Cancer Care Quality Program

Treatment Pathways

EFFECTIVE AUGUST 12, 2019
LAST REVIEWED MAY 28, 2019
Review and updates during 2nd quarter 2019

Kidney Cancer (Renal Cell Carcinoma)
- Pembrolizumab (Keytruda) and axitinib (Inlyta) combination regimen added as a pathway option in the following clinical scenario: ‘Metastatic Disease | First Line of Therapy (1st Line) | Clear Cell Carcinoma’
- The following regimens have been removed as a pathway option from the clinical scenario: ‘Metastatic Disease | First Line of Therapy (1st Line)’
  - High dose intravenous (IV) interleukin-2 (IL2, Proleukin)
  - Pazopanib (Votrient)
  - Sunitinib (Sutent)
  - Temsirolimus (Torisel)

Metastatic Melanoma
- Encorafenib (Braftovi) and binimetinib (Mektovi) combination regimen added as a pathway option AND vemurafenib (Zelboraf) and cobimetinib (Cotellic) removed as a pathway option from the following clinical scenarios:
  - ‘Metastatic Disease | First Line of Therapy (1st Line) | BRAF Mutated| Symptomatic Disease| ECOG PS 0-2’
  - ‘Metastatic Disease | Second and Subsequent Lines of Therapy (2nd Line +) | BRAF Mutated| Symptomatic Disease| 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.

Effective August 12, 2019
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Cancer Care Quality Program</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder Cancer (Urothelial) Pathways</td>
<td>5</td>
</tr>
<tr>
<td>Breast Cancer Pathways: Neoadjuvant</td>
<td>8</td>
</tr>
<tr>
<td>Breast Cancer Pathways: Adjuvant</td>
<td>12</td>
</tr>
<tr>
<td>Breast Cancer Pathways: Advanced/Metastatic Disease</td>
<td>16</td>
</tr>
<tr>
<td>Breast Cancer Pathways: Endocrine Therapy for Advanced/Metastatic Disease</td>
<td>22</td>
</tr>
<tr>
<td>Chronic Myelogenous Leukemia (CML) Pathways</td>
<td>26</td>
</tr>
<tr>
<td>Colorectal Cancer Pathways</td>
<td>30</td>
</tr>
<tr>
<td>Gastric, Esophageal, and Gastroesophageal Junction Cancer (Adenocarcinoma) Pathways</td>
<td>35</td>
</tr>
<tr>
<td>Head and Neck Cancer Pathways</td>
<td>39</td>
</tr>
<tr>
<td>Hodgkin Lymphoma Pathways</td>
<td>42</td>
</tr>
<tr>
<td>Kidney Cancer (Renal Cell Carcinoma) Pathways</td>
<td>45</td>
</tr>
<tr>
<td>Lung Cancer: Non-Small Cell Lung Cancer (NSCLC) Pathways</td>
<td>48</td>
</tr>
<tr>
<td>Lung Cancer: Small Cell Lung Cancer Pathways</td>
<td>55</td>
</tr>
<tr>
<td>Melanoma Pathways: Metastatic Melanoma</td>
<td>58</td>
</tr>
<tr>
<td>Myeloma Pathways: Multiple Myeloma</td>
<td>62</td>
</tr>
<tr>
<td>NHL: Chronic Lymphocytic Leukemia (CLL)/ Small Lymphocytic Lymphoma (SLL) Pathways</td>
<td>68</td>
</tr>
<tr>
<td>NHL: Diffuse Large B-Cell Lymphoma Pathways</td>
<td>72</td>
</tr>
<tr>
<td>NHL: Follicular and Marginal Zone Lymphoma Pathways</td>
<td>76</td>
</tr>
<tr>
<td>NHL: Mantle Cell Lymphoma Pathways</td>
<td>80</td>
</tr>
<tr>
<td>Ovarian Cancer (Epithelial) Pathways</td>
<td>83</td>
</tr>
<tr>
<td>Pancreatic Cancer (Adenocarcinoma) Pathways</td>
<td>87</td>
</tr>
<tr>
<td>Prostate Cancer (Adenocarcinoma) Pathways</td>
<td>90</td>
</tr>
<tr>
<td>Testicular (Germ Cell Tumors) Cancer Pathways</td>
<td>95</td>
</tr>
<tr>
<td>Uterine (Endometrial) Cancer Pathways</td>
<td>98</td>
</tr>
</tbody>
</table>

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Effective August 12, 2019
Cancer Care Quality Program

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

The Pathways are developed using a rigorous process of evidence-based medicine. Pathways differ from clinical practice guidelines in that the objective of a Pathway is to identify a subset of regimens supported by clinical evidence and practice guidelines with the goal of further reducing unwarranted variation in care and cost. Pathways are selected based on: clinical benefit (efficacy), safety/side effects (especially those leading to hospitalizations & impacting quality of life), strength of national guideline recommendations, and cost of regimens. The Pathways developed for this Program are intended to support quality cancer care.

Selecting a Pathway depends upon a number of factors – the type of cancer, the stage of disease, and the biomarkers or specific genetic profile of the cancer. Within each cancer type, separate Pathways are usually available for early stage and advanced cancer, sub-types of cancer (e.g. HER2 positive) and different lines of therapy.

Pathways are not available for every medical condition but are intended to be applicable for 80%-90% of individuals with the most common types of cancer. Selecting the best cancer treatment depends upon a number of factors – the type of cancer, the stage, the biomarkers or specific genetic profile of the cancer, and unique aspects of each individual’s medical condition. Given the complexity of cancer and all of the unique individual circumstances, it would not be possible to have a Pathway for every specific situation. The treating oncologist will determine if, in his/her medical opinion, a Pathway treatment regimen is the best option for a patient or whether, given his or her unique circumstances, another treatment regimen will be a better treatment for him or her.

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

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

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Effective August 12, 2019
## Bladder Cancer (Urothelial) Pathways

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

- **CMV**: cisplatin, methotrexate, and vinblastine 3 cycles\(^4,5\)
- Gemcitabine (Gemzar) and cisplatin 4 cycles\(^2\)

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

- **BCG**: bacillus calmette-guerin, intravesica\(^20\)\(^-\)\(^24\)
- Gemcitabine (Gemzar), intravesical (low-grade histology only)\(^19\)

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

- Gemcitabine (Gemzar)\(^6,17,18\)

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

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

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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.

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

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Effective August 12, 2019
BLADDERS (UROTHELIAL) REFERENCES

NCCN Practice Guidelines: Bladder Cancer Version 5.2018


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

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.

References


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Effective August 12, 2019

7
Breast Cancer Pathways: Neoadjuvant

<table>
<thead>
<tr>
<th>Neoadjuvant Therapy</th>
<th>HER2 Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ddAC → weekly T</strong></td>
<td>dose dense doxorubicin (Adriamycin) and cyclophosphamide followed by weekly paclitaxel[^8,11,12,39]</td>
</tr>
<tr>
<td><strong>TC</strong></td>
<td>docetaxel (Taxotere) and cyclophosphamide[^10,43]</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Neoadjuvant Therapy</th>
<th>HER2 Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AC → TH</strong></td>
<td>doxorubicin (Adriamycin) and cyclophosphamide followed by paclitaxel and trastuzumab (Herceptin)^[^1,14,23,24,26]</td>
</tr>
<tr>
<td><strong>TCH</strong></td>
<td>docetaxel (Taxotere), carboplatin, and trastuzumab (Herceptin)^[^25,49]</td>
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<table>
<thead>
<tr>
<th>Neoadjuvant Therapy</th>
<th>HER2 Positive</th>
<th>Hormone Receptor (ER/PR) Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TCH+P</strong></td>
<td>docetaxel (Taxotere), carboplatin, trastuzumab (Herceptin)^[^*], and pertuzumab (Perjeta)^[^50,51,54,55,57]</td>
<td></td>
</tr>
</tbody>
</table>

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

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Effective August 12, 2019
BREAST CANCER NEOADJUVANT REFERENCES

NCCN Clinical Practice Guidelines: Breast Cancer V4.2018


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

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References

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

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Effective August 12, 2019


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


58. Piccart-Gebhart MJ, Baselga J, et al. First results from the phase III ALTT0 trial (BIG 2-06; NCCTG[A11-063]) comparing one year of dual HER2 therapy with lapatinib (L) and trastuzumab (T), their sequence (T→L), or their combination (T+L) in the neoadjuvant treatment of HER2-positive early advanced breast cancer [EBC]. J Clin Oncol. 2014; 32(S5):LBA4.


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Breast Cancer Pathways: Adjuvant

### Adjuvant Therapy | HER2 Negative*

- ddAC → weekly T: dose dense doxorubicin (Adriamycin) and cyclophosphamide followed by weekly paclitaxel[^8,9,11,12,60]
- TC: docetaxel (Taxotere) and cyclophosphamide[^10,19]

### Adjuvant Therapy | HER2 Positive

- AC → TH: doxorubicin (Adriamycin) and cyclophosphamide followed by paclitaxel and trastuzumab (Herceptin)[^23,26,58]
- TCH: docetaxel (Taxotere), carboplatin, and trastuzumab (Herceptin)[^25,26,58]
- TH: paclitaxel and trastuzumab (Herceptin)[^34,58] *(Pathway for stage I, HER2 positive breast cancer only)*

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

- Capecitabine (Xeloda)[^56]

### Adjuvant Therapy | HER2 Positive | Residual Disease following Neoadjuvant Therapy - *Added effective 5/13/2019*

- Trastuzumab emtansine (Kadcyla)[^63] – *Added effective 5/13/2019*

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* Adjuvant chemotherapy pathways do NOT apply to individuals with hormone-receptor positive, lymph node negative, OncotypeDX™ LOW risk score

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

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BREAST CANCER ADJUVANT REFERENCES

NCCN Clinical Practice Guidelines: Breast Cancer V4.2018


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References

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Effective August 12, 2019


35. Slamon DJ, Swain SM, Buyse M, et al. [S1-03] Primary results from BETH, a phase 3 controlled study of adjuvant chemotherapy and trastuzumab + bevacizumab in patients with HER2-positive, node-negative or high risk node-negative breast cancer. Cancer Res. December 15, 2013;10;S1-03. Abstract S1-03.


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Effective August 12, 2019

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

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Breast Cancer Pathways: Advanced/Metastatic Disease

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

- Capecitabine (Xeloda)\(^4,24-26,28,60,65\)
- Doxorubicin (Adriamycin)\(^4,5,9,65\)
- Gemcitabine (Gemzar)\(^14,60\)
- Paclitaxel\(^28-20,65\)
- Vinorelbine (Navelbine)\(^15-17,65\)

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

- Olaparib (Lynparza)\(^87\)

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

- Capecitabine (Xeloda) and trastuzumab (Herceptin)\(^40,43\)
- Gemcitabine (Gemzar) and trastuzumab (Herceptin)\(^44,45\)
- Paclitaxel and trastuzumab (Herceptin)\(^35,36\)
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and docetaxel (Taxotere)\(^32,33,35\)
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and paclitaxel\(^34\)
- Vinorelbine (Navelbine) and trastuzumab (Herceptin)\(^46,47\)

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

- Ado-trastuzumab emtansine (Kadcyla)\(^59,61,62\)
- Capecitabine (Xeloda) and lapatinib (Tykerb)\(^51,52\)
- Capecitabine (Xeloda) and trastuzumab (Herceptin)\(^40,43\)
- Gemcitabine (Gemzar) and trastuzumab (Herceptin)\(^44,45\)
- Paclitaxel and trastuzumab (Herceptin)\(^35,36\)
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and docetaxel (Taxotere)\(^32,33,35,82\)
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and paclitaxel\(^34\)
- Trastuzumab (Herceptin) and lapatinib (Tykerb)\(^19,50\)
- Trastuzumab (Herceptin) monotherapy\(^37,48\)
- Vinorelbine (Navelbine) and trastuzumab (Herceptin)\(^46,47\)

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Effective August 12, 2019
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Effective August 12, 2019


Breast Cancer Pathways: Endocrine Therapy for Advanced/Metastatic Disease

**Advanced/Metastatic Disease | Hormone Receptor Positive | First Line of Therapy (1st Line)**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole (Arimidex)*</td>
<td>1,6,7,10,11,22,33</td>
</tr>
<tr>
<td>Anastrozole (Arimidex) and palbociclib (Ibrance)*</td>
<td>19,40,41</td>
</tr>
<tr>
<td>Anastrozole (Arimidex) and ribociclib (Kisqali)*</td>
<td>19,40,41</td>
</tr>
<tr>
<td>Fulvestrant (Faslodex)* high dose</td>
<td>5,7,22,26,33,42</td>
</tr>
<tr>
<td>Fulvestrant (Faslodex) and ribociclib (Kisqali)*</td>
<td>Added effective 5/13/2019</td>
</tr>
<tr>
<td>Letrozole (Femara)*</td>
<td>3,12,14,38</td>
</tr>
<tr>
<td>Letrozole (Femara) and palbociclib (Ibrance)*</td>
<td>19,40,41</td>
</tr>
<tr>
<td>Letrozole (Femara) and ribociclib (Kisqali)*</td>
<td>19,40,41,53</td>
</tr>
<tr>
<td>Tamoxifen†</td>
<td>12,26</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Note</th>
</tr>
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<tbody>
<tr>
<td>Anastrozole (Arimidex)*</td>
<td>1,6,7,10,11,22,33</td>
</tr>
<tr>
<td>Exemestane (Aromasin)*</td>
<td>4,20,21,39</td>
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<tr>
<td>Fulvestrant (Faslodex) high dose*</td>
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</tr>
<tr>
<td>Fulvestrant (Faslodex) and palbociclib (Ibrance)*‡</td>
<td>40</td>
</tr>
<tr>
<td>Letrozole (Femara)*</td>
<td>3,12,14,38</td>
</tr>
<tr>
<td>Tamoxifen†</td>
<td>12,26</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole (Arimidex) and trastuzumab (Herceptin)*</td>
<td>46</td>
</tr>
<tr>
<td>Letrozole (Femara) and trastuzumab (Herceptin)*</td>
<td>49</td>
</tr>
</tbody>
</table>

* With ovarian suppression for premenopausal individuals. Ovarian suppression utilizes LHRH agonists given as monthly injections. 3-month depot dosing does not reliably suppress estrogen levels.
† Tamoxifen is considered pathway for premenopausal individuals with or without ovarian suppression
‡ Palbociclib regimens are not considered pathway when continued in the second line setting if the patient has received an available CDK4/6 inhibitor regimen in the first line setting

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Effective August 12, 2019
References


35. Ellis MJ, Prahladan M, Green NL, Mari E, Robertson JFR. Abstract OT3-2-09: FALCON: A randomised, double-blind, multicentre, phase III study comparing fulvestrant 500 mg for postmenopausal women with hormone receptor-positive locally advanced or metastatic breast cancer who have not previously been treated with any hormonal therapy. Cancer Res. 2013 Dec 15;73:OT3-2-09. http://cancerres.aacrjournals.org/content/73/24_Supplement/OT3-2-09


44. Cristofanilli M, Bondarenko I, Ro J, et al. [P41301] PALOMA3: Phase 3 trial of fulvestrant with or without palbociclib in pre and postmenopausal women with hormone receptor positive, HER2negative metastatic breast cancer that progressed on prior endocrine therapy—confirmed efficacy and safety. San Antonio Breast Cancer Symposium. December 11, 2015. Abstract P4-13-01

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47. Kornblum NS, Klein P, et al. A randomized, double-blind, phase II trial of fulvestrant plus everolimus or placebo in postmenopausal women with hormone receptor (HR)-positive, HER2-negative metastatic breast cancer (MBC) resistant to aromatase inhibitor (AI) therapy. San Antonio Breast Cancer Symposium; San Antonio TX 2016. SABCS Abstract S1-02


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Chronic Myelogenous Leukemia (CML) Pathways

<table>
<thead>
<tr>
<th>First Line of Therapy (1st Line)</th>
<th>Low Risk Disease</th>
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<tbody>
<tr>
<td>Imatinib (Gleevec)1-4,6,8,30,33,35</td>
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<thead>
<tr>
<th>First Line of Therapy (1st Line)</th>
<th>Intermediate or High Risk Disease*</th>
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<tbody>
<tr>
<td>Dasatinib (Sprycel)1,2,30,37-39</td>
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<tr>
<td>Imatinib (Gleevec)1-4,6,8,30,33,35</td>
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</tr>
<tr>
<td>Nilotinib (Tasigna)6,8,31,32</td>
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<table>
<thead>
<tr>
<th>Second Line of Therapy (2nd Line)</th>
<th>Following Treatment Failure, Suboptimal Response†, or Intolerance to 1st Line</th>
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<tbody>
<tr>
<td>Bosutinib (Bosulif)23,33</td>
<td></td>
</tr>
<tr>
<td>Dasatinib (Sprycel)1,2,9,10,12,36</td>
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</tr>
<tr>
<td>Nilotinib (Tasigna)16-18,31,32</td>
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</tr>
<tr>
<td>Ponatinib (Iclusig)‡26</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Third Line of Therapy (3rd Line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ponatinib (Iclusig)26</td>
</tr>
</tbody>
</table>

* For patients with intermediate or high risk disease based on Sokal or Hasford score:
  - Sokal: Intermediate Risk=0.8-1.2; High Risk>1.2
  - Hasford: Intermediate Risk=781-1480; High Risk>1480

† Defined as lack of complete hematologic response or BCR-ABL1 transcripts > 10% (IS) or lack of partial cytogenetic response on bone marrow cytogenetics.

‡ Pathway option for second line therapy only after failure, suboptimal response, or intolerance of a second generation TKI has been used in the first line setting, or T315I mutation has been identified.

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

Effective August 12, 2019
CHRONIC MYELOGENOUS LEUKEMIA (CML) REFERENCES

NCCN Clinical Practice Guidelines: Chronic Myelogenous Leukemia V1.2019


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Effective August 12, 2019
## Colorectal Cancer Pathways

### Adjuvant Therapy*

- Capecitabine (Xeloda)\(^{52,69}\)
- **CAPOX**: capecitabine (Xeloda) and oxaliplatin (limited to 3 months duration)\(^{94}\)
- **FOLFOX**: fluorouracil (5-FU), leucovorin, and oxaliplatin\(^{7,8,50,51,60,69}\)
- **FULV**: fluorouracil (5FU) and leucovorin\(^{1,4,7,49,52,69}\)

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

- Capecitabine (Xeloda)\(^{27}\)
- **FOLFIRI**: fluorouracil (5FU), leucovorin, and irinotecan (Camptosar)\(^{18,23,30,32,34}\)
- **FOLFIRI + bevacizumab**: fluorouracil (5FU), leucovorin, and irinotecan (Camptosar) with bevacizumab (Avastin)\(^{21,23,31,36,44,45,58}\)
- **FOLFOX**: fluorouracil (5FU), leucovorin, and oxaliplatin\(^{24,26,28,30,34}\)
- **FOLFOX + bevacizumab**: fluorouracil (5FU), leucovorin, oxaliplatin, with bevacizumab (Avastin)\(^{25,26,28,33,44,45,70}\)
- **FULV**: fluorouracil (5FU) and leucovorin\(^{22,27,35}\)
- **FULV**: fluorouracil (5FU) and leucovorin with bevacizumab (Avastin)\(^{22,35}\)

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

- **FOLFIRI + panitumumab**: fluorouracil (5FU), leucovorin, and irinotecan (Camptosar) with panitumumab (Vectibix)\(^{11,62}\)
- **FOLFOX + panitumumab**: fluorouracil (5-FU), leucovorin, and oxaliplatin with panitumumab (Vectibix)\(^{12,53,59}\)
- Irinotecan (Camptosar) and panitumumab (Vectibix)\(^{47}\)

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

- Pembrolizumab (Keytruda)\(^{191}\)

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

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

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

---

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

Effective August 12, 2019
COLORECTAL CANCER REFERENCES


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

## Primary Therapy | Resectable and Unresectable Disease

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin and fluorouracil (5FU)</td>
<td>(^{3,4})</td>
</tr>
<tr>
<td>Fluorouracil (5FU) and cisplatin with concurrent radiation therapy (RT)</td>
<td>(^{35})</td>
</tr>
<tr>
<td><strong>FLOT</strong>: Fluorouracil (5FU), leucovorin, oxaliplatin, and docetaxel (Taxotere)</td>
<td>(^{47,48})</td>
</tr>
<tr>
<td>Pacitaxel and carboplatin with concurrent RT</td>
<td>(^{5})</td>
</tr>
</tbody>
</table>

## Post-Operative Treatment

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluorouracil (5FU) and leucovorin with concurrent RT</td>
<td>(^{38})</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin and fluorouracil (5FU)</td>
<td>(^{15,19,21,26})</td>
</tr>
<tr>
<td>Fluorouracil (5FU) and irinotecan (Camptosar)</td>
<td>(^{25,26})</td>
</tr>
<tr>
<td><strong>FLO/FOLFOX</strong>: fluorouracil (5FU), leucovorin, and oxaliplatin</td>
<td>(^{27})</td>
</tr>
<tr>
<td><strong>FLP</strong>: fluorouracil (5FU), leucovorin, and cisplatin</td>
<td>(^{27})</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin, fluorouracil (5FU), and trastuzumab (Herceptin)</td>
<td>(^{15})</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irinotecan (Camptosar)</td>
<td>(^{24,29})</td>
</tr>
<tr>
<td>Pacitaxel</td>
<td>(^{33})</td>
</tr>
</tbody>
</table>

---

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

Effective August 12, 2019
GASTRIC, ESOPHAGEAL, AND GASTROESOPHAGEAL JUNCTION (ADENOCARCINOMA) CANCERS REFERENCES


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(FLOT4-AIO): results from the phase 2 part of a multicentre, open-label, randomised phase 2/3 trial. Lancet Oncol. 2016;17(12):1697-708.PMID 27776843


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

Effective August 12, 2019
# Head and Neck Cancer Pathways

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

<table>
<thead>
<tr>
<th><em><em>High dose cisplatin</em> with concurrent RT</em>*</th>
<th><strong>Ref.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>3, 10, 37</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th><strong>Carboplatin, fluorouracil (5FU), and cetuximab (Erbitux)</strong></th>
<th><strong>Ref.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Cisplatin, fluorouracil (5FU), and cetuximab (Erbitux)</strong></th>
<th><strong>Ref.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th><strong>Nivolumab (Opdivo)</strong></th>
<th><strong>Ref.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>35</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Paclitaxel</strong></th>
<th><strong>Ref.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>23</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th><em><em>High dose cisplatin</em> with concurrent RT</em>*</th>
<th><strong>Ref.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>13, 37</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th><strong>Carboplatin</strong></th>
<th><strong>Ref.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
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<table>
<thead>
<tr>
<th><strong>Cisplatin</strong></th>
<th><strong>Ref.</strong></th>
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<tbody>
<tr>
<td>20, 22</td>
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</table>

<table>
<thead>
<tr>
<th><strong>Cisplatin† and gemcitabine (Gemzar)</strong></th>
<th><strong>Ref.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>29, 39</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Cisplatin† and paclitaxel</strong></th>
<th><strong>Ref.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>18, 22, 29</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Fluorouracil (5FU)</strong></th>
<th><strong>Ref.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>22</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Gemcitabine (Gemzar)</strong></th>
<th><strong>Ref.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>31</td>
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</table>

<table>
<thead>
<tr>
<th><strong>Methotrexate</strong></th>
<th><strong>Ref.</strong></th>
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</thead>
<tbody>
<tr>
<td>24, 26</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Paclitaxel</strong></th>
<th><strong>Ref.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>23</td>
<td></td>
</tr>
</tbody>
</table>

* Cisplatin dosed at 100 mg/m³ 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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HEAD AND NECK CANCER REFERENCES

NCCN Clinical Practice Guidelines: Head and Neck Cancers V1.2019


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Hodgkin Lymphoma Pathways

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

**ABVD:** doxorubicin (Adriamycin), bleomycin, vinblastine, and dacarbazine (DTIC) ± ISRT*1,5,30,35,36

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

**ABVD:** doxorubicin (Adriamycin), bleomycin, vinblastine, and dacarbazine (DTIC) ± ISRT*7,10,32

* ISRT – Involved site radiation therapy

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Effective August 12, 2019
REFERENCES

NCCN Clinical Practice Guidelines: Hodgkin Lymphoma V1.2018


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Effective August 12, 2019
## Kidney Cancer (Renal Cell Carcinoma) Pathways

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

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Effective Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose intravenous (IV) interleukin-2 (IL2, Proleukin)*[^17,18]</td>
<td>TERMED Effective 8/12/2019</td>
</tr>
<tr>
<td>Pazopanib (Votrient)[^4,5,7]</td>
<td>TERMED Effective 8/12/2019</td>
</tr>
<tr>
<td>Sunitinib (Sutent)[^1-3,37]</td>
<td>TERMED Effective 8/12/2019</td>
</tr>
<tr>
<td>Temsirolimus (Torisel)†[^12,23]</td>
<td>TERMED Effective 8/12/2019</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Effective Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab (Opdivo) and ipilimumab (Yervoy)</td>
<td>TERMED Effective 8/12/2019</td>
</tr>
<tr>
<td>Pembrolizumab (Keytruda) and axitinib (Inlyta)</td>
<td>ADDED Effective 8/12/2019</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Effective Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab (Opdivo)</td>
<td>TERMED Effective 8/12/2019</td>
</tr>
</tbody>
</table>

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


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NCCN Practice Guideline: Kidney Cancer V3.2019


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

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

- Cisplatin and etoposide with concurrent XRT\(^{88,89}\)
- Paclitaxel and carboplatin with concurrent XRT\(^{53}\)

#### Adjuvant Therapy

- Carboplatin and paclitaxel\(^{52}\)
- Cisplatin and gemcitabine (Gemzar)
- Cisplatin and vinorelbine (Navelbine)\(^{53}\)

#### Metastatic Disease

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

<table>
<thead>
<tr>
<th>Squamous</th>
<th>TPS &lt; 50%</th>
<th>First Line of Therapy (1st Line)</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembrolizumab (Keytruda)*, carboplatin, and paclitaxel(^{126})</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nonsquamous</th>
<th>ALK/EGFR Negative (ROS1 Negative or Unknown)</th>
<th>TPS &gt; 50%</th>
<th>First Line of Therapy (1st Line)</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembrolizumab (Keytruda)*(^{102,125})</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nonsquamous</th>
<th>ALK/EGFR Negative (ROS1 Negative or Unknown)</th>
<th>TPS &lt; 50%</th>
<th>First Line of Therapy (1st Line)</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin†, pemetrexed (Alimta), and pembrolizumab (Keytruda)*(^{124})</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Squamous or Nonsquamous</th>
<th>Immunotherapy-Ineligible</th>
<th>First Line of Therapy (1st Line)</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin† and paclitaxel(^{17,16,54})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carboplatin, paclitaxel, and bevacizumab (Avastin)(^{13,14,31}) (NON-SQUAMOUS ONLY)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisplatin† and gemcitabine (Gemzar)(^{8,11,13,22,25})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisplatin† and pemetrexed (Alimta)(^{17,18}) (NON-SQUAMOUS ONLY)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

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

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

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

Effective August 12, 2019
Lung Cancer: Non-Small Cell Lung Cancer (NSCLC) Pathways (continued)

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Non-Squamous</th>
<th>Maintenance</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuation bevacizumab (Avastin)(^{36,38})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuation pemetrexed (Alimta)(^{39,94})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pembrolizumab (Keytruda)* and pemetrexed (Alimta) (if previously treated with carboplatin†, pemetrexed, and pembrolizumab)(^{113})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Switch pemetrexed (Alimta)(^{41,94})</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Second or Subsequent Lines of Therapy (2(^{nd}) Line+)</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atezolizumab (Tecentriq)(^{104}) (if no prior checkpoint inhibitors)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nivolumab (Opdivo)(^{59,61,72,78}) (if no prior checkpoint inhibitors)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carboplatin† and paclitaxel(^{17,16,54})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carboplatin† and gemcitabine (Gemzar)(^{†})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carboplatin† and pemetrexed (Alimta)(^{†})</td>
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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>ALK Positive</th>
<th>First Line of Therapy (1(^{st}) Line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alectinib (Alecensa)(^{108})</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>EGFR Positive</th>
<th>First Line of Therapy (1(^{st}) Line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osimertinib (Tagrisso)(^{114})</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>ALK or EGFR Positive</th>
<th>Second or Subsequent Lines of Therapy (2(^{nd}) Line+)</th>
<th>ECOG PS: 0-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin† and paclitaxel(^{17,16,54})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisplatin† and gemcitabine (Gemzar)(^{8,11,13,22,25})</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Cisplatin† and pemetrexed (Alimta)(^{17,18})</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>EGFR Positive</th>
<th>ECOG PS: 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erlotinib (Tarceva)(^{42,48,50,51})</td>
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</tbody>
</table>

* Administered at a dose of 200 mg every 3 weeks per the FDA label OR 2 mg/kg (up to a maximum of 200 mg) every 3 weeks, as clinically appropriate
† In the setting of recurrent/metastatic NSCLC, a substitution of cisplatin for carboplatin (or vice-versa) will be considered a pathway option.
‡ Eligible only if immunotherapy alone was administered as first line treatment. Ineligible if chemotherapy was used in the first line setting.

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

Effective August 12, 2019
LUNG CANCER: NON-SMALL CELL LUNG CANCER (NSCLC)

REFERENCES

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


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References

14. FDA review documents

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

Effective August 12, 2019
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.
Garassino MC, Martelli O, et al. Erlotinib versus docetaxel as second-line treatment of patients with advanced non-small-cell lung cancer and wild-type EGFR tumours (TAILOR); a randomised controlled trial. Lancet Oncol. 2013 Sep;14(10):981-8. PMID: 23883922


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 Pathways

<table>
<thead>
<tr>
<th>Limited Stage</th>
<th>Primary, Adjuvant, or First Line of Therapy (1&lt;sup&gt;st&lt;/sup&gt; Line)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Carboplatin and etoposide ± XRT&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Cisplatin and etoposide ± XRT&lt;sup&gt;1,2&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Extensive Stage</th>
<th>First Line of Therapy (1&lt;sup&gt;st&lt;/sup&gt; Line)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Carboplatin and etoposide&lt;sup&gt;9&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Atezolizumab (Tecentriq), carboplatin, and etoposide&lt;sup&gt;31&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second and Subsequent Lines of Therapy (2&lt;sup&gt;nd&lt;/sup&gt; Line+)</th>
<th>Relapse Greater than Six (6) Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin and etoposide&lt;sup&gt;9&lt;/sup&gt;</td>
<td></td>
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</tbody>
</table>

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Effective August 12, 2019
LUNG CANCER: SMALL CELL LUNG CANCER REFERENCES


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Effective August 12, 2019 56
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# Melanoma Pathways: Metastatic Melanoma

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

Nivolumab (Opdivo)\(^59\)

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

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

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

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

Vemurafenib (Zelboraf) and cobimetinib (Cotellic)\(^{26,40,42}\) – **TERMED Effective 8/12/2019**

Encorafenib (Braftovi) and binimetinib (Mektovi)\(^66\) – **ADDED Effective 8/12/2019**

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

Vemurafenib (Zelboraf) and cobimetinib (Cotellic)\(^{26,40,42}\) – **TERMED Effective 8/12/2019**

Encorafenib (Braftovi) and binimetinib (Mektovi)\(^66\) – **ADDED Effective 8/12/2019**

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

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

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

\(\dagger\) BRAF mutations include V600E and V600K mutations

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Effective August 12, 2019
MELANOMA: METASTATIC MELANOMA REFERENCES

NCCN Clinical Practice Guidelines: Melanoma V2.2019

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Effective August 12, 2019


NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Melanoma. NCCN. Accessed May 1, 2019


Ascierto PA, McArthur GA, Dréno B, et. al. Cobimetinib combined with vemurafenib in advanced BRAF(V600)-mutant melanoma (coBRIM): updated efficacy results from a randomised, double-blind, phase 3 trial. Lancet Oncol. 2016 Sep;17(9):1248-60. PMID: 27480103


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Effective August 12, 2019
# Myeloma Pathways: Multiple Myeloma

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

| VRD/VDR: bortezomib (Velcade), lenalidomide (Revlimid), and dexamethasone[^10,12,79] |

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

| CyBorD or VDC: bortezomib (Velcade), cyclophosphamide, and dexamethasone[^9,10,84] |
| R-dex: lenalidomide (Revlimid) and low-dose dexamethasone[^10,11,13,73] |
| VRD/VDR: bortezomib (Velcade), lenalidomide (Revlimid), and dexamethasone[^50,12,79] |
| VD: bortezomib (Velcade) and dexamethasone[^1,3,12,24,89] |

## Maintenance Therapy | Post-Transplant

| Lenalidomide (Revlimid)^[^26,27,83,92] |

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

| CRd or KRd: carfilzomib (Kyprolis), lenalidomide (Revlimid), and dexamethasone[^82] |
| DRD: daratumumab (Darzalex), lenalidomide (Revlimid), and dexamethasone[^100] |
| DVD: daratumumab (Darzalex), bortezomib (Velcade), and dexamethasone[^103] |

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

| Daratumumab (Darzalex)^[^95] |
| Elotuzumab (Empliciti), lenalidomide (Revlimid), and dexamethasone[^97] |
| Elotuzumab (Empliciti), pomalidomide (Pomalyst), and dexamethasone[^*113] – Added Effective 5/13/2019 |

[^*]: Eligible only if patient has received prior therapy with lenalidomide and proteasome inhibitor

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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.*
MYELOMA: MULTIPLE MYELOMA REFERENCES

NCCN Clinical Practice Guidelines: Multiple Myeloma V2.2019


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Effective August 12, 2019


42. Anderson KC, Jagannath S, Jakubowiak A, et al. Phase II study of lenalidomide (Len), bortezomib (Bz), and dexamethasone (Dex) in patients (pts) with relapsed or relapsed and refractory multiple myeloma (MM). J Clin Oncol. 2008; 26(15S):A8545 Abstract 8545.


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

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Effective August 12, 2019
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NHL: Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Pathways

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

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

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

BR: bendamustine (Bendeka, Treanda) and rituximab\textsuperscript{13,15,39,51}

FCR: fludarabine (Fludara), cyclophosphamide, and rituximab*\textsuperscript{1,2,39,51}

Ibrutinib (Imbruvica)\textsuperscript{29,37,46,47}

Obinutuzumab (Gazyva) and chlorambucil (Leukeran)\textsuperscript{16}

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

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

Idelalisib (Zydelig)\textsuperscript{43}

Idelalisib (Zydelig) and rituximab*\textsuperscript{38}

Venetoclax (Venclexta) and rituximab\textsuperscript{59}

Second and Subsequent Lines of Therapy (2nd Line+) | Without 17p Deletion

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

Idelalisib (Zydelig)\textsuperscript{43}

Idelalisib (Zydelig) and rituximab\textsuperscript{38}

Venetoclax (Venclexta) and rituximab\textsuperscript{59}

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

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

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

Effective August 12, 2019
NHL: CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) / SMALL LYMPHOCYTIC LYMPHOMA (SLL) REFERENCES

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


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


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

Effective August 12, 2019
# NHL: Diffuse Large B-Cell Lymphoma Pathways

## First Line of Therapy (1st Line)

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

## First Line of Therapy (1st 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 (2nd 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 (2nd 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>  

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

Effective August 12, 2019
NHL: DIFFUSE LARGE B CELL LYMPHOMA REFERENCES


Note: Pathways are independent of specific health plan medical policy coverage criteria. Health plan medical policy/clinical guidelines should be consulted to determine whether proposed services will be covered.
Effective August 12, 2019


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Effective August 12, 2019
NHL: Follicular and Marginal Zone Lymphoma Pathways

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

Antibiotic therapy† for H. pylori eradication33,34

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

R rituximab monotherapy27,29,52,53

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

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

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

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

R rituximab monotherapy7,17,52,53

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

Chlorambucil (Leukeran)10

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

Cyclophosphamide11-13

Cyclophosphamide and rituximab§52,53

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

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

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

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

† Only generic antibiotics are considered pathway options for H. pylori eradication

‡ Splenectomy is also a recommended option for splenic marginal zone lymphoma (NCCN 2A)

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

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

Effective August 12, 2019
NHL: FOLLICULAR AND MARGINAL ZONE LYMPHOMA REFERENCES


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Effective August 12, 2019
### NHL: Mantle Cell Lymphoma Pathways

#### First Line of Therapy (1st Line) | ASCT Candidates

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

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

#### First Line of Therapy (1st Line) | Not an ASCT Candidate

- **BR**: bendamustine (Bendeka, Treanda) and rituximab*9,10

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

- Acalabrutinib (Calquence)42

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

- Bortezomib (Velcade)17

- Ibrutinib (Imbruvica)19,20

- Lenalidomide (Revlimid)20-23

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

Effective August 12, 2019
**NHL: MANTLE CELL LYMPHOMA REFERENCES**


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**References**


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

Effective August 12, 2019


40. Goy A, Bernstein SH, Kahl BS, et al. Bortezomib in relapsed or refractory mantle cell lymphoma who relapsed or progressed after or were refractory to bortezomib: phase II MCL-001 (EMERGE) study. J Clin Oncol. 2013 Oct 10;31(29):3688-3695. PMID: 24002500


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

Effective August 12, 2019
Ovarian Cancer (Epithelial) Pathways

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

**Adjuvant or Primary Therapy | Stage II, III, IV**
- Carboplatin and paclitaxel\(^6\)\(^-8\)\(^,45\) *(Administered weekly or every 3 weeks)*
- Intravenous (IV) paclitaxel and Intraperitoneal (IP) cisplatin and IP paclitaxel\(^1\)\(^-49\) *(Stage III only)*

**Recurrent Disease | First and Subsequent Lines of Therapy (1st Line+) | Platinum-Sensitive*\)**
- Carboplatin\(^8\)\(^,9\)\(^,12\)
- Carboplatin and gemcitabine (Gemzar)\(^12\)\(^,13\)
- Carboplatin and paclitaxel\(^8\)\(^,9\)\(^,15\)
- Carboplatin and weekly paclitaxel

**Recurrent Disease | Maintenance Therapy | Platinum-Sensitive*\)**
- Niraparib (Zejula)\(^54\)
- Olaparib (Lynparza)\(^55\)
- Rucaparib (Rubraca)\(^60\)

**Recurrent Disease | Second and Subsequent Lines of Therapy (2nd Line+) | Platinum Resistant\)**
- Bevacizumab (Avastin) monotherapy\(^42\)
- Docetaxel (Taxotere)\(^17\)
- Gemcitabine (Gemzar)\(^18\)\(^,20\)
- Liposomal doxorubicin (Doxil or Lipodox)\(^19\)\(^-21\)
- Paclitaxel (weekly)\(^22\)\(^,23\)
- Paclitaxel and bevacizumab (Avastin)\(^36\)\(^-38\)
- Tamoxifen\(^56\)
- Topotecan (Hycamtin)\(^21\)\(^,24\)
- Topotecan (Hycamtin) and bevacizumab (Avastin)\(^36\)\(^,37\)
- Vinorelbine (Navelbine)\(^34\)\(^,35\)

* 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.

Effective August 12, 2019
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)\textsuperscript{36,40}
  - **FULV**: fluorouracil (5FU) and leucovorin\textsuperscript{4,6,9}
  - Gemcitabine (Gemzar)\textsuperscript{1,3-7}
  - **mFOLFIRINOX**: fluorouracil (5FU), leucovorin, irinotecan (Camptosar), and oxaliplatin\textsuperscript{46}

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

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

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

- Gemcitabine (Gemzar)\textsuperscript{21}

* Modified FOLFIRINOX: Bolus 5-FU not administered

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**Effective August 12, 2019**
PANCREATIC CANCER (ADENOCARCINOMA) REFERENCES

NCCN Clinical Practice Guidelines: Pancreatic Adenocarcinoma V2.2018


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Effective August 12, 2019
34 Tempero MA, Cardin DB, Blankin A, et al. nab-paclitaxel (nab-P) plus gemcitabine (Gem) vs Gem alone as adjuvant treatment for resected pancreatic cancer (PC) in a phase III trial (APACT). J Clin Oncol 33, 2015 (suppl; abstr TPS4153). Abstract 4153
36 Neoptolemos J, Palmer D, Ghaney P, et al. ESPAC-4: A multicenter, international, open-label randomized controlled phase III trial of adjuvant combination chemotherapy of gemcitabine (GEM) and capecitabine (CAP) versus monotherapy gemcitabine in patients with resected pancreatic ductal adenocarcinoma*. J Clin Oncol 34, 2016 (supplement) Abstract LBA4006

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Effective August 12, 2019
Prostate Cancer (Adenocarcinoma) Pathways

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

- Goserelin (Zoladex)\(^1,2\)
- Leuprolide (Eligard/Lupron)\(^1,2\)
- Triptorelin (Trelstar)\(^1,2\)

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

- Goserelin (Zoladex)\(^3,5\)
- Leuprolide (Eligard/Lupron)\(^3,5\)
- Triptorelin (Trelstar)\(^3,5\)

**High Risk (T3a or Gleason 8-10), Very High Risk (T3b-T4), and Locally Advanced Prostate Cancer (LN+) | Primary Treatment with Radiotherapy (RT)**

- Goserelin (Zoladex)\(^4\)
- Goserelin (Zoladex)\(^*\) with abiraterone (Zytiga)\(^41\)
- Leuprolide (Eligard/Lupron)\(^*\)\(^4\)
- Leuprolide (Eligard/Lupron)\(^*\) with abiraterone (Zytiga)\(^41\)
- Triptorelin (Trelstar)\(^*\)\(^4\)
- Triptorelin (Trelstar) with abiraterone (Zytiga)\(^*\)\(^41\)

**Recurrent and Metastatic Disease | Hormone Sensitive**

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

Bilateral 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\(^*\) Line) setting

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Effective August 12, 2019
Prostate Cancer (Adenocarcinoma) Pathways (continued)

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

- Abiraterone (Zytiga) and prednisone with continued ADT†8,12,25-27
- Docetaxel (Taxotere) (every 3 weeks) with continued ADT†9,10,19
- Enzalutamide (Xtandi) with continued ADT
- 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†8,12,25-27
- Cabazitaxel (Jevtana) with ADT†11
- Docetaxel (Taxotere) (every 3 weeks) with continued ADT†9,10,19
- Docetaxel (Taxotere) rechallenge with ADT†21,22
- 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 ± dexamethasone13-16,24

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

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Effective August 12, 2019
NCCN Clinical Practice Guidelines: Prostate Cancer. Version 3.2018


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References


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37. De Bono J, Hardy-Bessard A, Kim C, et al. Phase III non-inferiority study of cabazitaxel (C) 20 mg/m2 (C20) versus 25 mg/m2 (C25) in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) previously treated with docetaxel (D). American Society of Clinical Oncology Annual Meeting; Chicago IL: American Society of Clinical Oncology; 2016 Abstract 5008


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Effective August 12, 2019
93
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Effective August 12, 2019
# Testicular (Germ Cell Tumors) Cancer Pathways

## Seminoma | Stage II-IIIA | Primary Therapy

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

**EP**: etoposide and cisplatin

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

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

## Nonseminoma | Stage II-IIIA | Primary Therapy

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

**EP**: etoposide and cisplatin

## Nonseminoma | Stage IIIB-C | Primary Therapy

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

## Nonseminoma | Adjuvant Therapy after RPLND†

**EP**: etoposide and cisplatin

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

† RPLND: Retroperitoneal lymph node dissection

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Effective August 12, 2019
TESTICULAR (GERM CELL TUMORS) CANCER REFERENCES


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Uterine (Endometrial) Cancer Pathways

<table>
<thead>
<tr>
<th>Adjuvant Therapy</th>
<th>Stage III-IV or High Risk Histologies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin and paclitaxel[^6]^6</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recurrent / Metastatic</th>
<th>First and Subsequent Lines of Therapy (1st Line+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin and paclitaxel[^27,29]^27,29</td>
<td></td>
</tr>
<tr>
<td>Cisplatin and doxorubicin (Adriamycin)[^24,25]^24,25</td>
<td></td>
</tr>
</tbody>
</table>

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

Effective August 12, 2019

[^6]: Reference 6
[^27]: Reference 27
[^29]: Reference 29
[^24]: Reference 24
[^25]: Reference 25
UTERINE (ENDOMETRIAL) CANCER REFERENCES


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References


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Effective August 12, 2019
39. Gunderson CC, Fader AN, Carson KA, Bristow RE. Oncologic and reproductive outcomes with progesterin therapy in women with endometrial hyperplasia and grade 1 adenocarcinoma: a systematic review. Gynecol Oncol. 2012 May;125(2):477-82. PMID: 22245711

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