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AIM Medical Oncology Program

The goal of the AIM Oncology program is to help provide access to quality and affordable cancer care. A key component of the program is AIM Cancer Treatment Pathways.

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. 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. 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 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.
## Bladder Cancer (Urothelial) Pathways

<table>
<thead>
<tr>
<th>Neoadjuvant Therapy</th>
<th>Clinical Stage II, III, or IV without evidence of metastases (cT2, cT3, cT4a, cT4b, M0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMV: cisplatin (Platinol), methotrexate, and vinblastine 3 cycles 4,5</td>
<td></td>
</tr>
<tr>
<td>Gemcitabine (Gemzar) and cisplatin (Platinol) 4 cycles 2</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adjuvant Therapy</th>
<th>Stage I or II after TURBT* or following resection of recurrent or persistent disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG: bacillus calmette-guerin, intravesical 20-24</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>First line therapy (1st line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemcitabine (Gemzar) and cisplatin** (Platinol) 6,17,18</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Second line therapy (2nd line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemcitabine (Gemzar) 9</td>
<td></td>
</tr>
<tr>
<td>Paclitaxel (Taxol) 14</td>
<td></td>
</tr>
</tbody>
</table>

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.

Note: Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.
BLADDER CANCER UROTHELIAL REFERENCES


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Breast Cancer Pathways: Adjuvant and Neoadjuvant

**Adjuvant | HER2 Negative** *(Note: adjuvant chemotherapy pathways do NOT apply to individuals with Hormone-Receptor positive, lymph node negative, OncotypeDx™ LOW risk score)*

AC → weekly T: doxorubicin (Adriamycin) and cyclophosphamide (Cytoxan) (every 3 weeks) followed by weekly paclitaxel (Taxol)8, 9, 11, 33
Dose dense (dd) AC → weekly T: dose dense doxorubicin (Adriamycin) and cyclophosphamide (Cytoxan) followed by weekly paclitaxel (Taxol) 8, 9, 11, 12, 60
TC: docetaxel (Taxotere) and cyclophosphamide (Cytoxan)10, 19

**Adjuvant | HER2 Positive**

AC → TH: doxorubicin (Adriamycin) and cyclophosphamide (Cytoxan) followed by paclitaxel (Taxol) and trastuzumab (Herceptin) 23-26
TCH: docetaxel (Taxotere), carboplatin (Paraplatin) and trastuzumab (Herceptin) 25, 26
TH: paclitaxel (Taxol) and trastuzumab (Herceptin)34 *(Pathway for stage I HER2+ breast cancer only)*

**Neoadjuvant | HER2 Negative**

AC → weekly T: doxorubicin (Adriamycin) and cyclophosphamide (Cytoxan) (every 3 weeks) followed by weekly paclitaxel (Taxol)8, 33, 42, 60
ddAC → weekly T: dose dense doxorubicin (Adriamycin) and cyclophosphamide (Cytoxan) followed by weekly paclitaxel (Taxol) 8, 11, 12, 39
TC: docetaxel (Taxotere) and cyclophosphamide (Cytoxan)10, 43

**Neoadjuvant | HER2 Positive**

TCH: docetaxel (Taxotere), carboplatin (Paraplatin) and trastuzumab (Herceptin)25, 49
AC → TH: doxorubicin (Adriamycin) and cyclophosphamide (Cytoxan) followed by paclitaxel (Taxol) and trastuzumab (Herceptin)1, 14, 23, 24, 26

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

TCH+P: docetaxel (Taxotere), carboplatin (Paraplatin), trastuzumab (Herceptin) and pertuzumab (Perjeta)50, 51, 54, 55, 57

Note: Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.


26 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-positive or high risk nodenegative breast cancer. Cancer Res. December 15, 2013 73; S1-03. Abstract S1-03


77 Seidman AD, Berry D, Cirrincione C, et al. Randomized phase III trial of weekly compared with every-3-weeks paclitaxel for metastatic breast cancer, with trastuzumab for all HER-2 overexpressors and random assignment to trastuzumab or not in HER-2 nonoverexpressors: final results of Cancer and Leukemia Group B protocol 9840. J Clin Oncol. 2008 Apr 1;26(10):1642-1649. PMID:18375893


Effective October 1, 2016


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# Breast Cancer Pathways:
## Advanced/Metastatic

### Metastatic disease | HER2 Negative | First and/or 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 (Taxol) 18-20,65
- Vinorelbine (Navelbine) 15-17,65

### 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 (Taxol) and trastuzumab (Herceptin) 35,36
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and docetaxel (Taxotere) 32,33,35
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and paclitaxel (Taxol) 34
- Vinorelbine (Navelbine) and trastuzumab (Herceptin) 46,47

### 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 (Taxol) and trastuzumab (Herceptin) 35,36
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and docetaxel (Taxotere) 32,33,35,82
- Pertuzumab (Perjeta), trastuzumab (Herceptin), and paclitaxel (Taxol) 34
- Trastuzumab (Herceptin) and lapatinib (Tykerb) 49,50
- Trastuzumab (Herceptin) monotherapy 37,48
- Vinorelbine (Navelbine) and trastuzumab (Herceptin) 46,47

*Note: Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.*
BREAST CANCER METASTATIC REFERENCES


# Breast Cancer Pathways: Endocrine Therapy for Recurrent or Metastatic Disease

## Post-Menopausal | ER or PR Positive | Recurrent or Metastatic disease | First line therapy (1st line)

<table>
<thead>
<tr>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole (Arimidex)</td>
</tr>
<tr>
<td>Fulvestrant, high dose (Faslodex)</td>
</tr>
<tr>
<td>Letrozole (Femara)</td>
</tr>
<tr>
<td>Letrozole (Femara) and palbociclib (Ibrance)</td>
</tr>
<tr>
<td>Tamoxifen</td>
</tr>
</tbody>
</table>

## Post-Menopausal | ER or PR Positive | Recurrent or Metastatic disease | Second and subsequent lines of therapy (2nd line +)*

<table>
<thead>
<tr>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole (Arimidex)</td>
</tr>
<tr>
<td>Exemestane (Aromasin)</td>
</tr>
<tr>
<td>Fulvestrant, high dose (Faslodex)</td>
</tr>
<tr>
<td>Fulvestrant (Faslodex) and palbociclib (Ibrance)</td>
</tr>
<tr>
<td>Letrozole (Femara)</td>
</tr>
<tr>
<td>Tamoxifen</td>
</tr>
</tbody>
</table>

## Pre-Menopausal | ER or PR Positive | Metastatic disease | First line of therapy (1st line)

<table>
<thead>
<tr>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole (Arimidex) with ovarian suppression</td>
</tr>
<tr>
<td>Letrozole (Femara) with ovarian suppression</td>
</tr>
<tr>
<td>Letrozole (Femara) and palbociclib (Ibrance) with ovarian suppression</td>
</tr>
<tr>
<td>Tamoxifen with ovarian suppression</td>
</tr>
<tr>
<td>Tamoxifen</td>
</tr>
</tbody>
</table>

* Ovarian suppression utilizes LHRH agonists given as monthly injections. 3-month depot dosing does not reliably suppress estrogen levels.

Note: Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required
Breast Cancer Pathways: Endocrine Therapy for Recurrent or Metastatic Disease (continued)

<table>
<thead>
<tr>
<th>Pre-Menopausal</th>
<th>ER or PR Positive</th>
<th>Metastatic disease</th>
<th>Second and subsequent lines of therapy (2nd line +)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrozole (Arimidex) with ovarian suppression 29</td>
<td>Exemestane (Aromasin) with ovarian suppression 32</td>
<td>Fulvestrant, high dose (Faslodex) with ovarian suppression 20</td>
<td>Fulvestrant (Faslodex) and palbociclib (Ibrance) with ovarian suppression 41</td>
</tr>
<tr>
<td>Letrozole* (Femara) with ovarian suppression 24</td>
<td>Tamoxifen with ovarian suppression* 30</td>
<td>Tamoxifen 30,31</td>
<td></td>
</tr>
</tbody>
</table>

* Ovarian suppression utilizes LHRH agonists given as monthly injections. 3-month depot dosing does not reliably suppress estrogen levels.

Note: Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.
BREAST CANCER ENDOCRINE THERAPY REFERENCES


20. Johnston SR, Kilburn LS, Ellis P, et al. Fulvestrant plus anastrozole or placebo versus exemestane alone after progression on non-steroidal aromatase inhibitors in postmenopausal patients with hormone-receptor-positive locally advanced or metastatic breast cancer (SoFEA); a composite, multicentre, phase 3 randomised trial. Lancet Oncol. 2013 Sep;14(10):989-998. PMID: 23902874


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 with anastrozole 1 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


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**Chronic Myelogenous Leukemia (CML) Pathways**

### First Line Therapy
- Imatinib (Gleevec) 1,4,6,8,30,33-35
- Dasatinib* (Sprycel) for **intermediate or high risk disease** 1,2,30,37-39
- Nilotinib* (Tasigna) for **intermediate or high risk disease** 6,8,31,32

### Second Line Therapy  
**Following treatment failure, suboptimal response †, or intolerance to first line therapy**
- Bosutinib (Bosulif) 23,33
- Dasatinib (Sprycel) 1,2,9,10,12,36
- Nilotinib (Tasigna) 16,17,18,31,32
- Ponatinib** (Iclusig) 26

### Third Line Therapy
- Ponatinib (Iclusig) 26

---

**Note:** Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.

*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

**Pathway option for 2nd 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.

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


Colorectal Cancer Pathways

Adjuvant*

Capecitabine (Xeloda) 52,69

FOLFOX: fluorouracil (5-FU), leucovorin and oxaliplatin (Eloxatin) 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 (Eloxatin) 24,26,28,30,34

FOLFOX + bevacizumab: fluorouracil (5FU), leucovorin oxaliplatin (Eloxatin) 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 (Eloxatin) with panitumumab (Vectibix) 12,53,59

Irinotecan (Camptosar) and panitumumab (Vectibix) 47

Metastatic disease | RAS WT | Third or subsequent lines of therapy (3rd line+)

Panitumumab (Vectibix) monotherapy 13,61,56

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

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

Note: Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.
COLORECTAL CANCER REFERENCES


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


Dutton SJ, Kenealy N, Love SB, Wasan HS, Sharma RA1; FOXFIRE Protocol Development Group and the NCRI Colorectal Clinical Study Group. FOXFIRE protocol: an open-label, randomised, phase III trial of 5-fluorouracil, oxaliplatin and folinic acid (OxMdG) with or without interventional Selective Internal Radiation Therapy (SIRT) as first-line treatment for patients with unresectable liver-only or liver-dominant metastatic colorectal cancer. BMC Cancer. 2014 Jul 9;14:497. PMID: 25011439


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

### Primary therapy | Resectable and unresectable disease

- Cisplatin (Platinol) and fluorouracil (5FU) \(^{3,4}\)
- **ECF:** epirubicin (Ellence), cisplatin (Platinol), and fluorouracil (5FU) \(^{1,2}\)
- Fluorouracil (5FU) and cisplatin (Platinol) with concurrent radiation therapy (RT) \(^{35}\)
- Paclitaxel (Taxol) and carboplatin (Paraplatin) with concurrent radiation therapy (RT) \(^{5}\)

### Post-operative treatment

- Fluorouracil (5FU) and leucovorin with concurrent radiation therapy (RT) \(^{38}\)

### Recurrent/metastatic or locally advanced/inoperable disease | HER2 Negative | First line

- Cisplatin (Platinol) and fluorouracil (5FU) \(^{15,19,21,26}\)
- Fluorouracil (5FU) and irinotecan (Camptosar) \(^{25,26}\)
- **FLO / FOLFOX:** fluorouracil (5FU), leucovorin, and oxaliplatin (Eloxatin) \(^{27}\)
- **FLP:** fluorouracil (5FU), leucovorin, and cisplatin (Platinol) \(^{27}\)

### Recurrent/metastatic or locally advanced/inoperable disease | HER2 positive | First line

- Cisplatin (Platinol), fluorouracil (5FU), and trastuzumab (Herceptin) \(^{15}\)

### Recurrent/metastatic or locally advanced/ inoperable disease | Second line

- Irinotecan (Camptosar) \(^{24,29}\)
- Paclitaxel (Taxol) \(^{33}\)

Note: Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.
GASTRIC, ESOPHAGEAL, AND GASTROESOPHAGEAL JUNCTION CANCERS REFERENCES


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Effective October 1, 2016
# Head and Neck Cancer Pathways

<table>
<thead>
<tr>
<th>Hypopharynx and larynx: candidate for local therapy (M0)</th>
<th>Primary systemic therapy &amp; concurrent radiation therapy (RT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose cisplatin (Platinol) * with concurrent radiation therapy (RT)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hypopharynx and larynx: candidate for local therapy (M0)</th>
<th>Post-operative systemic therapy &amp; concurrent radiation therapy (RT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose cisplatin (Platinol)* with concurrent radiation therapy (RT) 10</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lip, oral cavity, oropharynx, ethmoid sinus, maxillary sinus, occult primary: candidate for local therapy (M0)</th>
<th>Primary systemic therapy &amp; concurrent radiation therapy (RT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose cisplatin (Platinol)* with concurrent radiation therapy (RT)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Lip, oral cavity, oropharynx, ethmoid sinus, maxillary sinus, occult primary: candidate for local therapy (M0)</th>
<th>Post-operative systemic therapy &amp; concurrent radiation therapy (RT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose cisplatin (Platinol)* with concurrent radiation therapy (RT)</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nasopharynx: candidate for local therapy (M0)</th>
<th>Primary systemic therapy &amp; concurrent radiation therapy (RT) followed by adjuvant therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose cisplatin (Platinol)* with concurrent radiation therapy (RT), followed by adjuvant cisplatin (Platinol) and fluorouracil (5FU)</td>
<td></td>
</tr>
</tbody>
</table>

**Nasopharynx | Metastatic and recurrent disease | First Line and subsequent lines of therapy (1st line+) | Performance Status 0,1,2**

<table>
<thead>
<tr>
<th>Carboplatin (Paraplatin)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin (Platinol) 20,22</td>
</tr>
<tr>
<td>Cisplatin (Platinol)** and gemcitabine (Gemzar) 29</td>
</tr>
<tr>
<td>Cisplatin (Platinol)** and paclitaxel (Taxol) 18,29</td>
</tr>
<tr>
<td>Fluorouracil (5FU) 22</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar) 31</td>
</tr>
<tr>
<td>Gemcitabine (Gemzar) and vinorelbine (Navelbine) 30</td>
</tr>
<tr>
<td>Methotrexate 24,26</td>
</tr>
<tr>
<td>Paclitaxel (Taxol)23</td>
</tr>
</tbody>
</table>

**Non-Nasopharyngeal (Squamous cell) | Metastatic and recurrent disease | First Line | Performance Status 0,1,2**

| Carboplatin (Paraplatin), fluorouracil (5FU), and cetuximab (Erbitux) 14 |
| Cisplatin (Platinol), fluorouracil (5FU), and cetuximab (Erbitux) 14 |

**Non-nasopharyngeal (Squamous cell) | Metastatic and recurrent disease | Second Line and Subsequent lines of therapy | Performance Status 0,1,2**

| Paclitaxel (Taxol)23 |

---

*High dose cisplatin is defined as weekly dosing to achieve 200-300 mg/m² total cisplatin dose

**Substitution of carboplatin for cisplatin, and vice-versa, is acceptable for metastatic disease
HEAD AND NECK CANCER REFERENCES


37 Ferris RL, Blumenschein GR, Fayette J et al. Further evaluations of nivolumab (nivo) versus investigator’s choice (IC) chemotherapy for recurrent or metastatic (R/M) squamous cell carcinoma of the head and neck (SCCHN): CheckMate 141. J Clin Oncol 2016 34(15)_(supp; Abstract 6009)


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Hodgkin Lymphoma Pathways

Classical Hodgkin Lymphoma | Early Stage (Stage I-IIA, favorable and unfavorable risk)

**ABVD:** doxorubicin (Adriamycin), bleomycin (Blenoxane), vinblastine (Velban), and dacarbazine (DTIC) ± ISRT\(^1,3,4,5,30\)

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

**ABVD:** doxorubicin (Adriamycin), bleomycin (Blenoxane), vinblastine (Velban), and dacarbazine (DTIC) ± ISRT\(^7,8,9,10,32\)

Note: Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.
HODGKIN LYMPHOMA REFERENCES


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Kidney Cancer (Renal Cell Carcinoma) Pathways

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>First line therapy (1st line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dose intravenous (IV) interleukin-2 (IL2, Proleukin)(^{17,18}) (clear cell only)</td>
<td></td>
</tr>
<tr>
<td>Pazopanib (Votrient)(^{4,5,7})</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>First line therapy (1st line)</th>
<th>Poor prognosis* or non-clear cell histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temsirolimus (Torisel)(^{23})</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Second line or subsequent lines of therapy (2nd line+)</th>
<th>Clear cell carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab (Opdivo)(^{29})</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Poor prognosis patients have 3 or more of the following predictors of short survival:
- LDH greater than 1.5 x normal
- Hemoglobin less than normal (anemia)
- Corrected serum calcium (Ca) greater than 10 ng/dL
- Less than 1 year from diagnosis to the start of systemic therapy
- Karnofsky performance status ≤ 70 (Unable to carry on normal activity or do active work, but able to perform self-care)
- 2 or more sites of organ metastases

Note: Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.
KIDNEY CANCER REFERENCES


Effective October 1, 2016


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# Melanoma Pathways: Metastatic Melanoma

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>First and subsequent lines of therapy (1st line +)</th>
<th>Any BRAF status</th>
<th>ECOG PS: 0, 1, 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nivolumab (Opdivo)(^{20,31,32})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metastatic Disease</td>
<td>First line therapy (1st line)</td>
<td>BRAF mutated*</td>
<td>Symptomatic disease</td>
</tr>
<tr>
<td></td>
<td>Vemurafenib (Zelboraf) and cobimetinib (Cometriq)(^{26,40-42})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metastatic Disease</td>
<td>Second and subsequent lines of therapy (2nd line +)</td>
<td>BRAF mutated*</td>
<td>ECOG PS: 0, 1, 2</td>
</tr>
<tr>
<td></td>
<td>Vemurafenib (Zelboraf) and cobimetinib (Cometriq)(^{26,40-42})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metastatic Disease</td>
<td>Second and subsequent lines of therapy (2nd line +)</td>
<td>Any BRAF status</td>
<td>ECOG PS: 0, 1, 2</td>
</tr>
<tr>
<td></td>
<td>Ipilimumab (Yervoy)(^{1,14,15,35,36})</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*BRAF mutations include V600E and V600K mutations.

**Note:** Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.
MELANOMA: METASTATIC REFERENCES


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# Myeloma Pathways: Multiple Myeloma

## Primary/ First Line (1st line) Therapy | Transplant candidates

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

## Primary/ First Line (1st line) Therapy | Ineligible for transplant

- **CyBorD or VDC**: bortezomib (Velcade), cyclophosphamide (Cytoxan), 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>50,12,79</sup>
- **VD**: bortezomib (Velcade) and dexamethasone<sup>1,3,12,24,89</sup>

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

- **CRd or KRd**: carfilzomib (Kyprolis), lenalidomide (Revlimid) and dexamethasone<sup>82</sup>
- **CyBorD or VDC**: bortezomib (Velcade), cyclophosphamide (Cytoxan) and dexamethasone<sup>32,49,47</sup>
- Pomalidomide (Pomalyst) and low dose dexamethasone*<sup>54,55,74,75,78</sup>

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

- Daratuzumab (Darzalex)<sup>95</sup>
- Elotuzumab (Empliciti), lenalidomide (Revlimid), and dexamethasone<sup>97</sup>

*Use of pomalidomide may require 2 prior therapies to meet medical necessity criteria

**Note**: Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.
MYELOMA: MULTIPLE MYELOMA REFERENCES


Straka C, Vogel M, Muller J, et al. Results from two phase III studies of bortezomib (BTZ) consolidation vs observation (OBS) post-transplant in patients (pts) with newly diagnosed multiple myeloma (NDMM). J Clin Oncol. 33, 2015 (suppl; abstr 8511). Abstract 8511


93  San-Miguel, Hungria V TM, Yoon S-S, et al. 3026 Final Analysis of Overall Survival from the Phase 3 Panorama 1 Trial of Panobinostat Plus Bortezomib and Dexamethasone Versus Placebo Plus Bortezomib and Dexamethasone in Patients with Relapsed or Relapsed and Refractory Multiple Myeloma. ASH. December 6, 2015. Abstract 3026


96  Moreau P, Masszi T, Grzasko N, et al. Ixazomib, an Investigational Oral Proteasome Inhibitor (PI), in Combination with Lenalidomide and Dexamethasone (IRd), Significantly Extends Progression-Free Survival (PFS) for Patients (Pts) with Relapsed and/or Refractory Multiple Myeloma (RRMM): The Phase 3 Tourmaline-MM1 Study (NCT01564537). ASH. December 7, 2015. Abstract 727


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

**First line (1st line) therapy | With 17p Deletion**

BR: bendamustine (Treanda) and rituximab (Rituxan)\(^{13,14,15,39}\) *No Longer a Pathway as of 12/01/2016*

FCR: fludarabine (Fludara), cyclophosphamide (Cytoxan), and rituximab (Rituxan)\(^{1,2,39}\) *No Longer a Pathway as of 12/01/2016*

FR: fludarabine (Fludara) and rituximab (Rituxan)\(^*\) *No Longer a Pathway as of 12/01/2016*

Obinutuzumab (Gazyva) and chlorambucil (Leukeran)\(^{16}\) *No Longer a Pathway as of 12/01/2016*

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

**First line (1st line) therapy | Without 17p Deletion**

BR: bendamustine (Treanda) and rituximab (Rituxan)\(^{13,14,15,39,51}\)

FCR: fludarabine (Fludara), cyclophosphamide (Cytoxan), and rituximab (Rituxan)\(^{1,2,39,51}\)

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

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

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

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

BR: bendamustine (Treanda) and rituximab (Rituxan)\(^{13,14,15,42}\)

FCR: Fludarabine (Fludara), cyclophosphamide (Cytoxan), and rituximab (Rituxan)\(^{1,2,39}\) *No Longer a Pathway as of 12/01/2016*

FR: Fludarabine (Fludara) and rituximab (Rituxan)\(^4\) *No Longer a Pathway as of 12/01/2016*

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

Note: Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.

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

- WBC elevation above 200-300 x 10\(^9\)
- Signs of leukostasis
- Lymphocyte doubling time of less than 6 months
- In low or intermediate risk disease:
  - Significant disease-related symptoms such as severe fatigue, weight loss, night sweats, otherwise unexplained fever
  - Signs of end-organ damage
  - Significant or progressive bulky disease, such as massive splenomegaly (≥6 cm below the costal margin) or massive lymphadenopathy (≥ 10 cm in longest diameter)
  - Clinically significant progressive or symptomatic anemia or thrombocytopenia
    - Not caused by autoimmune etiology, unless poor response to conventional immunosuppressive therapy
- High risk disease, particularly with progressive cytopenias
NHL: CLL/SLL REFERENCES


39 Eichhorst B, Fink AM, Busch R, et al. Frontline Chemoimmunotherapy with Fludarabine (F), Cyclophosphamide (C), and Rituximab (R) (FCR) Shows Superior Efficacy in Comparison to Bendamustine (B) and Rituximab (BR) in Previously Untreated and Physically Fit Patients (pts) with Advanced Chronic Lymphocytic Leukemia (CLL): Final Analysis of an International, Randomized Study of the German CLL Study Group (GCLLSG) (CLL10 Study). Blood. 2011; 118:2085-2093. PMID: 21870470.


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# NHL: Diffuse Large B-Cell Lymphoma Pathways

## First line (1st line) therapy

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-CHOP</td>
<td>Cyclophosphamide (Cytoxan), doxorubicin (Adriamycin), vincristine (Oncovin), prednisone and rituximab (Rituxan)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-CEOP</td>
<td>Cyclophosphamide (Cytoxan), etoposide (Toposar), vincristine (Oncovin), prednisone and rituximab (Rituxan)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-GDP</td>
<td>Gemcitabine (Gemzar), dexamethasone, cisplatin (Platinol) and rituximab (Rituxan) OR gemcitabine (Gemzar), dexamethasone, carboplatin (Paraplatin) and rituximab (Rituxan)</td>
</tr>
<tr>
<td>R-ICE</td>
<td>Ifosfamide (Ifex), carboplatin (Paraplatin), etoposide (Toposar) and rituximab (Rituxan)</td>
</tr>
</tbody>
</table>

## Second and subsequent line of therapy (2nd line +)

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-R</td>
<td>Bendamustine (Treanda) and Rituximab (Rituxan)</td>
</tr>
<tr>
<td>R-GDP</td>
<td>Gemcitabine (Gemzar), dexamethasone, cisplatin (Platinol) and rituximab OR gemcitabine (Gemzar), dexamethasone, carboplatin (Paraplatin) and rituximab (Rituxan)</td>
</tr>
<tr>
<td>R-GemOx</td>
<td>Gemcitabine (Gemzar), oxaliplatin (Eloxatin) and rituximab (Rituxan)</td>
</tr>
<tr>
<td>R-ICE</td>
<td>Ifosfamide (Ifex), carboplatin (Paraplatin), etoposide (Toposar) and rituximab (Rituxan)</td>
</tr>
</tbody>
</table>

Rituximab monotherapy (Rituxan) reserved for frail patients

Note: Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.
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\(^{33,34}\)

**Splenic Marginal Zone Lymphoma** OR Gastric MALT Lymphoma: First Line Therapy (1st line)  

Rituximab monotherapy (Rituxan)\(^{27,28,29}\)

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

BR: Bendamustine (Treanda) and rituximab (Rituxan)\(^{5,6}\)

R-CHOP(21): Cyclophosphamide (Cytoxan), doxorubicin (Adriamycin), vincristine (Oncovin), prednisone, and rituximab (Rituxan) \(^{1,2,3,5}\)

R-CVP: Cyclophosphamide (Cytoxan), vincristine (Oncovin), prednisone, and rituximab (Rituxan) \(^{1,4}\)

Rituximab monotherapy (Rituxan) \(^{7,17}\)

**Follicular Lymphoma and other Marginal Zone Lymphomas | First Line Therapy (1st line) | additional options for the elderly or infirm**  

Chlorambucil (Leukeran)\(^{10}\)

Chlorambucil (Leukeran) and rituximab (Rituxan) \(^{10,11}\)

Cyclophosphamide (Cytoxan)\(^{11,12,13}\)

Cyclophosphamide (Cytoxan) and rituximab (Rituxan)

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

R-CHOP(21): Cyclophosphamide (Cytoxan), doxorubicin (Adriamycin), vincristine (Oncovin), prednisone, and rituximab (Rituxan)\(^{1,2,3,5}\)

R-CEOP: Cyclophosphamide (Cytoxan), etoposide (Toposar), vincristine (Oncovin), prednisone, and rituximab (Rituxan)\(^{13,35,36,37}\)

---

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

**Splenectomy is also a recommended option for Splenic Marginal Zone Lymphoma (NCCN 2A).**

**Note:** Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.
NHL: FOLLICULAR AND MARGINAL ZONE LYMPHOMA REFERENCES


# NHL: Mantle Cell Lymphoma Pathways

## First line therapy | ASCT Candidates

**Nordic Regimen**: dose intensified rituximab (Rituxan), cyclophosphamide (Cytoxan), vincristine (Marqibo), doxorubicin (Adriamycin), prednisone alternating with rituximab (Rituxan) and high dose cytarabine (Depocyt) ³

## First line therapy | Not ASCT Candidates

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

## Second and subsequent line therapy (2nd Line +)

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

- Bortezomib (Velcade)¹⁷
- Ibrutinib (Imbruvica)¹⁹,²⁰

---

Note: Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.
NHL: MANTLE CELL LYMPHOMA REFERENCES


13. Forstpointner R, Dreyling M, German Low-Grade Lymphoma Study Group, et al. The addition of rituximab to a combination of fludarabine, cyclophosphamide, mitoxantrone (FCM) significantly increases the response rate and prolongs survival as compared with FCM alone in patients with relapsed and refractory follicular and mantle cell lymphomas; results of a prospective randomized study of the German Low-Grade Lymphoma Study Group. *Blood*. 2004 Nov 15;104(10):3064-3071. PMID: 15284112


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

### Adjuvant

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin (Paraplatin) and paclitaxel (Taxol)</td>
<td>52</td>
</tr>
<tr>
<td>Cisplatin (Platinol) and gemcitabine (Gemzar)</td>
<td></td>
</tr>
<tr>
<td>Cisplatin (Platinol) and vinorelbine (Navelbine)</td>
<td>53,54</td>
</tr>
</tbody>
</table>

### Primary therapy | Locally advanced / Unresectable disease | Stage III

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin (Platinol) and etoposide (Vepesid) with concurrent XRT</td>
<td>88,89</td>
</tr>
<tr>
<td>Paclitaxel (Taxol) and carboplatin (Platinol) with concurrent XRT</td>
<td>92,93</td>
</tr>
</tbody>
</table>

### Metastatic disease | ALK positive or ROS1 positive | First Line (1st Line)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crizotinib (Xalkori)</td>
<td>1,58</td>
</tr>
</tbody>
</table>

### Metastatic disease | EGFR positive | First Line (1st line)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erlotinib (Tarceva)</td>
<td>2-5,63,73,87</td>
</tr>
</tbody>
</table>

### Metastatic disease | Non-squamous | First Line (1st line) | ECOG Performance status= 0, 1, 2

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin* (Paraplatin) and paclitaxel (Taxol)</td>
<td>7-13,15,16,54</td>
</tr>
<tr>
<td>Carboplatin (Paraplatin), paclitaxel (Taxol) and bevacizumab (Avastin)</td>
<td>13,14,30,31</td>
</tr>
<tr>
<td>Cisplatin* (Platinol) and gemcitabine (Gemzar)</td>
<td>8,11,13,22,24</td>
</tr>
<tr>
<td>Cisplatin* (Platinol) and pemetrexed (Alimta)</td>
<td>17,18,35</td>
</tr>
</tbody>
</table>

### Metastatic disease | Squamous | First Line (1st line) | ECOG Performance Status = 0, 1, 2

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin* (Paraplatin) and paclitaxel (Taxol)</td>
<td>7-13,15,16</td>
</tr>
<tr>
<td>Cisplatin* (Platinol) and gemcitabine (Gemzar)</td>
<td>8,11,13,17,22,23,25,75</td>
</tr>
</tbody>
</table>

### Metastatic disease | Non-squamous | Maintenance | ECOG Performance Status = 0, 1, 2

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuation bevacizumab (Avastin)</td>
<td>36,38</td>
</tr>
<tr>
<td>Continuation pemetrexed (Alimta)</td>
<td>39</td>
</tr>
<tr>
<td>Switch pemetrexed (Alimta)</td>
<td>41</td>
</tr>
</tbody>
</table>

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

** For patients with EGFR T790M mutation

**Note:** Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.

Effective October 1, 2016
## Non-Small Cell Lung Cancer (NSCLC) Pathways (cont.)

<table>
<thead>
<tr>
<th>Metastatic disease</th>
<th>EGFR T790M mutation</th>
<th>Second line (2nd line) after targeted 1st line therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Osimertinib (Tagrisso) ** 86, 90</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>ALK positive or EGFR positive</th>
<th>Second or subsequent lines of therapy (2nd line +)</th>
<th>ECOG Performance Status = 0, 1, 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Carboplatin* (Paraplatin) and paclitaxel (Taxol) 9</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cisplatin* (Platinol) and gemcitabine (Gemzar)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cisplatin* (Platinol) and pemetrexed (Alimta)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Osimertinib (Tagrisso) ** 86, 90</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>Second or subsequent lines of therapy (2nd line+)</th>
<th>ECOG Performance Status = 0, 1, 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nivolumab (Opdivo) 61,72 (any histology)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pemetrexed (Alimta) 43,44 (non-squamous histology)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic Disease</th>
<th>EGFR positive</th>
<th>ECOG Performance status = 3, 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Erlotinib (Tarceva) 35,48</td>
<td></td>
</tr>
</tbody>
</table>

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

** For patients with EGFR T790M mutation

Note: Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.
NON-SMALL CELL LUNG CANCER REFERENCES


14. FDA review documents


23 Grigorescu AC, Draghici IN, Nitipir C, et al. Gemcitabine (GEM) and carboplatin (CBDCA) versus cisplatin (CDDP) and vinblastine (VLB) in advanced non-

24 Helbækmo N, Sundstrøm SH, Norwegian Lung Cancer Study Group, et al. Vinorelbine/carboplatin vs gemcitabine/carboplatin in advanced NSCLC shows
similar efficacy, but different impact of toxicity. Br J Cancer. 2007 Aug 6;97(3):283-289. PMID: 17595658


1991;29(1):71-4. PMID: 1660354

30 Patel JD, Socinski MA, Garon EB, et al. PointBreak: a randomized phase III study of pemetrexed plus carboplatin and bevacizumab followed by
maintenance pemetrexed and bevacizumab versus paclitaxel plus carboplatin and bevacizumab followed by maintenance bevacizumab in patients
with stage IIIB or IV nonsquamous non-small-cell lung cancer. J Clin Oncol. 2013 Dec 1;31(34):4349-4357. PMID: 24145346


33 Binder D, Schweisfurth H, Grah C, et al. Docetaxel/gemcitabine or cisplatin/gemcitabine followed by docetaxel in the first-line treatment of patients with
PMID: 17031643


37 Barlesi F, Scherpereel A, Rittmeyer A, et al. Randomized phase III trial of maintenance bevacizumab with or without pemetrexed after first-line induction
20;31(24):3004-3011. PMID: 23835708

38 Johnson BE, Kabbinavar F, Fehrenbacher L, et al. ATLAS: randomized, double-blind, placebo-controlled, phase III trial comparing bevacizumab therapy
with or without erlotinib, after completion of chemotherapy, with bevacizumab for first-line treatment of advanced non-small-cell lung cancer. J Clin Oncol.
2013 Nov 1;31(31):3926-3934. PMID: 24101054

39 Paz-Ares LG, de Marinis F, Dediu M, et al. PARAMOUNT: Final overall survival results of the phase III study of maintenance pemetrexed versus placebo
10;31(23):2895-2902. PMID: 23835707

40 Cappuzzo F, Ciuleanu T, SATURN investigators, et al. Erlotinib as maintenance treatment in advanced non-small-cell lung cancer: a multicentre,

41 Ciuleanu T, Brodowicz T, Zielinski C, Kim JH, Krzakowski M, Laack E, Wu YL, Bover I, Begbie S, Tzekova V, Cucevic B, Pereira JR, Yang SH, Madhavan J,
Sugarman KP, Peterson P, John WJ, Krejcy J, Belani CP. Maintenance pemetrexed plus best supportive care versus placebo plus best supportive care for

PMID: 20818875

Shaharyar, Manegold C, Paul S, Paolotti P, Einhorn L, Bunn PA Jr. Randomized phase III trial of pemetrexed versus docetaxel in patients with non-small-cell


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# Ovarian Cancer (Epithelial) Pathways

**Adjuvant Therapy | Stage I A/B (Grade 2 or 3) or IC (Grade 1-3)**

- Carboplatin (Paraplatin) and dose dense (weekly) paclitaxel (Taxol)\(^6,7,8\)
- Carboplatin (Paraplatin) and paclitaxel (Taxol)\(^2,3,4,5,7\)

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

- Carboplatin (Paraplatin) and dose dense (weekly) paclitaxel (Taxol)\(^6,7,8,45\)
- Intravenous (IV) paclitaxel (Taxol) and Intraperitoneal (IP) cisplatin (Platinol) and IP paclitaxel (Taxol)\(^1,49\) **(Stage III only)**

**Recurrent Disease | First or subsequent lines of therapy (1st line +) | Platinum-sensitive*\(^\)**

- Carboplatin (Paraplatin)\(^8,9,12\)
- Carboplatin (Paraplatin) and gemcitabine (Gemzar)\(^12,13\)
- Carboplatin (Paraplatin) and paclitaxel (Taxol)\(^8,9,15\)
- Carboplatin (Paraplatin) and weekly paclitaxel (Taxol)

**Recurrent Disease | Second or subsequent lines of therapy (2nd line +) | Platinum resistant**

- Bevacizumab monotherapy (Avastin)\(^42\)
- Docetaxel (Taxotere)\(^17\)
- Gemcitabine (Gemzar)\(^19,20\)
- Liposomal doxorubicin (Doxil or Lipodox)\(^19,20,21\)
- Paclitaxel (weekly) (Taxol)\(^22,23\)
- Paclitaxel (Taxol) and bevacizumab (Avastin)\(^36,37,38\)
- Topotecan (Hycamtin)\(^21,24\)
- Topotecan (Hycamtin) and bevacizumab (Avastin)\(^36,37\)
- Vinorelbine (Navelbine)\(^34,35\)

---

*Platinum sensitive disease is defined as recurrence > 6 months after prior platinum-based therapy  
**Pathway selection for Stage III only

**Note:** Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.
OVARIAN CANCER (EPITHELIAL) REFERENCES


O’Malley DM, Richardson DL, Rheumae PS, et al. Addition of bevacizumab to weekly paclitaxel significantly improves progression-free survival in heavily pretreated recurrent epithelial ovarian cancer. *Gynecol Oncol.* 2011 May;121(2):269-72. PMID: 21315428


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


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Pancreatic Cancer (Adenocarcinoma) Pathways

**Adjuvant Therapy**

- FULV: fluorouracil (5FU) and leucovorin
- Gemcitabine monotherapy (Gemzar)

**Locally Advanced/Unresectable and Metastatic Disease | First Line Therapy (1st line) | ECOG Performance Status (PS): 0, 1**

- FOLFIRINOX: fluorouracil (5FU), leucovorin, irinotecan (Camptosar), and oxaliplatin (Eloxatin)
- Gemcitabine (Gemzar)
- Gemcitabine (Gemzar) and nab-paclitaxel (Abraxane)

**Locally Advanced/Unresectable and Metastatic Disease | Second Line Therapy (2nd line) | ECOG Performance Status (PS): 0, 1**

- Fluorouracil (5FU), leucovorin, and oxaliplatin (Eloxatin)
- Gemcitabine monotherapy (Gemzar)

Note: Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.
PANCREATIC CANCER (ADENOCARCINOMA) REFERENCES


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Effective October 1, 2016
Prostate Cancer (Adenocarcinoma) Pathways

<table>
<thead>
<tr>
<th>Adjuvant Therapy</th>
<th>Post- prostatectomy</th>
<th>Lymph node positive (LN+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gosereлин (Zoladex)(^{1,2})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leuprolide (Eligard/Lupron)(^{1,2})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triptorelin (Trelstar) (^{1,2})</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Intermediate risk</th>
<th>Primary treatment with radiotherapy (RT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gosereлин* (Zoladex)(^{3,5})</td>
<td></td>
</tr>
<tr>
<td>Leuprolide* (Eligard/Lupron)(^{3,5})</td>
<td></td>
</tr>
<tr>
<td>Triptorelin* (Trelstar)(^{3,5})</td>
<td></td>
</tr>
</tbody>
</table>

| High Risk (T3a or Gleason 8-10), Very High Risk (T3b-T4), and Locally Advanced Prostate Cancer (LN+) | Primary treatment with radiotherapy |
|------------------------------------------------------------------------------------------------------------------|
| Gosereлин* (Zoladex)\(^{4}\) |
| Leuprolide* (Eligard/Lupron)\(^{4}\) |
| Triptorelin* (Trelstar)\(^{4}\) |

<table>
<thead>
<tr>
<th>Recurrent and Metastatic disease</th>
<th>Hormone Sensitive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Docetaxel (q 3 wks) + Androgen Deprivation Therapy (ADT)**(^{19})</td>
<td></td>
</tr>
<tr>
<td>Gosereлин (Zoladex)(^{6})</td>
<td></td>
</tr>
<tr>
<td>Leuprolide (Eligard/Lupron)(^{6})</td>
<td></td>
</tr>
<tr>
<td>Triptorelin (Trelstar)(^{6})</td>
<td></td>
</tr>
</tbody>
</table>

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

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

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

Note: Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.
Prostate Cancer (Adenocarcinoma) Pathways (cont.)

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

<table>
<thead>
<tr>
<th>Medication</th>
<th>Description</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Abiraterone</strong> (Zytiga)</td>
<td>+ continue ADT</td>
<td><strong>8,12,25,26,27</strong></td>
</tr>
<tr>
<td><strong>Docetaxel</strong> (q3 wks)</td>
<td>+ continue ADT</td>
<td><strong>9,10,19</strong></td>
</tr>
<tr>
<td><strong>Enzalutamide</strong> (Xtandi) (oral)</td>
<td>160 mg qd + ADT</td>
<td><strong>10,19</strong></td>
</tr>
<tr>
<td><strong>Goserelin</strong> (Zoladex) + bicalutamide (Casodex)</td>
<td></td>
<td><strong>6,7</strong></td>
</tr>
<tr>
<td><strong>Leuprolide</strong> (Eligard/Lupron) + bicalutamide (Casodex)</td>
<td></td>
<td><strong>6,7</strong></td>
</tr>
<tr>
<td><strong>Triptorelin</strong> (Trelstar) + bicalutamide (Casodex)</td>
<td></td>
<td><strong>6,7</strong></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Medication</th>
<th>Description</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Abiraterone</strong> (Zytiga)** and prednisone</td>
<td>+ continue ADT</td>
<td><strong>8,12,25,26,27</strong> †</td>
</tr>
<tr>
<td><strong>Cabazitaxel</strong> (Jevtana) + ADT</td>
<td></td>
<td><strong>11</strong></td>
</tr>
<tr>
<td><strong>Docetaxel</strong> (q3 wks)</td>
<td>+ continue ADT</td>
<td><strong>9,10,19</strong> ‡</td>
</tr>
<tr>
<td><strong>Docetaxel rechallenge</strong></td>
<td>+ ADT</td>
<td><strong>21,22</strong></td>
</tr>
<tr>
<td><strong>Enzalutamide</strong> (Xtandi) (oral)</td>
<td>160 mg qd + ADT</td>
<td><strong>10,19</strong> †</td>
</tr>
<tr>
<td><strong>Goserelin</strong> (Zoladex) + bicalutamide (Casodex)</td>
<td></td>
<td><strong>6,7</strong> ‡</td>
</tr>
<tr>
<td><strong>Leuprolide</strong> (Eligard/Lupron) + bicalutamide (Casodex)</td>
<td></td>
<td><strong>6,7</strong> ‡</td>
</tr>
<tr>
<td><strong>Triptorelin</strong> (Trelstar)</td>
<td>+ bicalutamide (Casodex)</td>
<td><strong>6,7</strong> ‡</td>
</tr>
<tr>
<td><strong>Continued ADT</strong></td>
<td>with supportive care ± dexamethasone</td>
<td><strong>13,14,15,16,24</strong></td>
</tr>
</tbody>
</table>

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

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

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

† If neither abiraterone nor enzalutamide have been previously used

‡ If not previously used in the first line (1st Line) setting

**Note: Pathway lists are independent of specific health plan medical policy criteria. Verification of additional clinical criteria may be required.**
PROSTATE CANCER (ADENOCARCINOMA) REFERENCES


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