Locally Advanced/Unresectable and Metastatic Disease</th>
<th>First Line Therapy (1\textsuperscript{st} line)</th>
<th>ECOG PS: 0, 1, 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FOLIRINOX:</strong> fluorouracil (5FU), leucovorin, irinotecan (Camptosar), and oxaliplatin\textsuperscript{5,21}</td>
<td>Gemcitabine (Gemzar)\textsuperscript{5,15-21}</td>
<td>Gemcitabine (Gemzar) and nab-paclitaxel (Abraxane)\textsuperscript{5,15,33}</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Locally Advanced/Unresectable and Metastatic Disease</th>
<th>Second line of therapy (2\textsuperscript{nd} line)</th>
<th>ECOG PS: 0,1,2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OFF:</strong> Fluorouracil (5FU), leucovorin, and oxaliplatin\textsuperscript{32}</td>
<td>Gemcitabine (Gemzar) monotherapy\textsuperscript{21}</td>
<td></td>
</tr>
</tbody>
</table>
# Prostate Cancer (Adenocarcinoma) Pathways

## Adjuvant Therapy | Post-prostatectomy | Lymph node positive (LN+)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goserelin (Zoladex)</td>
<td></td>
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<tr>
<td>Leuprolide (Eligard/Lupron)</td>
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<tr>
<td>Triptorelin (Trelstar)</td>
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</table>

## Intermediate risk | Primary treatment with radiotherapy (RT)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Goserelin* (Zoladex)</td>
<td></td>
</tr>
<tr>
<td>Leuprolide* (Eligard/Lupron)</td>
<td></td>
</tr>
<tr>
<td>Triptorelin* (Trelstar)</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goserelin* (Zoladex)</td>
<td></td>
</tr>
<tr>
<td>Goserelin* (Zoladex) with abiraterone (Zytiga)</td>
<td>Added Effective 11/1/2017</td>
</tr>
<tr>
<td>Histrelin* (Vantas)</td>
<td>No Longer Effective 11/1/2017</td>
</tr>
<tr>
<td>Leuprolide* (Eligard/Lupron)</td>
<td></td>
</tr>
<tr>
<td>Leuprolide* (Eligard/Lupron) with abiraterone (Zytiga)</td>
<td>Added Effective 11/1/2017</td>
</tr>
<tr>
<td>Triptorelin* (Trelstar)</td>
<td></td>
</tr>
<tr>
<td>Triptorelin* (Trelstar) with abiraterone (Zytiga)</td>
<td>Added Effective 11/1/2017</td>
</tr>
</tbody>
</table>

## Recurrent and Metastatic disease | Hormone Sensitive

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abiraterone (Zytiga) and prednisone with Androgen Deprivation Therapy (ADT)</td>
<td>Added Effective 11/1/2017</td>
</tr>
<tr>
<td>Docetaxel (Taxotere) (every 3 weeks) with Androgen Deprivation Therapy (ADT)</td>
<td>Added Effective 11/1/2017</td>
</tr>
<tr>
<td>Goserelin (Zoladex)</td>
<td></td>
</tr>
<tr>
<td>Histrelin (Vantas)**</td>
<td>No Longer Effective 11/1/2017</td>
</tr>
<tr>
<td>Leuprolide (Eligard/Lupron)</td>
<td></td>
</tr>
<tr>
<td>Triptorelin (Trelstar)</td>
<td></td>
</tr>
</tbody>
</table>

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

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

† ADT Pathway options, when given as listed above: goserelin (Zoladex), leuprolide (Eligard/Lupron), triptorelin (Trelstar) or history of orchiectomy
Prostate Cancer (Adenocarcinoma) Pathways
(Continued)

**Recurrent and Metastatic Disease | Hormone Resistant | First and subsequent lines of therapy (1st line+) No Longer Effective 11/1/2017**

**Recurrent and Metastatic Disease | Hormone Resistant | First line of therapy (1st line) (Added Effective 11/1/2017)**

Abiraterone (Zytiga) and prednisone with continued ADT**8,12,25,26,27

Degarelix (Firmagon) with bicalutamide (Casodex)**7 No Longer Effective 11/1/2017

Docetaxel** (Taxotere) (every 3 weeks) with continued ADT**9,10,19

Enzalutamide (Xtandi) (Added Effective 11/1/2017)

Enzalutamide (Xtandi) with goserelin (Zoladex) (Added Effective 11/1/2017)

Enzalutamide (Xtandi) with leuprolide (Eligard/Lupron) (Added Effective 11/1/2017)

Enzalutamide (Xtandi) with triptorelin (Trelstar) (Added Effective 11/1/2017)

Goserelin (Zoladex) with bicalutamide (Casodex)6,7

Leuprolide (Eligard/Lupron) with bicalutamide (Casodex)6,7

Triptorelin (Trelstar) with bicalutamide (Casodex)6,7

**Recurrent and Metastatic Disease | Hormone Resistant | Second and subsequent lines of therapy (2nd line+)**

Abiraterone (Zytiga)** and prednisone with continued ADT**8,12,25,26,27 (Added Effective 11/1/2017)

Docetaxel** (Taxotere) (every 3 weeks) with continue ADT**9,10,19 (Added Effective 11/1/2017)

Docetaxel (Taxotere) rechallenge with ADT**21,22

Enzalutamide (Xtandi)** with ADT16 No Longer Effective 11/1/2017

Goserelin (Zoladex) with bicalutamide (Casodex)†6,7

Leuprolide (Eligard/Lupron) with bicalutamide (Casodex)†6,7

Triptorelin (Trelstar) with bicalutamide (Casodex)†6,7

Continued ADT** with supportive care ± dexamethasone13,14,15,16,24

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

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

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

† If neither abiraterone nor enzalutamide have been previously used

‡ If not previously used in the first line (1st Line) setting
## Testicular (Germ Cell Tumors) Cancer Pathways

<table>
<thead>
<tr>
<th>Stage</th>
<th>Risk Level</th>
<th>Therapy Type</th>
<th>BEP:</th>
<th>EP:</th>
</tr>
</thead>
<tbody>
<tr>
<td>II-IIIA</td>
<td></td>
<td>Primary</td>
<td>bleomycin, etoposide (Toposar), and cisplatin(^5)</td>
<td>etoposide (Toposar) and cisplatin(^4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nonseminoma</td>
<td>bleomycin, etoposide (Toposar), and cisplatin(^5,6)</td>
<td>etoposide (Toposar) and cisplatin(^4)</td>
</tr>
<tr>
<td></td>
<td>III-C</td>
<td>Seminoma</td>
<td>bleomycin, etoposide (Toposar), and cisplatin(^5,6)</td>
<td>etoposide (Toposar) and cisplatin(^4)</td>
</tr>
<tr>
<td></td>
<td>III-B-C</td>
<td>Nonseminoma</td>
<td>bleomycin, etoposide (Toposar), and cisplatin(^5,6)</td>
<td>etoposide (Toposar) and cisplatin(^4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nonseminoma</td>
<td>etoposide (Toposar) and cisplatin(^8,9,26)</td>
<td>etoposide (Toposar) and cisplatin(^8,9,26)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After RPLND*</td>
<td>etoposide (Toposar) and cisplatin(^8,9,26)</td>
<td>etoposide (Toposar) and cisplatin(^8,9,26)</td>
</tr>
</tbody>
</table>

*RPLND: Retroperitoneal Lymph Node Dissection
Uterine (Endometrial) Cancer Pathways

**Adjuvant Therapy | Stage III-IV or High Risk Histologies**

Carboplatin and paclitaxel\(^5,6\)

**Recurrence / Metastatic | First and Subsequent Lines of Therapy (1\(^{st}\) line +)**

Carboplatin and paclitaxel\(^5,27-29\)

Cisplatin and doxorubicin (Adriamycin)\(^24,25\)
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14. FDA review documents


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NHL: FOLLICULAR LYMPHOMA AND MARGINAL ZONE LYMPHOMA
PATHWAYS REFERENCES


NHL: MANTLE CELL LYMPHOMA PATHWAYS REFERENCES


Ovarian Cancer Pathways References


PANCREATIC CANCER PATHWAYS REFERENCES


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