



# Cancer Therapy Pathways Program



With the rapid approval of new cancer therapies, along with the rising cost of cancer care, the goal of our Cancer Therapy Pathways Program is to help improve quality and value of cancer care for our members. We identify anti-cancer regimens supported by evidence-based guidelines, such as the clinical benefit (efficacy) and side-effect profile (toxicity). Among regimens with comparable efficacy and toxicity, we give additional consideration to the frequency of hospitalizations during therapy, duration of therapy, drug costs and total cost of care.



Please remember that this program isn't a substitute for the provider's therapy recommendation or care decision made between the provider and patient. Participating providers must use independent medical judgment in the context of individual clinical circumstances to determine a patient's care or treatment.

# Symbol definitions

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 in combination with  alone or in combination with  followed by

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Please note that the therapy regimens within each of these programs are in no particular order of preference. You may use any of the therapy regimens within each program.

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This section summarizes the updates to the program since it began in 2020.

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To request a list of reference documentation, please email [unitedoncology@uhc.com](mailto:unitedoncology@uhc.com).

### **Bladder Cancer (Non-Muscle Invasive): Neoadjuvant/Adjuvant**

- Intravesical BCG (Bacillus Calmette-Guerin)
- Intravesical Gemcitabine

### **Bladder Cancer (Muscle Invasive): Neoadjuvant/Adjuvant**

- Gemcitabine + Cisplatin
- Nivolumab (adjuvant only)

### **Bladder Cancer: Radiosensitizing Chemotherapy for Organ-Preserving Chemoradiation**

- Cisplatin + Fluorouracil (5FU)
- Gemcitabine

### **Bladder Cancer: Locally Advanced or Metastatic: 1st Line of Therapy**

- Gemcitabine + Cisplatin or Carboplatin

### **Bladder Cancer: Locally Advanced or Metastatic: Maintenance Post 1st Line of Therapy and No Progression**

- Avelumab

### **Bladder Cancer: Locally Advanced or Metastatic: 2nd + Subsequent Lines of Therapy**

- Avelumab (if IO not used previously)
- Gemcitabine + Cisplatin or Carboplatin (if platinum-based therapy not used previously)
- Enfortumab vedotin-ejfv
- Erdafitinib (FGFR3 mutation positive)
- Nivolumab (if IO not used previously)
- Pembrolizumab (if IO not used previously)

## Breast Cancer: Neoadjuvant/Adjuvant

### HER2 NEGATIVE:

- Docetaxel + Cyclophosphamide (TC)
- Doxorubicin + Cyclophosphamide (dose dense) → Paclitaxel every 2 weeks (ddAC → q2w T)
- Doxorubicin + Cyclophosphamide (dose dense) → Paclitaxel weekly (ddAC → weekly T)
- Olaparib (for BRCA 1/2 mutation positive; adjuvant therapy only)
- Pembrolizumab + Carboplatin + Paclitaxel → Pembrolizumab + Cyclophosphamide + Doxorubicin or Epirubicin → adjuvant Pembrolizumab (for high-risk TNBC only)

### HER2 POSITIVE:

- Docetaxel + Carboplatin + Trastuzumab\* (TCH)
- Doxorubicin + Cyclophosphamide → Paclitaxel weekly + Trastuzumab\* (AC → TH)
- Paclitaxel + Trastuzumab\*

## Breast Cancer: Adjuvant (Residual Disease Post-Neoadjuvant Treatment)

### TRIPLE NEGATIVE BREAST CANCER:

- Capecitabine
- Pembrolizumab (continuation in TNBC following Pembrolizumab + chemotherapy)

### HER2 POSITIVE:

- Ado-trastuzumab Emtansine (T-DM1)
- Trastuzumab

## Breast Cancer: Metastatic and Recurrent – Endocrine Therapy

### HER2 NEGATIVE:

#### 1st Line of Therapy

- Anastrozole + Abemaciclib
- Anastrozole + Palbociclib
- Exemestane + Abemaciclib
- Exemestane + Palbociclib
- Fulvestrant + Anastrozole
- Fulvestrant + Letrozole
- Letrozole + Abemaciclib
- Letrozole + Palbociclib

#### 1st + Subsequent Lines of Therapy

- Anastrozole
- Exemestane
- Fulvestrant
- Letrozole
- Tamoxifen

#### 2nd + Subsequent Lines of Therapy

- Anastrozole
- Exemestane
- Fulvestrant
- Fulvestrant + Abemaciclib
- Fulvestrant + Palbociclib
- Letrozole
- Tamoxifen

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**HER2 POSITIVE:**

- Anastrozole + Lapatinib
- Anastrozole + Trastuzumab\*
- Exemestane + Lapatinib
- Exemestane + Trastuzumab\*
- Letrozole + Lapatinib
- Letrozole + Trastuzumab\*

## Breast Cancer: Metastatic and Recurrent – Chemotherapy

### HER2 NEGATIVE:

#### 1st + Subsequent Lines of Therapy

- Capecitabine
- Carboplatin (Germline BRCA 1/2 mutation positive and TNBC)
- Cisplatin (Germline BRCA 1/2 mutation positive and TNBC)
- Docetaxel
- Doxorubicin
- Gemcitabine
- Olaparib (Germline BRCA 1/2 mutation positive)
- Paclitaxel
- Pembrolizumab + Gemcitabine + Carboplatin (mTNBC and PD-L1 expression threshold for positivity combined positive score  $\geq 10$ )
- Pembrolizumab + Paclitaxel (mTNBC and PD-L1 expression threshold for positivity combined positive score  $\geq 10$ )
- Sacituzumab Govitecan-hziy (HR+, HER2-)
- Vinorelbine

#### 2nd + Subsequent Lines of Therapy

- Fam-trastuzumab deruxtecan-nxki (for HER2 IHC 1+ or 2+ and ISH negative, who have received at least 1 prior line of chemotherapy for metastatic disease and, if tumor is HR+, are refractory to endocrine therapy)

#### 3rd + Subsequent Lines of Therapy

- Sacituzumab Govitecan-hziy (mTNBC and after 2 prior therapies for metastatic disease)

### HER2 POSITIVE:

#### 1st Line of Therapy

- Docetaxel + Trastuzumab\* + Pertuzumab
- Paclitaxel + Trastuzumab\* + Pertuzumab

#### 2nd + Subsequent Lines of therapy

- Ado-Trastuzumab Emtansine (T-DM1)
- Fam-trastuzumab deruxtecan-nxki
- Tucatinib + Trastuzumab\* + Capecitabine (in patients with brain mets)

#### 3rd + Subsequent Lines of therapy

- Capecitabine + Lapatinib
- Capecitabine + Trastuzumab\*
- Gemcitabine + Trastuzumab\*
- Paclitaxel + Trastuzumab\*
- Tucatinib + Trastuzumab\* + Capecitabine
- Vinorelbine + Trastuzumab\*

\* Kanjinti® and Trazimera® are the preferred medications for UnitedHealthcare commercial plans. Kanjinti is preferred for UnitedHealthcare Community Plan in most markets. Kanjinti, Trazimera and trastuzumab are preferred for UnitedHealthcare® Medicare Advantage plan.

## Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)

### 1st line of therapy

- Acalabrutinib
- Bendamustine + Rituximab\* (without del(17p)/TP53 mutation)
- Ibrutinib
- Venetoclax + Obinutuzumab

### 2nd + Subsequent lines of therapy

- Acalabrutinib
- Bendamustine + Rituximab\* (without del(17p)/TP53 mutation)
- Ibrutinib
- Venetoclax + Rituximab\*

\*Truxima and Ruxience are the preferred products for most UnitedHealthcare Community Plans and UnitedHealthcare commercial plans. Truxima, Ruxience and rituximab are preferred for UnitedHealthcare Medicare Advantage plan.

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## **Chronic Myeloid Leukemia (CML)**

### **1st line of therapy**

- Imatinib

### **2nd + Subsequent lines of therapy**

- Imatinib
- Nilotinib
- Ponatinib (T315I mutation only)

### **3rd + Subsequent lines of therapy**

- Asciminib (without T315I mutation only)



## Colon/Rectal Cancer: Adjuvant

- Capecitabine + Oxaliplatin (CAPEOX)
- Fluorouracil (5-FU)/Leucovorin
- Fluorouracil + Leucovorin + Oxaliplatin (FOLFOX)

## Colon/Rectal Cancer: Metastatic KRAS/NRAS: Unknown/Mutant 1st and 2nd Lines of Therapy

- Capecitabine
- Fluorouracil + Leucovorin + Irinotecan (FOLFIRI) +/- Bevacizumab\*
- Fluorouracil + Leucovorin + Oxaliplatin (FOLFOX) +/- Bevacizumab\*
- Fluorouracil + Leucovorin +/- Bevacizumab\*

## Colon/Rectal Cancer: Metastatic KRAS/NRAS: Wild Type 1st + Subsequent Lines of therapy

- Capecitabine
- Fluorouracil + Leucovorin + Irinotecan (FOLFIRI) + Cetuximab
- Fluorouracil + Leucovorin + Irinotecan (FOLFIRI) + Panitumumab
- Fluorouracil + Leucovorin + Irinotecan (FOLFIRI) +/- Bevacizumab\*
- Fluorouracil + Leucovorin + Oxaliplatin (FOLFOX) + Cetuximab
- Fluorouracil + Leucovorin + Oxaliplatin (FOLFOX) + Panitumumab
- Fluorouracil + Leucovorin + Oxaliplatin (FOLFOX) +/- Bevacizumab\*
- Fluorouracil + Leucovorin +/- Bevacizumab\*

## 2nd + Subsequent Lines of Therapy

- Encorafenib + Cetuximab (BRAF V600E mutation positive)
- Encorafenib + Panitumumab (BRAF V600E mutation positive)

## 3rd + Subsequent Lines of Therapy

- Trifluridine + Tipiracil + Bevacizumab\*

\* Mvasi® is the preferred medication for most UnitedHealthcare Community Plans and UnitedHealthcare commercial plans. Mvasi and bevacizumab are preferred for UnitedHealthcare Medicare Advantage plan.

## Colon/Rectal Cancer: Metastatic MSI-H/dMMR

### 1st Line of Therapy

- Pembrolizumab

### 2nd + Subsequent Lines of Therapy

- Capecitabine
- Encorafenib + Cetuximab (BRAF V600E mutation positive)
- Encorafenib + Panitumumab (BRAF V600E mutation positive)
- Fluorouracil + Leucovorin + Irinotecan (FOLFIRI) + Cetuximab
- Fluorouracil + Leucovorin + Irinotecan (FOLFIRI) + Panitumumab
- Fluorouracil + Leucovorin + Irinotecan (FOLFIRI) +/- Bevacizumab\*
- Fluorouracil + Leucovorin + Oxaliplatin (FOLFOX) + Cetuximab
- Fluorouracil + Leucovorin + Oxaliplatin (FOLFOX) + Panitumumab
- Fluorouracil + Leucovorin + Oxaliplatin (FOLFOX) +/- Bevacizumab\*
- Fluorouracil + Leucovorin +/- Bevacizumab\*

### 3rd + Subsequent Lines of Therapy

- Trifluridine + Tipiracil + Bevacizumab\*

## **Endometrial Carcinoma: Adjuvant**

- Carboplatin + Paclitaxel
- Carboplatin + Paclitaxel + Dostarlimab-gxly (stage III-IV tumors)

## **Endometrial Carcinoma: Metastatic or Recurrent**

### **1st Line of Therapy**

- Carboplatin + Paclitaxel
- Carboplatin + Paclitaxel + Dostarlimab-gxly (for patients who are ICI naïve)
- Carboplatin + Paclitaxel + Trastuzumab (for stage III/IV or recurrent HER2-positive uterine serous carcinoma only)
- Lenvatinib + Pembrolizumab (for pMMR tumors after prior platinum-based therapy, including neoadjuvant and adjuvant)

### **2nd + Subsequent Lines of Therapy**

- Docetaxel
- Doxorubicin
- Lenvatinib + Pembrolizumab (for pMMR tumors after prior platinum-based therapy, including neoadjuvant and adjuvant)
- Liposomal Doxorubicin
- Paclitaxel

## Esophageal and Esophagogastric Cancers

### Preoperative or Definitive chemoradiotherapy

- Capecitabine + Cisplatin + Radiotherapy
- Capecitabine + Oxaliplatin + Radiotherapy
- Fluorouracil ± Leucovorin + Cisplatin + Radiotherapy
- Fluorouracil ± Leucovorin + Oxaliplatin + Radiotherapy
- Paclitaxel + Carboplatin + Radiotherapy

### Perioperative

- Capecitabine + Cisplatin
- Capecitabine + Oxaliplatin
- Fluorouracil + Leucovorin + Oxaliplatin + Docetaxel (FLOT)
- Fluorouracil ± Leucovorin + Cisplatin
- Fluorouracil ± Leucovorin + Oxaliplatin

### Recurrent/Metastatic/Unresectable locally advanced disease; 1st line of therapy

#### HER2-negative or Unknown

- Capecitabine + Cisplatin
- Capecitabine + Cisplatin + Nivolumab (squamous cell carcinoma and CPS ≥ 1)
- Capecitabine + Cisplatin + Pembrolizumab (PD-L1 CPS ≥ 10)
- Capecitabine + Oxaliplatin
- Capecitabine + Oxaliplatin + Nivolumab (for adenocarcinoma and PD-L1 CPS ≥ 5 or squamous cell carcinoma)
- Capecitabine + Oxaliplatin + Pembrolizumab (PD-L1 CPS ≥ 10)
- Fluorouracil ± Leucovorin + Cisplatin
- Fluorouracil ± Leucovorin + Cisplatin + Nivolumab (squamous cell carcinoma and CPS ≥ 1)
- Fluorouracil ± Leucovorin + Cisplatin + Pembrolizumab (PD-L1 CPS ≥ 10)
- Fluorouracil ± Leucovorin + Oxaliplatin
- Fluorouracil ± Leucovorin + Oxaliplatin + Nivolumab (for adenocarcinoma and PD-L1 CPS ≥ 5 or squamous cell carcinoma)
- Fluorouracil ± Leucovorin + Oxaliplatin + Pembrolizumab (PD-L1 CPS ≥ 10)

#### HER2-positive

- Capecitabine + Cisplatin + Trastuzumab
- Capecitabine + Oxaliplatin + Trastuzumab
- Capecitabine + Cisplatin + Trastuzumab + Pembrolizumab (CPS ≥ 1)
- Capecitabine + Oxaliplatin + Trastuzumab + Pembrolizumab (CPS ≥ 1)
- Fluorouracil ± Leucovorin + Cisplatin + Trastuzumab
- Fluorouracil ± Leucovorin + Oxaliplatin + Trastuzumab
- Fluorouracil ± Leucovorin + Cisplatin + Trastuzumab + Pembrolizumab (CPS ≥ 1)
- Fluorouracil ± Leucovorin + Oxaliplatin + Trastuzumab + Pembrolizumab (CPS ≥ 1)

**Recurrent/Metastatic/Unresectable locally advanced disease; 2nd + subsequent lines of therapy**

- Docetaxel
- Fam-trastuzumab deruxtecan-nxki (for HER2-positive adenocarcinoma only)
- Irinotecan
- Paclitaxel
- Paclitaxel + Ramucirumab (for adenocarcinoma)

## Gastric Cancer

### Perioperative

- Capecitabine + Cisplatin
- Capecitabine + Oxaliplatin
- Fluorouracil + Leucovorin + Oxaliplatin + Docetaxel (FLOT)
- Fluorouracil ± Leucovorin + Cisplatin
- Fluorouracil ± Leucovorin + Oxaliplatin

### Postoperative chemotherapy or chemoradiotherapy

- Capecitabine + Oxaliplatin
- Capecitabine ± Radiotherapy
- Fluorouracil ± Radiotherapy

### Recurrent/Metastatic/Unresectable locally advanced disease; 1st line of therapy

#### HER2-negative or Unknown

- Capecitabine + Cisplatin
- Capecitabine + Cisplatin + Pembrolizumab (PD-L1 CPS ≥ 10)
- Capecitabine + Oxaliplatin
- Capecitabine + Oxaliplatin + Nivolumab (for PD-L1 CPS ≥ 5)
- Capecitabine + Oxaliplatin + Pembrolizumab (PD-L1 CPS ≥ 10)
- Fluorouracil ± Leucovorin + Cisplatin
- Fluorouracil ± Leucovorin + Cisplatin + Pembrolizumab (PD-L1 CPS ≥ 10)
- Fluorouracil ± Leucovorin + Oxaliplatin
- Fluorouracil ± Leucovorin + Oxaliplatin + Nivolumab (for PD-L1 CPS ≥ 5)
- Fluorouracil ± Leucovorin + Oxaliplatin + Pembrolizumab (PD-L1 CPS ≥ 10)

#### HER2-positive

- Capecitabine + Cisplatin + Trastuzumab
- Capecitabine + Cisplatin + Trastuzumab + Pembrolizumab (CPS ≥ 1)
- Capecitabine + Oxaliplatin + Trastuzumab
- Capecitabine + Oxaliplatin + Trastuzumab + Pembrolizumab (CPS ≥ 1)
- Fluorouracil ± Leucovorin + Cisplatin + Trastuzumab
- Fluorouracil ± Leucovorin + Cisplatin + Trastuzumab + Pembrolizumab (CPS ≥ 1)
- Fluorouracil ± Leucovorin + Oxaliplatin + Trastuzumab
- Fluorouracil ± Leucovorin + Oxaliplatin + Trastuzumab + Pembrolizumab (CPS ≥ 1)

**Recurrent/Metastatic/Unresectable locally advanced disease; 2nd + subsequent lines of therapy**

- Docetaxel
- Fam-trastuzumab deruxtecan-nxki (for HER2-positive adenocarcinoma only)
- Irinotecan
- Paclitaxel
- Paclitaxel + Ramucirumab (for adenocarcinoma)

## Head and Neck Cancer: Primary Definitive Therapy

### Non-Nasopharyngeal

- Cisplatin + Concurrent Radiation Therapy

### Nasopharyngeal

- Cisplatin + Concurrent Radiation Therapy
- Cisplatin + Gemcitabine

## Head and Neck Cancer: Adjuvant Therapy

### Non-Nasopharyngeal

- Cisplatin + Concurrent Radiation Therapy

### Nasopharyngeal

- Carboplatin + Fluorouracil (5FU)
- Cisplatin + Fluorouracil (5FU)

## Head and Neck Cancer: Recurrent/Metastatic/Unresectable

### Non-Nasopharyngeal: 1st Line of Therapy

- Carboplatin + Paclitaxel + Pembrolizumab (for combined positive score (CPS)  $\geq 1$  only)
- Cisplatin + Fluorouracil (5FU)
- Cisplatin or Carboplatin + Docetaxel
- Cisplatin or Carboplatin + Fluorouracil (5FU) + Cetuximab
- Cisplatin or Carboplatin + Fluorouracil (5FU) + Pembrolizumab (for combined positive score (CPS)  $\geq 1$  only)
- Cisplatin or Carboplatin + Paclitaxel
- Pembrolizumab (for combined positive score (CPS)  $\geq 1$  only)

### Non-Nasopharyngeal: Maintenance

- Cetuximab
- Pembrolizumab (for combined positive score (CPS)  $\geq 1$  only)

### Non-Nasopharyngeal: 2nd + Subsequent Lines of Therapy

- Cisplatin + Fluorouracil (5FU)
- Cisplatin or Carboplatin + Docetaxel
- Cisplatin or Carboplatin + Fluorouracil (5FU) + Cetuximab
- Cisplatin or Carboplatin + Paclitaxel
- Nivolumab (if IO not used previously)
- Pembrolizumab (if IO not used previously)

### Nasopharyngeal: 1st Line of Therapy

- Cisplatin + Gemcitabine
- Cisplatin + Gemcitabine + Toripalimab-tpzi



## Hepatobiliary cancer

### Hepatocellular Carcinoma: Unresectable, Not a Transplant Candidate, Metastatic Disease, Inoperable by PS or Comorbidity

#### 1st Line of Therapy

- Atezolizumab + Bevacizumab\*
- Durvalumab
- Tremelimumab-actl + Durvalumab

#### 2nd + Subsequent Lines of Therapy

- Cabozantinib
- Lenvatinib
- Regorafenib
- Sorafenib

### Biliary Tract Cancers (Gallbladder, Intrahepatic and Extrahepatic Cholangiocarcinoma): Adjuvant Therapy

- Capecitabine

### Biliary Tract Cancers (Gallbladder, Intrahepatic and Extrahepatic Cholangiocarcinoma): Unresectable/Metastatic

#### 1st Line of Therapy

- Gemcitabine + Cisplatin

#### 2nd + Subsequent Lines of Therapy

- Fluorouracil/Leucovorin + Oxaliplatin (FOLFOX)
- Ivosidenib (in IDH1 Mutation Cholangiocarcinoma)

\* Mvasi is the preferred medication for most UnitedHealthcare Community Plans and UnitedHealthcare commercial plans. Mvasi and bevacizumab are preferred for UnitedHealthcare Medicare Advantage plan.

## **Kidney Cancer**

### **Adjuvant**

- Pembrolizumab

### **Relapsed or Metastatic (Clear Cell): 1st Line of Therapy**

- Axitinib + Avelumab
- Axitinib + Pembrolizumab
- Cabozantinib + Nivolumab
- Lenvatinib + Pembrolizumab
- Ipilimumab + Nivolumab

### **Relapsed or Metastatic (Clear Cell): 2nd + Subsequent lines of therapy**

- Axitinib
- Cabozantinib
- Nivolumab (if immune checkpoint inhibitor not received previously)
- Pazopanib
- Sunitinib
- Tivozanib (who received  $\geq 2$  prior systemic therapies)

## **Lung Cancer, Non-Small Cell: Neoadjuvant/Adjuvant**

### **Nonsquamous**

- Alectinib (ALK rearrangement positive; adjuvant only)
- Carboplatin + Paclitaxel ± Concurrent Radiation Therapy (RT)
- Carboplatin + Pemetrexed ± Concurrent Radiation Therapy (RT)
- Cisplatin + Etoposide + Concurrent Radiation Therapy (RT)
- Cisplatin + Pemetrexed ± Concurrent Radiation Therapy (RT)
- Cisplatin + Vinorelbine
- Nivolumab + Carboplatin or Cisplatin + Paclitaxel (Neoadjuvant only)
- Nivolumab + Carboplatin or Cisplatin + Pemetrexed (Neoadjuvant only)
- Osimertinib (in completely resected stage IB - IIIA EGFR [exon 19del, L858R] directly following completion of adjuvant chemotherapy or are ineligible to receive platinum-based chemotherapy)

### **Squamous**

- Alectinib (ALK rearrangement positive; adjuvant only)
- Carboplatin + Paclitaxel ± Concurrent Radiation Therapy (RT)
- Cisplatin + Etoposide + Concurrent Radiation Therapy (RT)
- Cisplatin + Vinorelbine
- Nivolumab + Carboplatin or Cisplatin + Gemcitabine (Neoadjuvant only)
- Nivolumab + Carboplatin or Cisplatin + Paclitaxel (Neoadjuvant only)
- Osimertinib (in completely resected stage IB - IIIA EGFR [exon 19del, L858R] directly following completion of adjuvant chemotherapy or are ineligible to receive platinum-based chemotherapy)

## **Lung Cancer, Non-Small Cell: Consolidation: Stage III Unresectable, No Progression and PS 0-1**

- Durvalumab

## **Lung Cancer, Non-Small Cell: Advanced/Metastatic: EGFR exon 19 deletion, L858R, S768I, L861Q, and/or G719X Mutation Positive**

### **1st + Subsequent Lines of Therapy**

- Dacomitinib
- Osimertinib

## **Lung Cancer, Non-Small Cell: Advanced/Metastatic: ALK Rearrangement Positive**

### **1st + Subsequent Lines of Therapy**

- Alectinib
- Brigatinib

## **Lung Cancer, Non-Small Cell: Advanced/Metastatic (Excluding EGFR, ALK, RET, ROS1 and/or MET genomic aberration)**

### **Nonsquamous: 1st Line of Therapy**

- Atezolizumab (PD-L1  $\geq$  50% only)
- Carboplatin/Cisplatin + Paclitaxel (Immunotherapy ineligible)
- Carboplatin/Cisplatin + Pemetrexed (Immunotherapy ineligible)
- Carboplatin/Cisplatin + Pemetrexed + Pembrolizumab (PD-L1: < 1%, 1-49% and  $\geq$  50%)
- Carboplatin/Cisplatin + Pemetrexed/Paclitaxel + Cemiplimab-rwlc (PD-L1: < 1%, 1 - 49%, and  $\geq$  50%)
- Cemiplimab-rwlc (PD-L1  $\geq$  50% only)
- Pembrolizumab Single Agent (PD-L1  $\geq$  50% only)

### **Nonsquamous: Maintenance**

- Cemiplimab-rwlc  $\pm$  Pemetrexed
- Pembrolizumab
- Pembrolizumab + Pemetrexed
- Pemetrexed

### **Nonsquamous: 2nd + Subsequent Lines of Therapy**

- Docetaxel
- Gemcitabine
- Pemetrexed

### **Squamous: 1st Line of Therapy**

- Atezolizumab (PD-L1  $\geq$  50% only)
- Carboplatin + Paclitaxel + Cemiplimab-rwlc (PD-L1: < 1%, 1 - 49%, and  $\geq$  50%)
- Carboplatin + Paclitaxel + Pembrolizumab (PD-L1: < 1%, 1-49% and  $\geq$  50%)
- Carboplatin/Cisplatin + Gemcitabine (Immunotherapy ineligible)
- Carboplatin/Cisplatin + Paclitaxel (Immunotherapy ineligible)
- Cemiplimab-rwlc (PD-L1  $\geq$  50% only)
- Pembrolizumab Single Agent (PD-L1  $\geq$  50% only)

### **Squamous: Maintenance**

- Cemiplimab-rwlc
- Pembrolizumab

### **Squamous: 2nd + Subsequent Lines of Therapy**

- Docetaxel
- Gemcitabine

### **Lung Cancer, Small Cell: Limited Stage – Adjuvant or Primary Therapy**

- Carboplatin + Etoposide
- Cisplatin + Etoposide
- Durvalumab

### **Lung Cancer, Small Cell: Extensive Stage – Adjuvant or Primary Therapy**

- Carboplatin + Etoposide
- Carboplatin + Etoposide + Atezolizumab
- Carboplatin + Etoposide + Durvalumab
- Cisplatin + Etoposide
- Cisplatin + Etoposide + Durvalumab

### **Lung Cancer, Small Cell: Extensive Stage – Adjuvant or Primary Therapy – Maintenance**

- Atezolizumab
- Durvalumab

### **Lung Cancer, Small Cell: Subsequent Therapy: Relapse $\leq$ 6 months**

- Irinotecan
- Paclitaxel
- Topotecan IV

### **Lung Cancer, Small Cell: Subsequent Therapy: Relapse $>$ 6 months**

- Carboplatin + Etoposide
- Cisplatin + Etoposide
- Irinotecan
- Topotecan IV

## **Lymphoma, Classic Hodgkin (cHL)**

### **1st Line of Therapy**

- Doxorubicin + Bleomycin + Vinblastine + Dacarbazine (ABVD)
- Doxorubicin + Vinblastine + Dacarbazine (AVD)
- Escalated bleomycin + etoposide + doxorubicin + cyclophosphamide + vincristine + procarbazine + prednisone (escBEACOPP)

## Lymphoma, Diffuse Large B-Cell\*

### 1st Line of Therapy

- Rituximab\*\*–CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone)
- Rituximab\*\*–DA-EPOCH (Etoposide, Prednisone, Vincristine, Cyclophosphamide, Doxorubicin) (For Primary Mediastinal B-Cell Lymphoma (PMBCL) only)
- Rituximab\*\*–mini-CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone)

### 2nd + Subsequent Lines of Therapy

- Rituximab\*\* ± DHAP (Dexamethasone, Cisplatin, Cytarabine)
- Rituximab\*\* ± GDP (Gemcitabine, Dexamethasone, Cisplatin or Carboplatin)
- Rituximab\*\* ± ICE (Ifosfamide, Carboplatin, Etoposide)

## Lymphoma, Diffuse Large B-Cell With Translocations of MYC and BCL2 and/or BCL6 (Double-/Triple-Hit Lymphoma)\*

- Rituximab\*\*–DA-EPOCH (Etoposide, Prednisone, Vincristine, Cyclophosphamide, Doxorubicin)

\* Therapies that are administered at Centers of Excellence, including stem cell transplant or CAR T-cell therapy, are not included in our pathways. Patients eligible for transplant or CAR T-cell therapy should be referred appropriately for evaluation.

\*\* Truxima and Ruxience are the preferred products for most UnitedHealthcare Community Plans and UnitedHealthcare commercial plans. Truxima, Ruxience and rituximab are preferred for UnitedHealthcare Medicare Advantage plan.



## **Lymphoma, Follicular (Grade 1-2)\***

### **1st Line of Therapy**

- Bendamustine + Rituximab\*\* (BR)
- Rituximab\*\* (weekly for 4 doses)

### **2nd + Subsequent Lines of Therapy (Non-Refractory Disease)**

- Bendamustine + Rituximab\*\* (BR)
- CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone) + Rituximab\*\*
- CVP (Cyclophosphamide, Vincristine, Prednisone) + Rituximab\*\*
- Rituximab\*\*

### **2nd + Subsequent Lines of Therapy (Refractory Disease)**

- Bendamustine + Obinutuzumab
- Bendamustine + Rituximab\*\* (BR)
- CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone) + Rituximab\*\*
- CVP (Cyclophosphamide, Vincristine, Prednisone) + Rituximab\*\*
- Rituximab\*\*

## **Lymphoma, High-Grade Follicular (Grade 3)\*\***

### **1st Line of Therapy**

- Rituximab\*\*-CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone)

### **2nd + Subsequent Lines of Therapy**

- Rituximab\*\* ± GDP (Gemcitabine, Dexamethasone, Cisplatin or Carboplatin)
- Rituximab\*\* ± ICE (Ifosfamide, Carboplatin, Etoposide)
- Rituximab\*\* ± DHAP (Dexamethasone, Cisplatin, cytarabine)

\* Therapies that are administered at Centers of Excellence, including stem cell transplant or CAR T-cell therapy, are not included in our pathways. Patients eligible for transplant or CAR T-cell therapy should be referred appropriately for evaluation.

\*\* Truxima and Ruxience are the preferred products for most UnitedHealthcare Community Plans and UnitedHealthcare commercial plans. Truxima, Ruxience and rituximab are preferred for UnitedHealthcare Medicare Advantage plan.

## **Lymphoma, Mantle Cell\***

### **1st Line of Therapy**

- Bendamustine + Rituximab\*\*
- Hyper-CVAD (Cyclophosphamide, Vincristine, Doxorubicin and Dexamethasone Alternating With High-Dose Methotrexate and Cytarabine) + Rituximab\*\*
- Nordic Regimen (Dose-Intensified Induction Immunochemotherapy With Rituximab + Cyclophosphamide, Vincristine, Doxorubicin, Prednisone [Maxi-CHOP]) Alternating With Rituximab + High-Dose Cytarabine
- VR-CAP (Bortezomib, Rituximab, Cyclophosphamide, Doxorubicin and Prednisone)\*\*

### **Maintenance After 1st Line of Therapy**

- Rituximab\*\* (after HDT/ASCR only)

### **2nd Line of Therapy**

- Acalabrutinib
- Bendamustine + Rituximab\*\* (BR)
- Ibrutinib
- Zanubrutinib

### **3rd + Subsequent Lines of Therapy**

- Acalabrutinib
- Bendamustine + Rituximab\*\* (BR)
- Ibrutinib
- Lenalidomide
- Zanubrutinib

\*Therapies that are administered at Centers of Excellence, including stem cell transplant or CAR T-cell therapy, are not included in our pathways. Patients eligible for transplant or CAR T-cell therapy should be referred appropriately for evaluation.

\*\*Truxima and Ruxience are the preferred products for most UnitedHealthcare Community Plans and UnitedHealthcare commercial plans. Truxima, Ruxience and rituximab are preferred for UnitedHealthcare Medicare Advantage plan.

## Lymphoma, Marginal Zone\*

### 1st Line of Therapy

- Bendamustine + Rituximab\*\* (BR)
- Helicobacter Pylori (H. pylori) Eradication Therapy (Gastric MALT Lymphoma only)
- Rituximab (weekly for 4 doses)

### 2nd + Subsequent Lines of Therapy (Non-Refractory Disease)

- Bendamustine + Rituximab\*\* (BR)
- Chlorambucil ± Rituximab\*\*
- CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone) + Rituximab\*\*
- CVP (Cyclophosphamide, Vincristine, Prednisone) + Rituximab\*\*
- Rituximab (weekly for 4 doses)

### 2nd + Subsequent Lines of Therapy (Refractory Disease)

- Bendamustine + Obinutuzumab
- Bendamustine + Rituximab\*\* (BR)
- Chlorambucil ± Rituximab\*\*
- CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone) + Rituximab\*\*
- CVP (Cyclophosphamide, Vincristine, Prednisone) + Rituximab\*\*
- Rituximab (weekly for 4 doses)

## Lymphoma, High-Grade Marginal Zone (Grade 3)\*\*

### 1st Line of Therapy

- Rituximab\*\*-CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone)

### 2nd + Subsequent Lines of Therapy

- Rituximab\*\* ± DHAP (Dexamethasone, Cisplatin, Cytarabine)
- Rituximab\*\* ± GDP (Gemcitabine, Dexamethasone, Cisplatin or Carboplatin)
- Rituximab\*\* ± ICE (Ifosfamide, Carboplatin, Etoposide)

\*Therapies that are administered at Centers of Excellence, including stem cell transplant or CAR T-cell therapy, are not included in our pathways. Patients eligible for transplant or CAR T-cell therapy should be referred appropriately for evaluation.

\*\*Truxima and Ruxience are the preferred products for most UnitedHealthcare Community Plans and UnitedHealthcare commercial plans. Truxima, Ruxience and rituximab are preferred for UnitedHealthcare Medicare Advantage plan.

### **Melanoma: Neoadjuvant (Resectable; Stage III)**

- Nivolumab + Ipilimumab (2 cycles)

### **Melanoma: Adjuvant (Resectable; Stage III)**

- Nivolumab
- Pembrolizumab

### **Melanoma: Adjuvant (Resectable; Stage III)- (BRAF Mutated)**

- Dabrafenib + Trametinib
- Nivolumab
- Pembrolizumab

### **Melanoma: Metastatic/Unresectable (BRAF Mutated/Symptomatic)**

- Dabrafenib + Trametinib
- Vemurafenib + Cobimetinib

### **Melanoma: Metastatic/Unresectable (BRAF Wild Type/Mutated/Unknown)**

#### **1st + Subsequent Lines of Therapy**

- Nivolumab
- Nivolumab + Ipilimumab
- Pembrolizumab

## Multiple Myeloma: Primary Therapy\*

### Transplant Eligible

- Bortezomib + Cyclophosphamide + Dexamethasone (CyBorD or VCD)
- Bortezomib + Lenalidomide + Dexamethasone (VRD)
- Daratumumab + Bortezomib + Lenalidomide + Dexamethasone (D-VRD)

### Transplant Ineligible

- Bortezomib + Cyclophosphamide + Dexamethasone (CyBorD or VCD)
- Bortezomib + Lenalidomide + Dexamethasone (VRD)

## Multiple Myeloma: Maintenance Therapy\*

### Transplant Eligible or Ineligible

- Bortezomib
- Lenalidomide

## Multiple Myeloma: Relapsed or Refractory\*

### 1st Relapse

- Bortezomib + Cyclophosphamide + Dexamethasone (CyBorD or VCD)
- Bortezomib + Lenalidomide + Dexamethasone (VRD)
- Daratumumab + Bortezomib + Dexamethasone (DVD)
- Daratumumab + Lenalidomide + Dexamethasone (DRD)

### 2nd Relapse

- Bortezomib + Cyclophosphamide + Dexamethasone (CyBorD or VCD)
- Bortezomib + Lenalidomide + Dexamethasone (VRD)
- Carfilzomib + Lenalidomide + Dexamethasone (KRD)
- Daratumumab + Bortezomib + Dexamethasone (DVD)
- Daratumumab + Lenalidomide + Dexamethasone (DRD)
- Daratumumab + Pomalidomide + Dexamethasone (DPD)
- Elotuzumab + Pomalidomide + Dexamethasone (EPD)
- Isatuximab-irfc + Pomalidomide + Dexamethasone (Isa-PD)
- Pomalidomide + Bortezomib + Dexamethasone (PVD)

\*Therapies that are administered at Centers of Excellence, including stem cell transplant or CAR T-cell therapy, are not included in our pathways. Patients eligible for transplant or CAR T-cell therapy should be referred appropriately for evaluation.

## **Ovarian, Fallopian and Primary Peritoneal Cancer: Neoadjuvant Therapy**

- Carboplatin + Paclitaxel\*

## **Ovarian, Fallopian and Primary Peritoneal Cancer: Adjuvant or Primary Therapy**

- Carboplatin + Paclitaxel\*

## **Ovarian, Fallopian and Primary Peritoneal Cancer: Maintenance Therapy After Primary Therapy**

- Niraparib
- Olaparib (Germline/Somatic BRCA Mutation only)

## **Ovarian, Fallopian and Primary Peritoneal Cancer: Platinum – Sensitive Recurrent Disease**

### **1st + Subsequent Lines of Therapy**

- Carboplatin + Gemcitabine
- Carboplatin + Liposomal Doxorubicin
- Carboplatin + Paclitaxel

### **Maintenance Therapy**

- Niraparib
- Olaparib

## **Ovarian, Fallopian and Primary Peritoneal Cancer: Platinum – Resistant Recurrent Disease**

### **1st + Subsequent Lines of Therapy**

- Gemcitabine
- Liposomal Doxorubicin
- Liposomal Doxorubicin + Bevacizumab\*\*
- Mirvetuximab soravtansine-gynx (FR $\alpha$  expressing tumors,  $\geq$ 75% positive tumor cells)
- Paclitaxel (weekly)
- Paclitaxel (weekly) + Bevacizumab\*\*
- Tamoxifen

\* Only intravenous carboplatin + paclitaxel are pathway regimens.

\*\* Mvasi® is the preferred medication for most UnitedHealthcare Community Plans and UnitedHealthcare commercial plans. Mvasi and bevacizumab are preferred for UnitedHealthcare Medicare Advantage plan.

## **Pancreatic Cancer: Neoadjuvant (Resectable/Borderline Resectable)**

- Fluorouracil/Leucovorin + Oxaliplatin + Irinotecan (FOLFIRINOX/mFOLFIRINOX)
- Gemcitabine + Albumin-Bound Paclitaxel (G-nP)

## **Pancreatic Cancer: Adjuvant (Resectable)**

Pancreatic Cancer: Adjuvant (Resectable)

- Fluorouracil/Leucovorin + Oxaliplatin + Irinotecan (mFOLFIRINOX)
- Gemcitabine + Capecitabine
- Gemcitabine

## **Pancreatic Cancer: Locally Advanced/Metastatic**

### **1st Line of Therapy**

- Fluorouracil/Leucovorin + Oxaliplatin + Irinotecan (FOLFIRINOX/mFOLFIRINOX)
- Gemcitabine + Albumin-Bound Paclitaxel (G-nP)
- Gemcitabine

### **2nd + Subsequent Lines of Therapy**

- Gemcitabine + Albumin-Bound Paclitaxel (G-nP)
- Gemcitabine
- Fluorouracil/Leucovorin
- Fluorouracil/Leucovorin + Oxaliplatin (OFF)
- Fluorouracil/Leucovorin + Oxaliplatin (FOLFOX)
- Fluorouracil/Leucovorin + Irinotecan (FOLFIRI)
- Fluorouracil/Leucovorin + Oxaliplatin + Irinotecan (FOLFIRINOX/mFOLFIRINOX)

### **Maintenance**

- Capecitabine
- Fluorouracil/Leucovorin

## Prostate Cancer

### Adjuvant/Neoadjuvant; Castration-sensitive disease

- Goserelin
- Leuprolide
- Triptorelin

### Recurrent/Metastatic; Castration-sensitive disease

- Goserelin ± Abiraterone/Prednisone ± docetaxel
- Leuprolide ± Abiraterone/Prednisone ± docetaxel
- Triptorelin ± Abiraterone/Prednisone ± docetaxel

### Recurrent/Metastatic; Castration-resistant disease

- Goserelin + Cabazitaxel (after prior docetaxel therapy)
- Goserelin + Enzalutamide (after prior abiraterone therapy)
- Goserelin ± Abiraterone/Prednisone or docetaxel
- Leuprolide + Cabazitaxel (after prior docetaxel therapy)
- Leuprolide + Enzalutamide (after prior abiraterone therapy)
- Leuprolide ± Abiraterone/Prednisone or docetaxel
- Olaparib + abiraterone (BRCA1/2 mutations positive)
- Olaparib + abiraterone (Homologous recombination repair (HRR) mutations positive)
- Triptorelin + Cabazitaxel (after prior docetaxel therapy)
- Triptorelin + Enzalutamide (after prior abiraterone therapy)
- Triptorelin ± Abiraterone/Prednisone or docetaxel



## List of updates

Date	Changes
<b>July 1, 2020</b>	Added change control New pathways - Small Cell Lung Cancer and Hepatobiliary Cancer Updates to existing pathways <ul style="list-style-type: none"> <li>• Melanoma pathways:                             <ul style="list-style-type: none"> <li>- Removed “Stages IIIB and IIIC” from Adjuvant</li> </ul> </li> <li>• Colon pathways:                             <ul style="list-style-type: none"> <li>- Updated name to “Colon/Rectal” to reflect pathways for rectal cancer</li> <li>- Removed FOLFOX/FOLFIRI + Cetuximab regimen from Colon Cancer: Metastatic KRAS/ NRAS: Wild Type - 1st and 2nd Lines of Therapy</li> </ul> </li> </ul>
<b>Aug. 1, 2020</b>	New pathways - Ovarian Cancer
<b>Oct. 1, 2020</b>	New pathways - Non-Small-Cell Lung Cancer Updates to existing pathways <ul style="list-style-type: none"> <li>• Breast pathways:                             <ul style="list-style-type: none"> <li>- Added capecitabine + lapatinib to pathways for HER2 POSITIVE: 1st + Subsequent Lines of Therapy</li> </ul> </li> <li>• Pancreatic pathways:                             <ul style="list-style-type: none"> <li>- Added fluorouracil/leucovorin to Locally Advanced/Metastatic: 2nd + Subsequent Lines of Therapy</li> </ul> </li> <li>• Colon/Rectal pathways:                             <ul style="list-style-type: none"> <li>- Added capecitabine + oxaliplatin (CAPEOX) to pathways for Adjuvant</li> <li>- Added new category of pathways for Metastatic: MSI/dMMR: 1st + Subsequent Lines of Therapy</li> </ul> </li> </ul>
<b>Nov. 1, 2020</b>	New pathways - Head and Neck Cancer Updates to existing pathways <ul style="list-style-type: none"> <li>• Melanoma pathways:                             <ul style="list-style-type: none"> <li>- Removed Nivolumab single agent from Adjuvant and Metastatic/Unresectable</li> </ul> </li> </ul>
<b>Jan. 1, 2021</b>	New pathways - Multiple Myeloma
<b>March 1, 2021</b>	New pathways - Diffuse Large B-Cell Lymphoma Updates to existing pathways <ul style="list-style-type: none"> <li>• Hepatocellular Carcinoma:                             <ul style="list-style-type: none"> <li>- Added Atezolizumab + Bevacizumab regimen to pathways as 1st Line of Therapy and 2nd + Subsequent Lines of Therapy</li> <li>- Added Sorafenib or Lenvatinib to 2nd + Subsequent Lines of Therapy</li> </ul> </li> <li>• Biliary tract cancers:                             <ul style="list-style-type: none"> <li>- Added FOLFOX, Pemigatinib (in FGFR2 mutation cholangiocarcinoma), and Ivosidenib (in IDH1 mutation cholangiocarcinoma) to pathways as 2nd + subsequent lines of therapy</li> </ul> </li> </ul>

## List of updates

Date	Changes
<b>May 1, 2021</b>	New pathways – Follicular Lymphoma and Marginal Zone Lymphoma
<b>June 1, 2021</b>	New pathways – Mantle Cell Lymphoma Updates to existing pathways <ul style="list-style-type: none"> <li>• Follicular Lymphoma and Marginal Zone Lymphoma                             <ul style="list-style-type: none"> <li>- Added pathway options for refractory disease</li> </ul> </li> </ul>
<b>July 1, 2021</b>	Updates to existing pathways <ul style="list-style-type: none"> <li>• Mantle Cell Lymphoma                             <ul style="list-style-type: none"> <li>- Added pathway option for maintenance after first line of therapy</li> </ul> </li> </ul>
<b>Sept. 1, 2021</b>	Updates to existing pathways <ul style="list-style-type: none"> <li>• Ovarian Cancer                             <ul style="list-style-type: none"> <li>- Added carboplatin to pathways as Primary/Adjuvant Therapy</li> </ul> </li> <li>• Head and Neck Cancer                             <ul style="list-style-type: none"> <li>- Added “Cisplatin/Carboplatin + 5FU + Cetuximab → Cetuximab Maintenance (Extreme regimen),” “Cisplatin/Carboplatin + Docetaxel/Paclitaxel,” and “Cisplatin + 5FU” regimens to pathways as non-nasopharyngeal: recurrent/metastatic unresectable: 2nd + subsequent line of therapy</li> </ul> </li> </ul>
<b>Oct. 1, 2021</b>	New pathways – Bladder Cancer
<b>Dec. 1, 2021</b>	Updates to existing pathways <ul style="list-style-type: none"> <li>• Breast pathways:                             <ul style="list-style-type: none"> <li>- Added olaparib (for BRCA 1/2 mutation positive) to pathways for Neoadjuvant/Adjuvant</li> <li>- HER2 Negative</li> <li>- Added trastuzumab to pathways for Adjuvant (residual disease post-neoadjuvant therapy) - HER2 Positive</li> <li>- Removed atezolizumab + nab-paclitaxel (in PD-L1 Positive and metastatic TNBC) from pathways</li> </ul> </li> <li>• Pancreatic pathways:                             <ul style="list-style-type: none"> <li>- Added FOLFIRINOX/mFOLFIRINOX to pathways for locally advanced or metastatic – 2nd + Subsequent Lines of Therapy</li> </ul> </li> <li>• Colon/Rectal pathways:                             <ul style="list-style-type: none"> <li>- Added fluorouracil + leucovorin ± bevacizumab to pathways for metastatic disease</li> </ul> </li> <li>• Melanoma                             <ul style="list-style-type: none"> <li>- Added pembrolizumab to pathways for Adjuvant (Resectable): BRAF Mutated</li> </ul> </li> </ul>

## List of updates

Date	Changes
<b>March 1, 2022</b>	<p>Updates to existing pathways</p> <ul style="list-style-type: none"> <li>• Breast pathways:               <ul style="list-style-type: none"> <li>- Added pembrolizumab + paclitaxel (mTNBC and PD-L1 expression threshold for positivity combined positive score <math>\geq 10</math>) to pathways</li> <li>- Added pembrolizumab + gemcitabine + carboplatin (mTNBC and PD-L1 expression threshold for positivity combined positive score <math>\geq 10</math>) to pathways</li> <li>- Added sacituzumab govitecan-hziy (mTNBC and after 2 prior therapies for metastatic disease) to pathways</li> <li>- Added fam-trastuzumab deruxtecan-nxki to pathways for 2nd + Subsequent Lines of Therapy in HER2 Positive metastatic disease</li> </ul> </li> <li>• Multiple Myeloma               <ul style="list-style-type: none"> <li>- Removed Bortezomib + Thalidomide + Dexamethasone (VTD) from relapsed or refractory disease</li> <li>- Removed Carfilzomib + Pomalidomide + Dexamethasone (KPD) from relapsed or refractory disease: 2nd Line of Therapy</li> </ul> </li> <li>• Lymphoma, Diffuse Large B-Cell               <ul style="list-style-type: none"> <li>- Added rituximab*-mini-CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone) to pathways for 1st Line of Therapy</li> </ul> </li> <li>• Lymphoma, Follicular               <ul style="list-style-type: none"> <li>- Removed 3rd + Subsequent Lines of Therapy (refractory disease) category and changed “2nd Line of Therapy (refractory disease)” to “2nd + Subsequent Lines of Therapy (refractory disease)”</li> <li>- Removed Duvelisib, Idelalisib, Umbralisib from pathways</li> </ul> </li> <li>• Lymphoma, Marginal Zone               <ul style="list-style-type: none"> <li>- Removed 3rd + Subsequent Lines of Therapy (refractory disease) category and changed “2nd Line of Therapy (refractory disease)” to “2nd + Subsequent Lines of Therapy (refractory disease)”</li> <li>- Removed Duvelisib, Idelalisib, Umbralisib from pathways</li> </ul> </li> </ul>
<b>April 1, 2022</b>	<p>Updates to existing pathways</p> <ul style="list-style-type: none"> <li>• Multiple Myeloma               <ul style="list-style-type: none"> <li>- Removed Panobinostat + Bortezomib + Dexamethasone from relapsed or refractory disease</li> </ul> </li> <li>• Small Cell Lung Cancer               <ul style="list-style-type: none"> <li>- Added topotecan, paclitaxel, and irinotecan to pathways for subsequent line(s), relapse &gt; 6 months</li> </ul> </li> <li>• Non-Small Cell Lung Cancer               <ul style="list-style-type: none"> <li>- Removed pathways for advanced/metastatic, ROS1 rearrangement, MET Exon 14 skipping, BRAF V600E, RET rearrangement, and NTRK gene fusion</li> </ul> </li> </ul>

## List of updates

Date	Changes
<b>May 1, 2022</b>	Updates to existing pathways <ul style="list-style-type: none"> <li>• Hepatobiliary Tract Cancers                             <ul style="list-style-type: none"> <li>- Removed pemigatinib (for FGFR2 mutated cholangiocarcinoma)</li> </ul> </li> </ul>
<b>July 1, 2022</b>	New pathway - Hodgkin Lymphoma and Kidney Cancer
<b>Aug. 1, 2022</b>	New pathway - Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)
<b>Sept. 1, 2022</b>	New pathway - Uterine (Endometrial) Cancer
<b>Nov. 1, 2022</b>	Updates to existing pathways <ul style="list-style-type: none"> <li>• Breast Cancer                             <ul style="list-style-type: none"> <li>- Added Fam-trastuzumab deruxtecan-nxki to HER2 IHC 1+ or 2+/ISH negative metastatic or recurrent disease: 2nd + subsequent lines of therapy</li> <li>- Removed Talazoparib (Germline BRCA 1/2 Mutation Positive) from Metastatic and Recurrent - Chemotherapy, HER2 NEGATIVE: 1st + subsequent lines of therapy</li> </ul> </li> <li>• Bladder Cancer                             <ul style="list-style-type: none"> <li>- Removed Cisplatin + Methotrexate + Vinblastine (CMV) from Neoadjuvant/Adjuvant</li> </ul> </li> <li>• Colon/Rectal Cancer                             <ul style="list-style-type: none"> <li>- Added Fluorouracil + Leucovorin + Oxaliplatin (FOLFOX) + Cetuximab and Fluorouracil + Leucovorin + Irinotecan (FOLFIRI) + Cetuximab to Metastatic KRAS/NRAS: Wild Type: 1st and 2nd line of therapy and MSI-H/dMMR: 1st + subsequent lines of therapy</li> </ul> </li> <li>• Melanoma                             <ul style="list-style-type: none"> <li>- Added Nivolumab single agent to Adjuvant and Metastatic/Unresectable</li> <li>- Added Dabrafenib + Trametinib to Metastatic/Unresectable (BRAF Mutated/Symptomatic)</li> </ul> </li> </ul>
<b>Feb. 1, 2023</b>	New pathways - Chronic Myeloid Leukemia (CML), Esophageal and Esophagogastric Cancers, Gastric Cancer, and Prostate Cancer Updates to existing pathways <ul style="list-style-type: none"> <li>• Colon/Rectal Cancer                             <ul style="list-style-type: none"> <li>- Removed Fluorouracil + Leucovorin + Oxaliplatin (FOLFOX) + Cetuximab and Fluorouracil + Leucovorin + Irinotecan (FOLFIRI) + Cetuximab to Metastatic KRAS/NRAS: Wild Type: 1st and 2nd line of therapy and MSI-H/dMMR: 1st + subsequent lines therapy</li> </ul> </li> </ul>

## List of updates

Date	Changes
<b>May 1, 2023</b>	<p>Updates to existing pathways</p> <ul style="list-style-type: none"> <li>• Lung cancer                             <ul style="list-style-type: none"> <li>- Added Carboplatin/Cisplatin + Pemetrexed/Paclitaxel + Cemiplimab-rwlc (PD-L1: &lt; 1%, 1 - 49%, and ≥ 50%) to Advanced/Metastatic - Nonsquamous (EGFR, ALK, RET WT) - 1st line of therapy</li> <li>- Added Carboplatin + Paclitaxel + Cemiplimab-rwlc (PD-L1: &lt; 1%, 1 - 49%, and ≥ 50%) to Advanced/Metastatic - Squamous (EGFR, ALK, RET WT) - 1st line of therapy</li> <li>- Added Cemiplimab-rwlc ± Pemetrexed to Advanced/Metastatic - Nonsquamous (EGFR, ALK, RET WT) - Maintenance</li> <li>- Added Cemiplimab-rwlc to Advanced/Metastatic - Squamous (EGFR, ALK, RET WT) - Maintenance</li> </ul> </li> </ul>
<b>June 1, 2023</b>	<p>Updates to existing pathways</p> <ul style="list-style-type: none"> <li>• Hepatocellular carcinoma                             <ul style="list-style-type: none"> <li>- Added Tremelimumab-actl + Durvalumab and Durvalumab to Hepatocellular cancer - Unresectable &amp; not a transplant candidate, metastatic disease, inoperable by PS or comorbidity - 1st + line of therapy</li> </ul> </li> <li>• Biliary Tract Cancers                             <ul style="list-style-type: none"> <li>- Added Gemcitabine + Cisplatin + Durvalumab to Unresectable/Metastatic - 1st line of therapy</li> </ul> </li> </ul>
<b>Aug. 1, 2023</b>	<p>Updates to existing pathways</p> <ul style="list-style-type: none"> <li>• Breast Cancer                             <ul style="list-style-type: none"> <li>- Added cisplatin and carboplatin (Germline BRCA1/2 mutation positive and TNBC) to Breast cancer - Metastatic and Recurrent - Chemotherapy, HER2 NEGATIVE: 1st + Subsequent Lines of Therapy.</li> </ul> </li> <li>• Colon/Rectal Cancer                             <ul style="list-style-type: none"> <li>- Added Fluorouracil + Leucovorin + Oxaliplatin (FOLFOX) + Cetuximab and Fluorouracil + Leucovorin + Irinotecan (FOLFIRI) + Cetuximab to Metastatic KRAS/NRAS: Wild Type: 1st and 2nd line of therapy and MSI-H/dMMR: 1st + subsequent lines of therapy</li> </ul> </li> </ul>

## List of updates

Date	Changes
<p><b>Oct. 1, 2023</b></p>	<p>Updates to existing pathways</p> <ul style="list-style-type: none"> <li>• Ovarian Cancer                             <ul style="list-style-type: none"> <li>- Removed carboplatin from pathways as Primary/Adjuvant Therapy</li> </ul> </li> <li>• Uterine/Endometrial cancer                             <ul style="list-style-type: none"> <li>- Added Carboplatin + Paclitaxel + Dostarlimab-gxly (for patients who are ICI naïve) and Lenvatinib + Pembrolizumab (for pMMR tumors after prior platinum-based therapy, including neoadjuvant and adjuvant) as Metastatic or Recurrent: 1st line of therapy</li> <li>- Added Lenvatinib + Pembrolizumab (for pMMR tumors after prior platinum-based therapy, including neoadjuvant and adjuvant) as Metastatic or Recurrent: 2nd + Subsequent lines of therapy</li> <li>- Removed Pembrolizumab (for TMB-H or dMMR/MSI-H tumors), Dostarlimab-gxly (for dMMR/MSI-H tumors), Nivolumab (for dMMR/MSI-H tumors), and Avelumab (for dMMR/MSI-H tumors) from pathways as Metastatic or Recurrent: 2nd + Subsequent lines of therapy</li> </ul> </li> <li>• Bladder Cancer                             <ul style="list-style-type: none"> <li>- Added Nivolumab (adjuvant only; PD-L1 <math>\geq</math> 1%; high-risk) as Neoadjuvant/Adjuvant: Muscle Invasive Bladder Cancer (MIBC)</li> </ul> </li> <li>• Colon/Rectal Cancer                             <ul style="list-style-type: none"> <li>- Added Pembrolizumab to Metastatic; MSI-H/dMMR - 1st line of therapy</li> <li>- Removed Pembrolizumab from pathways as Metastatic; MSI-H/dMMR - 2nd + subsequent lines of therapy</li> </ul> </li> </ul>
<p><b>Jan. 1, 2024</b></p>	<p>Updates to existing pathways</p> <ul style="list-style-type: none"> <li>• Esophageal and Esophagogastric Cancer                             <ul style="list-style-type: none"> <li>- Added Pembrolizumab + fluoropyrimidine + oxaliplatin or cisplatin (PD-L1 CPS <math>\geq</math> 10) to Recurrent/Metastatic/Unresectable locally advanced disease; 1st line of therapy HER2-negative or Unknown</li> </ul> </li> <li>• Gastric Cancer                             <ul style="list-style-type: none"> <li>- Added Pembrolizumab + fluoropyrimidine + oxaliplatin or cisplatin (PD-L1 CPS <math>\geq</math> 10) to Recurrent/Metastatic/Unresectable locally advanced disease; 1st line of therapy HER2-negative or Unknown</li> </ul> </li> </ul>

## List of updates

Date	Changes
<p><b>March 1, 2024</b></p>	<p>Updates to existing pathways</p> <ul style="list-style-type: none"> <li>• Non-Small Cell Lung Cancer                             <ul style="list-style-type: none"> <li>- Added Carboplatin + Pemetrexed ± Concurrent RT to Neoadjuvant/Adjuvant, nonsquamous</li> <li>- Added Nivolumab + Carboplatin or Cisplatin + Paclitaxel and Nivolumab + Carboplatin or Cisplatin + Pemetrexed (Neoadjuvant only) to Neoadjuvant/Adjuvant, nonsquamous</li> <li>- Added Nivolumab + Carboplatin or Cisplatin + Paclitaxel and Nivolumab + Carboplatin or Cisplatin + Gemcitabine (Neoadjuvant only) to Neoadjuvant/Adjuvant, squamous</li> <li>- Added Carboplatin/Cisplatin + Paclitaxel and Carboplatin/Cisplatin + Pemetrexed (immunotherapy ineligible) to Advanced/Metastatic - Nonsquamous (EGFR, ALK, RET WT), 1st line of therapy</li> <li>- Added Carboplatin/Cisplatin + Paclitaxel and Carboplatin/Cisplatin + Gemcitabine (immunotherapy ineligible) to Advanced/Metastatic - Squamous (EGFR, ALK, RET WT), 1st line of therapy</li> <li>- Added Gemcitabine to Advanced/Metastatic - Nonsquamous/Squamous, 2nd + subsequent lines of therapy</li> </ul> </li> <li>• Prostate Cancer                             <ul style="list-style-type: none"> <li>- Added Olaparib + abiraterone (BRCA1/2 mutations positive) and Olaparib + abiraterone (Homologous recombination repair (HRR) mutations positive) to Recurrent/Metastatic; Castration-resistant disease</li> </ul> </li> <li>• Small Cell Lung Cancer                             <ul style="list-style-type: none"> <li>- Removed Paclitaxel from pathways as Subsequent Therapy: Relapse &gt; 6 months</li> </ul> </li> </ul>
<p><b>May 1, 2024</b></p>	<p>Updates to existing pathways</p> <ul style="list-style-type: none"> <li>• Biliary Tract Cancers                             <ul style="list-style-type: none"> <li>- Removed Gemcitabine + Cisplatin + Durvalumab from pathways for Unresectable/Metastatic; 1st Line of Therapy</li> </ul> </li> <li>• Chronic Myeloid Leukemia                             <ul style="list-style-type: none"> <li>- Removed Omacetaxine (T315I mutation only) from pathways for 2nd + Subsequent Lines of Therapy</li> <li>- Added Dasatinib, Imatinib, Nilotinib, and T315I mutation only comment to Ponatinib to pathways for 2nd + Subsequent Lines of Therapy</li> <li>- Added Asciminib to pathways for 3rd + Subsequent Lines of Therapy</li> </ul> </li> <li>• Hepatocellular Carcinoma                             <ul style="list-style-type: none"> <li>- Removed Lenvatinib and Sorafenib from pathways for Unresectable, Not a Transplant Candidate, Metastatic Disease, Inoperable by PS or Comorbidity; 1st Line of Therapy</li> <li>- Removed Atezolizumab + Bevacizumab from pathways for Unresectable, Not a Transplant Candidate, Metastatic Disease, Inoperable by PS or Comorbidity; 2nd + Subsequent Lines of Therapy</li> </ul> </li> </ul>

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Date	Changes
<b>May 1, 2024 (cont.)</b>	<ul style="list-style-type: none"> <li>• Pancreatic Cancer                             <ul style="list-style-type: none"> <li>- Added Fluorouracil/Leucovorin and Capecitabine to pathways for Locally Advanced/Metastatic; Maintenance</li> </ul> </li> <li>• Multiple Myeloma                             <ul style="list-style-type: none"> <li>- Removed Bortezomib + Thalidomide + Dexamethasone (VTD) from pathways for Primary Therapy; Transplant Eligible</li> <li>- Added Daratumumab + Bortezomib + Lenalidomide + Dexamethasone (D-VRD) to pathways for Primary Therapy; Transplant Eligible</li> <li>- Removed Isatuximab-irfc + Pomalidomide + Dexamethasone (Isa-PD) from pathways for Relapsed or Refractory; 1st Relapse</li> <li>- Added Daratumumab + Pomalidomide + Dexamethasone (DPD) to pathways for Relapsed or Refractory; 2nd Relapse</li> </ul> </li> </ul>
<b>Aug. 1, 2024</b>	<p>Updates to existing pathways</p> <ul style="list-style-type: none"> <li>• Head and Neck Cancer                             <ul style="list-style-type: none"> <li>- Added Carboplatin + Paclitaxel + Pembrolizumab (for combined positive score (CPS) <math>\geq 1</math> only) to pathways for Non-Nasopharyngeal: 1st Line of Therapy</li> <li>- Added Cisplatin + Gemcitabine + Toripalimab-tpzi to pathways for Nasopharyngeal: 1st Line of Therapy</li> </ul> </li> <li>• Kidney Cancer                             <ul style="list-style-type: none"> <li>- Added Pembrolizumab to pathways for Adjuvant therapy</li> <li>- Added Nivolumab + Ipilimumab to pathways for Relapsed or Metastatic (Clear Cell): 1st Line of Therapy</li> </ul> </li> <li>• Follicular Lymphoma                             <ul style="list-style-type: none"> <li>- Added Rituximab (weekly for 4 doses) to pathways for 1st Line of Therapy</li> </ul> </li> <li>• Mantle Cell Lymphoma                             <ul style="list-style-type: none"> <li>- Removed Alternating RCHOP/RDHAP (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Prednisone)/(Rituximab, Dexamethasone, Cytarabine, Cisplatin) from pathways for 1st Line of Therapy</li> </ul> </li> <li>• Marginal Zone Lymphoma                             <ul style="list-style-type: none"> <li>- Removed Chlorambucil <math>\pm</math> Rituximab from pathways for 1st Line of Therapy</li> </ul> </li> </ul>



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Date	Changes
<b>Sept. 1, 2024</b>	<p>Updates to existing pathways</p> <ul style="list-style-type: none"> <li>• Breast Cancer                             <ul style="list-style-type: none"> <li>- Reformatted Metastatic and Recurrent - Chemotherapy HER2 Negative</li> <li>- Added Sacituzumab Govitecan-hziy (HR+, HER2-) to Metastatic and Recurrent - Chemotherapy HER2 Negative: 1st + Subsequent Lines of Therapy</li> <li>- Added Tucatinib + Trastuzumab + Capecitabine (in patients with brain mets) to Metastatic and Recurrent - Chemotherapy, HER2 Positive: 2nd + Subsequent lines of therapy</li> <li>- Added Tucatinib + Trastuzumab + Capecitabine to Metastatic and Recurrent - Chemotherapy, HER2 Positive: 3rd + Subsequent lines of therapy</li> </ul> </li> <li>• Chronic Lymphocytic Leukemia/Small Lymphocytic (CLL/SLL)                             <ul style="list-style-type: none"> <li>- Removed Zanubrutinib from pathways</li> </ul> </li> <li>• Melanoma                             <ul style="list-style-type: none"> <li>- Added Nivolumab + Ipilimumab (2 cycles) to Neoadjuvant therapy</li> </ul> </li> </ul>
<b>Jan. 1, 2025</b>	<p>Updates to existing pathways</p> <ul style="list-style-type: none"> <li>• Breast Cancer                             <ul style="list-style-type: none"> <li>- Added Pembrolizumab + Carboplatin + Paclitaxel, followed by Pembrolizumab + Cyclophosphamide + Doxorubicin or Epirubicin, followed by adjuvant Pembrolizumab (for high-risk TNBC only) to Neoadjuvant/Adjuvant; HER2 Negative.</li> <li>- Added Pembrolizumab (continuation in TNBC following pembrolizumab + chemotherapy to Adjuvant (Residual Disease Post-Neoadjuvant Treatment); Triple Negative Breast Cancer.</li> </ul> </li> <li>• Non Small Cell Lung Cancer                             <ul style="list-style-type: none"> <li>- Added Alectinib (ALK rearrangement positive; adjuvant only) to neoadjuvant/adjuvant non-small cell lung cancer Non Squamous and Squamous</li> </ul> </li> <li>• Lung Cancer, Non-Small Cell: Advanced/Metastatic:                             <ul style="list-style-type: none"> <li>- Changed EFR, ALK, RET Wild Type to say: Excluding EGFR, ALK, RET, ROS1 and/or MET genomic aberration)</li> </ul> </li> <li>• Small Cell Lung Cancer                             <ul style="list-style-type: none"> <li>- Added Durvalumab to Limited Stage (Adjuvant or Primary)</li> </ul> </li> </ul>

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Date	Changes
<b>Jan. 1, 2025 (cont.)</b>	<ul style="list-style-type: none"> <li>• Gastric Cancer                             <ul style="list-style-type: none"> <li>- Added Fluorouracil ± Leucovorin + Cisplatin + Trastuzumab + Pembrolizumab (CPS ≥ 1), Fluorouracil ± Leucovorin + Oxaliplatin + Trastuzumab + Pembrolizumab (CPS ≥ 1), Capecitabine + Cisplatin + Trastuzumab + Pembrolizumab (CPS ≥ 1), Capecitabine + Oxaliplatin + Trastuzumab + Pembrolizumab (CPS ≥ 1) to Recurrent/Metastatic/Unresectable locally advanced disease; 1st line of therapy, HER2-positive</li> </ul> </li> <li>• Ovarian, Fallopian and Primary Peritoneal Cancer                             <ul style="list-style-type: none"> <li>- Added Mirvetuximab soravtansine-gynx (FRα expressing tumors, ≥75% positive tumor cells) to Platinum – Resistant Recurrent Disease 1st + Subsequent Lines of Therapy</li> </ul> </li> </ul>
<b>March 1, 2025</b>	<p>Updates to existing pathways</p> <ul style="list-style-type: none"> <li>• Breast Cancer                             <ul style="list-style-type: none"> <li>- Added Pembrolizumab + Carboplatin + Paclitaxel, followed by Pembrolizumab + Cyclophosphamide + Doxorubicin or Epirubicin, followed by adjuvant Pembrolizumab (for high-risk TNBC only) to Neoadjuvant/Adjuvant; HER2 Negative</li> <li>- Added Pembrolizumab (continuation in TNBC following pembrolizumab + chemotherapy to Adjuvant (Residual Disease Post-Neoadjuvant Treatment); Triple Negative Breast Cancer</li> </ul> </li> <li>• Lung Cancer, Small Cell                             <ul style="list-style-type: none"> <li>- Added Durvalumab to Limited Stage (Adjuvant or Primary)</li> </ul> </li> <li>• Lung Cancer, Non-Small Cell                             <ul style="list-style-type: none"> <li>- Added Alectinib (ALK rearrangement positive; adjuvant only) to neoadjuvant/adjuvant non-small cell lung cancer</li> <li>- Advanced/Metastatic: Changed (EFFF, ALK, RET Wild Type) to (Excluding EGFR, ALK, RET, ROS1 and/or MET genomic aberration)</li> </ul> </li> </ul>

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