

# AIM Cancer Treatment Pathways

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## Review and updates during 4<sup>th</sup> quarter 2018

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### Head and Neck Cancer

- High dose cisplatin footer was updated to reflect the evidence-based dosing scenario '100 mg/m<sup>2</sup> every 3 weeks over the course of radiotherapy'

### Lung Cancer: Small Cell Lung Cancer

- Atezolizumab (Tecentriq), carboplatin and etoposide combination regimen added as a pathway option in the following clinical scenario: '**Extensive Stage | First Line of Therapy (1st Line)**'

### NHL: Follicular and Marginal Zone Lymphoma

- Footer was added to clarify that pathway eligibility for antibiotic therapy for *H. pylori* eradication is limited to generic antibiotic drugs only.

### Pancreatic Cancer (Adenocarcinoma)

- **OFF:** Fluorouracil (5FU), leucovorin, and oxaliplatin combination regimen was removed as a pathway option from the following clinical scenario: '**Locally Advanced/Unresectable and Metastatic Disease | Second Line of Therapy (2nd Line) | ECOG PS: 0-2**'

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

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# 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<sup>4,5</sup>

Gemcitabine (Gemzar) and cisplatin 4 cycles<sup>2</sup>

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

**BCG:** bacillus calmette-guerin, intravesical<sup>20-24</sup>

Gemcitabine (Gemzar), intravesical (**low-grade histology only**)<sup>40</sup>

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

Gemcitabine (Gemzar) and cisplatin<sup>†6,17,18</sup>

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

Gemcitabine (Gemzar)<sup>9</sup>

Paclitaxel<sup>14</sup>

Pembrolizumab (Keytruda)<sup>37</sup>

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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

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# BLADDER CANCER (UROTHELIAL) REFERENCES

## NCCN Practice Guidelines: Bladder Cancer Version 5.2018

Referenced with permission from NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer V5.2018. Available at: <http://www.nccn.org>. Accessed July 31, 2018 © National Comprehensive Cancer Network, 2018. To view the most recent complete version of the Guideline, go to [www.nccn.org](http://www.nccn.org).

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

The NCCN Guidelines® are a statement of consensus of its authors regarding their views of currently accepted approaches to treatment. Any clinical seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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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<sup>8,11,12,39</sup>

**TC:** docetaxel (Taxotere) and cyclophosphamide<sup>10,43</sup>

## Neoadjuvant Therapy | HER2 Positive

**AC → TH:** doxorubicin (Adriamycin) and cyclophosphamide followed by paclitaxel and trastuzumab (Herceptin)<sup>\*1,14,23,24,26</sup>

**TCH:** docetaxel (Taxotere), carboplatin, and trastuzumab (Herceptin)<sup>\*25,49</sup>

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

**TCH+P:** docetaxel (Taxotere), carboplatin, trastuzumab (Herceptin)<sup>\*</sup>, and pertuzumab (Perjeta)<sup>50,51,54,55,57</sup>

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

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# BREAST CANCER NEOADJUVANT REFERENCES

## NCCN Clinical Practice Guidelines: Breast Cancer V1.2018

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

The NCCN Guidelines® are a statement of consensus of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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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<sup>8,9,11,12,60</sup>

**TC:** docetaxel (Taxotere) and cyclophosphamide<sup>10,19</sup>

## Adjuvant Therapy | HER2 Positive

**AC → TH:** doxorubicin (Adriamycin) and cyclophosphamide followed by paclitaxel and trastuzumab (Herceptin)<sup>†23-26,58</sup>

**TCH:** docetaxel (Taxotere), carboplatin, and trastuzumab (Herceptin)<sup>†25,26,58</sup>

**TH:** paclitaxel and trastuzumab (Herceptin)<sup>†34,58</sup> **(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)<sup>56</sup>

\* 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

## NCCN Clinical Practice Guidelines: Breast Cancer V1.2018

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

The NCCN Guidelines® are a statement of consensus of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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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)<sup>4,24-26,28,60,65</sup>

Doxorubicin (Adriamycin)<sup>4,5,9,65</sup>

Gemcitabine (Gemzar)<sup>14,60</sup>

Paclitaxel<sup>18-20,65</sup>

Vinorelbine (Navelbine)<sup>15-17,65</sup>

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

Olaparib (Lynparza)<sup>87</sup>

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

Capecitabine (Xeloda) and trastuzumab (Herceptin)<sup>40-43</sup>

Gemcitabine (Gemzar) and trastuzumab (Herceptin)<sup>44,45</sup>

Paclitaxel and trastuzumab (Herceptin)<sup>35,36</sup>

Pertuzumab (Perjeta), trastuzumab (Herceptin), and docetaxel (Taxotere)<sup>32,33,35</sup>

Pertuzumab (Perjeta), trastuzumab (Herceptin), and paclitaxel<sup>34</sup>

Vinorelbine (Navelbine) and trastuzumab (Herceptin)<sup>46,47</sup>

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

Ado-trastuzumab emtansine (Kadcyla)<sup>59,61,62</sup>

Capecitabine (Xeloda) and lapatinib (Tykerb)<sup>51,52</sup>

Capecitabine (Xeloda) and trastuzumab (Herceptin)<sup>40-43</sup>

Gemcitabine (Gemzar) and trastuzumab (Herceptin)<sup>44,45</sup>

Paclitaxel and trastuzumab (Herceptin)<sup>35,36</sup>

Pertuzumab (Perjeta), trastuzumab (Herceptin), and docetaxel (Taxotere)<sup>32,33,35,82</sup>

Pertuzumab (Perjeta), trastuzumab (Herceptin), and paclitaxel<sup>34</sup>

Trastuzumab (Herceptin) and lapatinib (Tykerb)<sup>49,50</sup>

Trastuzumab (Herceptin) monotherapy<sup>37,48</sup>

Vinorelbine (Navelbine) and trastuzumab (Herceptin)<sup>46,47</sup>

**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.**



# BREAST CANCER ADVANCED/METASTATIC REFERENCES

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

The NCCN Guidelines® are a statement of consensus of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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# Breast Cancer Pathways: Endocrine Therapy for Advanced/Metastatic Disease

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

Anastrozole (Arimidex)\*<sup>1,6,7,10,11,22,33</sup>

Anastrozole (Arimidex) and palbociclib (Ibrance)\*<sup>19,40,41</sup>

Anastrozole (Arimidex) and ribociclib (Kisqali)\*<sup>19,40,41</sup>

Fulvestrant (Faslodex)\* high dose<sup>5-7,22,26,33,42</sup>

Letrozole (Femara)\*<sup>3,12-14,38</sup>

Letrozole (Femara) and palbociclib (Ibrance)\*<sup>19,40,41</sup>

Letrozole (Femara) and ribociclib (Kisqali)\*<sup>19,40,41,53</sup>

Tamoxifen†<sup>12,26</sup>

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

Anastrozole (Arimidex)\*<sup>1,6,7,10,11,22,33</sup>

Exemestane (Aromasin)\*<sup>4,20,21,39</sup>

Fulvestrant (Faslodex) high dose\*

Fulvestrant (Faslodex) and palbociclib (Ibrance)\*‡<sup>40</sup>

Letrozole (Femara)\*<sup>3,12-14,38</sup>

Tamoxifen†<sup>12,26</sup>

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

Anastrozole (Arimidex) and trastuzumab (Herceptin)\*<sup>46</sup>

Letrozole (Femara) and trastuzumab (Herceptin)\*<sup>49</sup>

\* 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

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

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

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# Chronic Myelogenous Leukemia (CML) Pathways

## First Line of Therapy (1<sup>st</sup> Line) | Low Risk Disease

Imatinib (Gleevec)<sup>1-4,6-8,30,33-35</sup>

## First Line of Therapy (1<sup>st</sup> Line) | Intermediate or High Risk Disease\*

Dasatinib (Sprycel)<sup>1,2,30,37-39</sup>

Imatinib (Gleevec)<sup>1-4,6-8,30,33-35</sup>

Nilotinib (Tasigna)<sup>6-8,31,32</sup>

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

Bosutinib (Bosulif)<sup>23,33</sup>

Dasatinib (Sprycel)<sup>1,2,9,10,12,36</sup>

Nilotinib (Tasigna)<sup>16-18,31,32</sup>

Ponatinib (Iclusig)<sup>‡26</sup>

## Third Line of Therapy (3<sup>rd</sup> Line)

Ponatinib (Iclusig)<sup>26</sup>

\* 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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# CHRONIC MYELOGENOUS LEUKEMIA (CML) REFERENCES

## NCCN Clinical Practice Guidelines: Chronic Myelogenous Leukemia V4.2018

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# Colorectal Cancer Pathways

## Adjuvant Therapy\*

Capecitabine (Xeloda)<sup>52,69</sup>

**CAPOX:** capecitabine (Xeloda) and oxaliplatin (limited to 3 months duration)<sup>†94</sup>

**FOLFOX:** fluorouracil (5-FU), leucovorin, and oxaliplatin<sup>7,8,50,51,60,69</sup>

**FULV:** fluorouracil (5FU) and leucovorin<sup>1,4,7,49,52,69</sup>

## Metastatic Disease | RAS Wild Type (WT) or Mutant (MT)<sup>‡</sup> | First or Second Lines of Therapy (1<sup>st</sup> or 2<sup>nd</sup> Line)

Capecitabine (Xeloda)<sup>27</sup>

**FOLFIRI:** fluorouracil (5FU), leucovorin, and irinotecan (Camptosar)<sup>18,23,30,32,34</sup>

**FOLFIRI + bevacizumab:** fluorouracil (5FU), leucovorin, and irinotecan (Camptosar) with bevacizumab (Avastin)<sup>21,23,31,36,44,45,58</sup>

**FOLFOX:** fluorouracil (5FU), leucovorin, and oxaliplatin<sup>24,26,28,30,34</sup>

**FOLFOX + bevacizumab:** fluorouracil (5FU), leucovorin, oxaliplatin, with bevacizumab (Avastin)<sup>25,26,28,33,44,45,70</sup>

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

**FULV:** fluorouracil (5FU) and leucovorin<sup>22,27,35</sup>

**FULV:** fluorouracil (5FU) and leucovorin with bevacizumab (Avastin)<sup>22,35</sup>

## Metastatic Disease | RAS Wild Type (WT) | First or Second Lines of Therapy (1<sup>st</sup> or 2<sup>nd</sup> Line)

**FOLFIRI + panitumumab:** fluorouracil (5FU), leucovorin, and irinotecan (Camptosar) with panitumumab (Vectibix)<sup>§11,62</sup>

**FOLFOX + panitumumab:** fluorouracil (5-FU), leucovorin, and oxaliplatin with panitumumab (Vectibix)<sup>§12,53,59</sup>

Irinotecan (Camptosar) and panitumumab (Vectibix)<sup>§47</sup>

## Metastatic Disease | MSI-H or dMMR | Second Line of Therapy (2<sup>nd</sup> Line)

Pembrolizumab (Keytruda)<sup>91</sup>

## Metastatic Disease | RAS Wild Type (WT) | Third or Subsequent Lines of Therapy (3<sup>rd</sup> Line+)

Panitumumab (Vectibix) monotherapy<sup>§13,61,56</sup>

\* Adjuvant Pathways do not apply to stage II MSI-H (microsatellite instability-high) disease

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

‡ Exon 2 KRAS, non-exon 2 KRAS, and NRAS mutations; testing recommended for all patients with metastatic disease

§ Limit to one line of therapy

**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.**

# COLORECTAL CANCER REFERENCES

## NCCN Clinical Practice Guidelines: Colon Cancer. Version 2.2018; Rectal Cancer. Version 2.2018

Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Colon Cancer V2.2018 and Rectal Cancer V2.2018. Available at: <http://www.nccn.org>. Accessed July 31, 2018 ©National Comprehensive Cancer Network, 2018. To view the most recent and complete version of the Guideline, go online to [www.nccn.org](http://www.nccn.org).

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

The NCCN Guidelines® are a statement of consensus of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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

## Primary Therapy | Resectable and Unresectable Disease

Cisplatin and fluorouracil (5FU)<sup>3,4</sup>

Fluorouracil (5FU) and cisplatin with concurrent radiation therapy (RT)<sup>35</sup>

**FLOT:** Fluorouracil (5FU), leucovorin, oxaliplatin, and docetaxel (Taxotere)<sup>47,48</sup>

Paclitaxel and carboplatin with concurrent RT<sup>5</sup>

## Post-Operative Treatment

Fluorouracil (5FU) and leucovorin with concurrent RT<sup>38</sup>

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

Cisplatin and fluorouracil (5FU)<sup>15,19,21,26</sup>

Fluorouracil (5FU) and irinotecan (Camptosar)<sup>25,26</sup>

**FLO/FOLFOX:** fluorouracil (5FU), leucovorin, and oxaliplatin<sup>27</sup>

**FLP:** fluorouracil (5FU), leucovorin, and cisplatin<sup>27</sup>

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

Cisplatin, fluorouracil (5FU), and trastuzumab (Herceptin)<sup>15</sup>

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

Irinotecan (Camptosar)<sup>24,29</sup>

Paclitaxel<sup>33</sup>

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# GASTRIC, ESOPHAGEAL, AND GASTROESOPHAGEAL JUNCTION (ADENOCARCINOMA) CANCERS REFERENCES

## NCCN Clinical Practice Guidelines: Gastric Cancer. Version 5.2017; Esophageal and Esophagogastric Junction Cancers. Version 4.2017

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

The NCCN Guidelines® are a statement of consensus of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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

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# Head and Neck Cancer Pathways

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

High dose cisplatin\* with concurrent RT<sup>3,10,37</sup>

## Non-Nasopharyngeal (Squamous Cell Carcinoma) | Metastatic and Recurrent Disease | First Line of Therapy (1<sup>st</sup> line)

Carboplatin, fluorouracil (5FU), and cetuximab (Erbix)<sup>14</sup>

Cisplatin, fluorouracil (5FU), and cetuximab (Erbix)<sup>14</sup>

## Non-Nasopharyngeal (Squamous Cell Carcinoma) | Metastatic and Recurrent Disease | Second and Subsequent Lines of Therapy (2<sup>nd</sup> line+)

Nivolumab (Opdivo)<sup>35</sup>

Paclitaxel<sup>23</sup>

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

High dose cisplatin\* with concurrent RT<sup>13,37</sup>

## Nasopharynx | Metastatic and Recurrent Disease | First and Subsequent Lines of Therapy (1<sup>st</sup> Line+)

Carboplatin<sup>21</sup>

Cisplatin<sup>20,22</sup>

Cisplatin† and gemcitabine (Gemzar)<sup>29,39</sup>

Cisplatin† and paclitaxel<sup>18,22,29</sup>

Fluorouracil (5FU)<sup>22</sup>

Gemcitabine (Gemzar)<sup>31</sup>

Methotrexate<sup>24,26</sup>

Paclitaxel<sup>23</sup>

\* Cisplatin dosed at 100 mg/m<sup>2</sup> 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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These Guidelines are a work in progress that may be refined as often as new significant data becomes available.

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

# Hodgkin Lymphoma Pathways

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

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

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

**ABVD:** doxorubicin (Adriamycin), bleomycin, vinblastine, and dacarbazine (DTIC) ± ISRT\*<sup>7-10,32</sup>

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\* ISRT – Involved site radiation therapy

**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.**



# HODGKIN LYMPHOMA REFERENCES

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

# Kidney Cancer (Renal Cell Carcinoma) Pathways

## Metastatic Disease | First Line of Therapy (1<sup>st</sup> Line)

High dose intravenous (IV) interleukin-2 (IL2, Proleukin)\*<sup>17,18</sup>

Nivolumab (Opdivo) and ipilimumab (Yervoy)\*<sup>46</sup>

Pazopanib (Votrient)<sup>4,5,7</sup>

Sunitinib (Sutent)<sup>1-3,37</sup>

Temsirolimus (Torisel)<sup>†12,23</sup>

## Metastatic Disease | Second or Subsequent Lines of Therapy (2<sup>nd</sup> Line+) | Clear Cell Carcinoma

Nivolumab (Opdivo)<sup>29,30,32</sup>

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

† Indicated only for poor prognosis and non-clear cell histology. Poor prognosis is based on the Motzer criteria (<https://www.mdcalc.com/memorial-sloan-kettering-cancer-center-mskcc-motzer-score-metastatic-renal-cell-carcinoma-rcc>)

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

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

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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<sup>88,89</sup>

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

## Adjuvant Therapy

Carboplatin and paclitaxel<sup>52</sup>

Cisplatin and gemcitabine (Gemzar)

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

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

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

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

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

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

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

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

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

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

Carboplatin<sup>†</sup> and paclitaxel<sup>7-16,54</sup>

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

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

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

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

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

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

Continuation bevacizumab (Avastin)<sup>36-38</sup>

Continuation pemetrexed (Alimta)<sup>39,94</sup>

Pembrolizumab (Keytruda) and pemetrexed (Alimta) (if previously treated with carboplatin<sup>†</sup>, pemetrexed, and pembrolizumab)<sup>113</sup>

Switch pemetrexed (Alimta)<sup>41,94</sup>

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

Atezolizumab (Tecentriq)<sup>104</sup> (if no prior checkpoint inhibitors)

Nivolumab (Opdivo)<sup>59,61,72,78</sup> (if no prior checkpoint inhibitors)

Carboplatin<sup>†</sup> and paclitaxel<sup>‡</sup><sup>7-16,54</sup>

Carboplatin<sup>†</sup> and gemcitabine (Gemzar)<sup>‡</sup>

Carboplatin<sup>†</sup> and pemetrexed (Alimta)<sup>‡</sup>

## Metastatic Disease | ALK Positive | First Line of Therapy (1<sup>st</sup> Line)

Alectinib (Alecensa)<sup>108</sup>

## Metastatic Disease | EGFR Positive | First Line of Therapy (1<sup>st</sup> Line)

Osimertinib (Tagrisso)<sup>114</sup>

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

Carboplatin<sup>†</sup> and paclitaxel<sup>‡</sup><sup>7-16,54</sup>

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

Cisplatin<sup>†</sup> and pemetrexed (Alimta)<sup>17,18</sup>

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

Erlotinib (Tarceva)<sup>42,48,50,51</sup>

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

† In the setting of recurrent/metastatic NSCLC, a substitution of 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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# Lung Cancer: Small Cell Lung Cancer Pathways

## Limited Stage | Primary, Adjuvant, or First Line of Therapy (1<sup>st</sup> Line)

Carboplatin and etoposide ± XRT<sup>3</sup>

Cisplatin and etoposide ± XRT<sup>1,2</sup>

## Extensive Stage | First Line of Therapy (1<sup>st</sup> Line)

Carboplatin and etoposide<sup>9</sup>

Atezolizumab (Tecentriq), carboplatin, and etoposide<sup>31</sup> – Added effective 2/4/2019

## Second and Subsequent Lines of Therapy (2<sup>nd</sup> Line+) | Relapse Greater than Six (6) Months

Carboplatin and etoposide<sup>9</sup>

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

# LUNG CANCER: SMALL CELL LUNG CANCER REFERENCES

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# Melanoma Pathways: Metastatic Melanoma

## Stage IIIB/IIIC (Resected) | Adjuvant Therapy

Nivolumab (Opdivo)<sup>59</sup>

## Metastatic Disease | First and Subsequent Lines of Therapy (1<sup>st</sup> Line+) | Any BRAF Status | ECOG PS: 0-2

Pembrolizumab (Keytruda)<sup>\*35,45,55,56</sup>

Nivolumab (Opdivo) and ipilimumab (Yervoy)<sup>65</sup>

## Metastatic Disease | First Line of Therapy (1<sup>st</sup> Line) | BRAF Mutated† | Symptomatic Disease | ECOG PS: 0-2

Vemurafenib (Zelboraf) and cobimetinib (Cotellic)<sup>26,40-42</sup>

## Metastatic Disease | Second and Subsequent Lines of Therapy (2<sup>nd</sup> Line+) | BRAF Mutated† | ECOG PS: 0-2

Vemurafenib (Zelboraf) and cobimetinib (Cotellic)<sup>26,40-42</sup>

## Metastatic Disease | Second and Subsequent Lines of Therapy (2<sup>nd</sup> Line+) | Any BRAF Status | ECOG PS: 0-2

Ipilimumab (Yervoy)<sup>1,14,15,35,36</sup>

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

† BRAF mutations include V600E and V600K mutations

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# Myeloma Pathways: Multiple Myeloma

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

**VRD/VDR:** bortezomib (Velcade), lenalidomide (Revlimid), and dexamethasone<sup>10,12,79</sup>

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

**CyBorD or VDC:** bortezomib (Velcade), cyclophosphamide, and dexamethasone<sup>9,10,84</sup>

**R-dex:** lenalidomide (Revlimid) and low-dose dexamethasone<sup>10,11,13,73</sup>

**VRD/VDR:** bortezomib (Velcade), lenalidomide (Revlimid), and dexamethasone<sup>10,12,79</sup>

**VD:** bortezomib (Velcade) and dexamethasone<sup>1,3,12,24,89</sup>

## Maintenance Therapy | Post-Transplant

Lenalidomide (Revlimid)<sup>26,27,83,92</sup>

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

**CRd or KRd:** carfilzomib (Kyprolis), lenalidomide (Revlimid), and dexamethasone<sup>82</sup>

**DRD:** daratumumab (Darzalex), lenalidomide (Revlimid), and dexamethasone<sup>100</sup>

**DVD:** daratumumab (Darzalex), bortezomib (Velcade), and dexamethasone<sup>103</sup>

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

Daratumumab (Darzalex)<sup>95</sup>

Elotuzumab (Empliciti), lenalidomide (Revlimid), and dexamethasone<sup>97</sup>

**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.**

# MYELOMA: MULTIPLE MYELOMA REFERENCES

## NCCN Clinical Practice Guidelines: Multiple Myeloma V3.2018

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The NCCN Guidelines® are a statement of consensus of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

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# NHL: Chronic Lymphocytic Leukemia (CLL)/ Small Lymphocytic Lymphoma (SLL) Pathways

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

Ibrutinib (Imbruvica)<sup>28,37,41,46,47</sup>

## First Line of Therapy (1<sup>st</sup> Line) | Without 17p Deletion

**BR:** bendamustine (Bendeka, Treanda) and rituximab<sup>13-15,39,51</sup>

**FCR:** fludarabine (Fludara), cyclophosphamide, and rituximab\*<sup>1,2,39,51</sup>

Ibrutinib (Imbruvica)<sup>29,37,46,47</sup>

Obinutuzumab (Gazyva) and chlorambucil (Leukeran)<sup>16</sup>

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

Ibrutinib (Imbruvica)<sup>28,37,41,46,47</sup>

Idelalisib (Zydelig)<sup>43</sup>

Idelalisib (Zydelig) and rituximab\*<sup>38</sup>

Venetoclax (Venclexta) and rituximab<sup>59</sup>

## Second and Subsequent Lines of Therapy (2<sup>nd</sup> Line+) | Without 17p Deletion

Ibrutinib (Imbruvica)<sup>28,37,41,46,47</sup>

Idelalisib (Zydelig)<sup>43</sup>

Idelalisib (Zydelig) and rituximab<sup>38</sup>

Venetoclax (Venclexta) and rituximab<sup>59</sup>

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Primary treatment for CLL should be initiated in accordance with the guidelines established by the Working Group on CLL<sup>58</sup>

\* 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.**

# NHL: CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) / SMALL LYMPHOCYTIC LYMPHOMA (SLL) REFERENCES

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

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

The NCCN Guidelines® are a statement of consensus of its authors regarding their views of currently accepted approaches to treatment. Any clinical seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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# NHL: Diffuse Large B-Cell Lymphoma Pathways

## First Line of Therapy (1<sup>st</sup> Line)

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

## First Line of Therapy (1<sup>st</sup> Line) | Contraindication to Anthracycline

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

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

**R-GDP:** gemcitabine (Gemzar), dexamethasone, cisplatin, and rituximab\*<sup>23,24,43,52,53</sup>

**R-GDP:** gemcitabine (Gemzar), dexamethasone, carboplatin, and rituximab\*<sup>23,24,43,52,53</sup>

**R-ICE:** ifosfamide (Ifex), carboplatin, etoposide, and rituximab\*<sup>18,19,29,52,53</sup>

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

**BR:** bendamustine (Bendeka, Treanda) and Rituximab\*<sup>32,33,52,53</sup>

**R-GDP:** gemcitabine (Gemzar), dexamethasone, cisplatin, and rituximab\*<sup>23,24,52,53</sup>

**R-GDP:** gemcitabine (Gemzar), dexamethasone, carboplatin, and rituximab\*<sup>23,24,52,53</sup>

**R-GemOx:** gemcitabine (Gemzar), oxaliplatin, and rituximab\*<sup>25-27,52,53</sup>

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

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# NHL: DIFFUSE LARGE B CELL LYMPHOMA REFERENCES

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# NHL: Follicular and Marginal Zone Lymphoma Pathways

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

Antibiotic therapy† for *H. pylori* eradication<sup>33,34</sup>

## Splenic Marginal Zone‡ or Gastric MALT Lymphoma | First Line of Therapy (1<sup>st</sup> Line)

Rituximab§ monotherapy<sup>27-29,52,53</sup>

## Follicular (Grade I-IIIa) and Other Marginal Zone Lymphomas | First Line of Therapy (1<sup>st</sup> Line)

**BR:** Bendamustine (Bendeka, Treanda) and rituximab<sup>5,6,52,53</sup>

**R-CHOP(21):** Cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, and rituximab<sup>1-3,5,52,53</sup>

**R-CVP:** Cyclophosphamide, vincristine (Vincasar), prednisone, and rituximab<sup>1,4,52,53</sup>

Rituximab§ monotherapy<sup>7,17,52,53</sup>

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

Chlorambucil (Leukeran)<sup>10</sup>

Chlorambucil (Leukeran) and rituximab<sup>10,11,52,53</sup>

Cyclophosphamide<sup>11-13</sup>

Cyclophosphamide and rituximab<sup>52,53</sup>

## Follicular Lymphoma (Grade III) | First Line of Therapy (1<sup>st</sup> Line)

**R-CHOP(21):** Cyclophosphamide, doxorubicin (Adriamycin), vincristine (Vincasar), prednisone, and rituximab<sup>1-5,52,53</sup>

**R-CEOP:** Cyclophosphamide, etoposide, vincristine (Vincasar), prednisone, and rituximab<sup>13,35-37,52,53</sup>

\* 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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# NHL: FOLLICULAR AND MARGINAL ZONE LYMPHOMA REFERENCES

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# NHL: Mantle Cell Lymphoma Pathways

## First Line of Therapy (1<sup>st</sup> Line) | ASCT Candidates

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

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

## First Line of Therapy (1<sup>st</sup> Line) | Not an ASCT Candidate

**BR:** bendamustine (Bendeka, Treanda) and rituximab\*<sup>9,10</sup>

## Second and Subsequent Lines of Therapy (2<sup>nd</sup> Line+)

Acalabrutinib (Calquence)<sup>42</sup>

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

Bortezomib (Velcade)<sup>17</sup>

Ibrutinib (Imbruvica)<sup>19,20</sup>

Lenalidomide (Revlimid)<sup>20-23</sup>

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

**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.**

# NHL: MANTLE CELL LYMPHOMA REFERENCES

## NCCN Practice Guidelines: Non-Hodgkin Lymphomas: B-Cell Lymphomas Version 1.2019.

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

The NCCN Guidelines® are a statement of consensus of its authors regarding their views of currently accepted approaches to treatment. Any clinical seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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# Ovarian Cancer (Epithelial) Pathways

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

Carboplatin and dose dense paclitaxel<sup>6-8</sup>

Carboplatin and paclitaxel<sup>2-5,7</sup>

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

Carboplatin and paclitaxel<sup>6-8,45</sup> **(Administered weekly or every 3 weeks)**

Intravenous (IV) paclitaxel and Intraperitoneal (IP) cisplatin and IP paclitaxel<sup>1,49</sup> **(Stage III only)**

## Recurrent Disease | First and Subsequent Lines of Therapy (1st Line+) | Platinum-Sensitive\*

Carboplatin<sup>8,9,12</sup>

Carboplatin and gemcitabine (Gemzar)<sup>12,13</sup>

Carboplatin and paclitaxel<sup>8,9,15</sup>

Carboplatin and weekly paclitaxel

## Recurrent Disease | Maintenance Therapy | Platinum-Sensitive\*

Niraparib (Zejula)<sup>54</sup>

Olaparib (Lynparza)<sup>55</sup>

Rucaparib (Rubraca)<sup>60</sup>

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

Bevacizumab (Avastin) monotherapy<sup>42</sup>

Docetaxel (Taxotere)<sup>17</sup>

Gemcitabine (Gemzar)<sup>19,20</sup>

Liposomal doxorubicin (Doxil or Lipodox)<sup>19-21</sup>

Paclitaxel (weekly)<sup>22,23</sup>

Paclitaxel and bevacizumab (Avastin)<sup>36-38</sup>

Tamoxifen<sup>56</sup>

Topotecan (Hycamtin)<sup>21,24</sup>

Topotecan (Hycamtin) and bevacizumab (Avastin)<sup>36,37</sup>

Vinorelbine (Navelbine)<sup>34,35</sup>

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

**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.**



# OVARIAN CANCER (EPITHELIAL) REFERENCES

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

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# Pancreatic Cancer (Adenocarcinoma) Pathways

## Adjuvant Therapy

Capecitabine (Xeloda) and gemcitabine (Gemzar)<sup>36,40</sup>

**FULV:** fluorouracil (5FU) and leucovorin<sup>4,6,9</sup>

Gemcitabine (Gemzar)<sup>1,3-7</sup>

**mFOLFIRINOX\*:** fluorouracil (5FU), leucovorin, irinotecan (Camptosar), and oxaliplatin<sup>46</sup>

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

**FOLFIRINOX:** fluorouracil (5FU), leucovorin, irinotecan (Camptosar), and oxaliplatin<sup>5,21</sup>

Gemcitabine (Gemzar)<sup>5,15-21</sup>

Gemcitabine (Gemzar) and nab-paclitaxel (Abraxane)<sup>5,15,33</sup>

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

Gemcitabine (Gemzar)<sup>21</sup>

**OFF:** Fluorouracil (5FU), leucovorin, and oxaliplatin<sup>32</sup> – **Termed effective 2/4/2019**

\* Modified FOLFIRINOX: Bolus 5-FU not administered

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# PANCREATIC CANCER (ADENOCARCINOMA) REFERENCES

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

# Prostate Cancer (Adenocarcinoma) Pathways

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

Goserelin (Zoladex)<sup>1,2</sup>  
Leuprolide (Eligard/Lupron)<sup>1,2</sup>  
Triptorelin (Trelstar)<sup>1,2</sup>

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

Goserelin (Zoladex)<sup>\*3,5</sup>  
Leuprolide (Eligard/Lupron)<sup>\*3,5</sup>  
Triptorelin (Trelstar)<sup>\*3,5</sup>

## 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)<sup>\*4</sup>  
Goserelin (Zoladex)<sup>\*</sup> with abiraterone (Zytiga)<sup>41</sup>  
Leuprolide (Eligard/Lupron)<sup>\*4</sup>  
Leuprolide (Eligard/Lupron)<sup>\*</sup> with abiraterone (Zytiga)<sup>41</sup>  
Triptorelin (Trelstar)<sup>\*4</sup>  
Triptorelin (Trelstar) with abiraterone (Zytiga)<sup>\*41</sup>

## Recurrent and Metastatic Disease | Hormone Sensitive

Abiraterone (Zytiga) and prednisone with Androgen Deprivation Therapy (ADT)<sup>†39,41</sup>  
Docetaxel (Taxotere) (every 3 weeks) with Androgen Deprivation Therapy (ADT)<sup>†19</sup>  
Goserelin (Zoladex)<sup>6</sup>  
Leuprolide (Eligard/Lupron)<sup>6</sup>  
Triptorelin (Trelstar)<sup>6</sup>

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

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

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

‡ If neither abiraterone nor enzalutamide have been previously used

§ If not previously used in the first line (1<sup>st</sup> Line) setting

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

# Prostate Cancer (Adenocarcinoma) Pathways (continued)

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

Abiraterone (Zytiga) and prednisone with continued ADT†<sup>8,12,25-27</sup>

Docetaxel (Taxotere) (every 3 weeks) with continued ADT†<sup>9,10,19</sup>

Enzalutamide (Xtandi) with continued ADT†

Goserelin (Zoladex) with bicalutamide (Casodex)<sup>6,7</sup>

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

Triptorelin (Trelstar) with bicalutamide (Casodex)<sup>6,7</sup>

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

Abiraterone (Zytiga)‡ and prednisone with continued ADT†<sup>8,12,25-27</sup>

Cabazitaxel (Jevtana) with ADT†<sup>11</sup>

Docetaxel (Taxotere) (every 3 weeks) with continued ADT†<sup>9,10,19</sup>

Docetaxel (Taxotere) rechallenge with ADT†<sup>21,22</sup>

Goserelin (Zoladex) with bicalutamide (Casodex)<sup>§6,7</sup>

Leuprolide (Eligard/Lupron) with bicalutamide (Casodex)<sup>§6,7</sup>

Triptorelin (Trelstar) with bicalutamide (Casodex)<sup>§6,7</sup>

Continued ADT† with supportive care ± dexamethasone<sup>13-16,24</sup>

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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

‡ If neither abiraterone nor enzalutamide have been previously used

§ If not previously used in the first line (1<sup>st</sup> Line) setting

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



# PROSTATE CANCER (ADENOCARCINOMA) REFERENCES

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# Testicular (Germ Cell Tumors) Cancer Pathways

## Seminoma | Stage II-III A | Primary Therapy

**BEP:** bleomycin, etoposide, and cisplatin<sup>5</sup>

**EP:** etoposide and cisplatin<sup>4</sup>

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

**BEP:** bleomycin, etoposide, and cisplatin\*<sup>5,6</sup>

## Nonseminoma | Stage II-III A | Primary Therapy

**BEP:** bleomycin, etoposide, and cisplatin<sup>5,6</sup>

**EP:** etoposide and cisplatin<sup>4</sup>

## Nonseminoma | Stage IIIB-C | Primary Therapy

**BEP:** bleomycin, etoposide, and cisplatin<sup>5,6</sup>

## Nonseminoma | Adjuvant Therapy after RPLND<sup>†</sup>

**EP:** etoposide and cisplatin<sup>8,9,26</sup>

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

† RPLND: Retroperitoneal lymph node dissection

**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.**

# TESTICULAR (GERM CELL TUMORS) CANCER REFERENCES

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

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# Uterine (Endometrial) Cancer Pathways

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

Carboplatin and paclitaxel<sup>5,6</sup>

## Recurrent /Metastatic | First and Subsequent Lines of Therapy (1<sup>st</sup> Line+)

Carboplatin and paclitaxel<sup>5,27-29</sup>

Cisplatin and doxorubicin (Adriamycin)<sup>24,25</sup>

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

# UTERINE (ENDOMETRIAL) CANCER REFERENCES

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Referenced with permission from NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Uterine Neoplasms V1.2018. Available at: <http://www.nccn.org>. Accessed May 9, 2018© National Comprehensive Cancer Network, 2018. To view the most recent complete version of the Guideline, go to [www.nccn.org](http://www.nccn.org).

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

The NCCN Guidelines® are a statement of consensus of its authors regarding their views of currently accepted approaches to treatment. Any clinical seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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