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OVERVIEW

Cancer Therapy Pathways Program

With the rapid approval of new therapies, along with the rising cost of cancer care, pathways serve a critical role in the delivery of high-quality and high-value cancer treatments while reducing an unwarranted variation in care. The UnitedHealthcare Cancer Therapy Pathways Program aims to improve quality and value in cancer care by identifying anti-cancer regimens supported by evidence-based guidelines to help reduce total cost of care and improve outcomes.

The program’s regimens are selected on the basis of clinical benefit (efficacy) and side-effect profile (toxicity). Among regimens with comparable efficacy and toxicity, additional consideration is given to the frequency of hospitalizations during therapy, duration of therapy, drug costs and total cost of care.

Care decisions are between the physician and the patient

The Cancer Therapy Pathways Program is not a substitute for the experience and judgment of a physician or other health care professional. Any clinician participating in the program must use independent medical judgment in the context of individual clinical circumstances to determine any patient’s care or treatment. Care decisions are between the physician and patient.
Breast Cancer: Neoadjuvant/Adjuvant

HER2 NEGATIVE:
• Doxorubicin + Cyclophosphamide (dose dense) → Paclitaxel weekly (ddAC → weekly T)
• Doxorubicin + Cyclophosphamide (dose dense) → Paclitaxel every 2 weeks (ddAC → q2w T)
• Docetaxel + Cyclophosphamide (TC)

HER2 POSITIVE:
• Doxorubicin + Cyclophosphamide → Paclitaxel weekly + Trastuzumab* (AC → TH)
• Docetaxel + Carboplatin + Trastuzumab* (TCH)
• Paclitaxel + Trastuzumab*

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

TRIPLE NEGATIVE BREAST CANCER:
• Capecitabine

HER2 POSITIVE:
• Ado-trastuzumab emtansine (T-DM1)

Breast Cancer: Metastatic and Recurrent – Endocrine Therapy

HER2 NEGATIVE:
1st Line of Therapy
• Fulvestrant + Anastrozole
• Anastrozole + Palbociclib
• Letrozole + Palbociclib
• Exemestane + Palbociclib
• Anastrozole + Abemaciclib
• Letrozole + Abemaciclib
• Exemestane + Abemaciclib

1st + Subsequent Lines of Therapy
• Anastrozole
• Letrozole
• Exemestane
• Tamoxifen
• Fulvestrant

2nd + Subsequent Lines of Therapy
• Anastrozole
• Letrozole
• Exemestane
• Tamoxifen
• Fulvestrant
• Fulvestrant + Palbociclib
• Fulvestrant + Abemaciclib
HER2 POSITIVE:
- Anastrozole + Trastuzumab*
- Letrozole + Trastuzumab*
- Exemestane + Trastuzumab*
- Anastrozole + Lapatinib
- Letrozole + Lapatinib
- Exemestane + Lapatinib

Breast Cancer: Metastatic and Recurrent – Chemotherapy

HER2 NEGATIVE:
1st + Subsequent Lines of Therapy
- Doxorubicin
- Paclitaxel
- Docetaxel
- Capecitabine
- Gemcitabine
- Vinorelbine
- Atezolizumab + Nab-Paclitaxel (in PD-L1+ mTNBC only)

HER2 POSITIVE:
1st + Subsequent Lines of Therapy
- Docetaxel + Trastuzumab* + Pertuzumab
- Paclitaxel + Trastuzumab* + Pertuzumab
- Ado-Trastuzumab Emtansine (T-DM1)
- Capecitabine + Lapatinib
- Paclitaxel + Trastuzumab*
- Vinorelbine + Trastuzumab*
- Gemcitabine + Trastuzumab*
- Capecitabine + Trastuzumab*

*Kanjinti™ and Trazimera™ are the preferred products under UnitedHealthcare commercial plans, Kanjinti™ is the preferred product under UnitedHealthcare Community Plans (in most markets) and all products are preferred under UnitedHealthcare Medicare plans.
References


12. Mackey, J.R., Pieńkowski, T., Crown, J., et al. (June 2016). Long-Term Outcomes After Adjuvant Treatment of Sequential Versus Combination Docetaxel With Doxorubicin and Cyclophosphamide in


103. Tutt, A., Tovey, H., Cheang, M.C., et al. (May 2018). Carboplatin in BRCA1/2-Mutated and Triple-Negative Breast Cancer BRCAness Subgroups: The TNT Trial. Retrieved from ncbi.nlm.nih.gov/pmc/articles/PMC6372067


Pancreatic Cancer: Neoadjuvant (Resectable/Borderline Resectable)

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

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)
References:


Melanoma: Adjuvant (Resectable)

- Pembrolizumab

Melanoma: Adjuvant (Resectable) – (BRAF Mutated)

- Dabrafenib + Trametinib

Melanoma: Metastatic/Unresectable (BRAF Mutated/Symptomatic)

- Vemurafenib + Cobimetinib

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

1st + Subsequent Lines of Therapy

- Pembrolizumab
- Nivolumab + Ipilimumab
References:


5. ClinicalTrials.gov. An Investigational Immuno-Therapy Study of Nivolumab Combined With Ipilimumab Compared to Nivolumab by Itself after Complete Surgical Removal of Stage IIIb/c/d or Stage IV Melanoma. Retrieved from clinicaltrials.gov/ct2/show/NCT03068455


34. ESMO 2018: CheckMate 067: 4-Year Follow-Up of Nivolumab Plus Ipilimumab in Advanced Melanoma. Retrieved from ascopost.com/News/59415


Colon/Rectal Cancer: Adjuvant

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

Colon/Rectal Cancer: Metastatic KRAS/NRAS: Unknown/Mutant

1st and 2nd Lines of Therapy

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

Colon/Rectal Cancer: Metastatic KRAS/NRAS: Wild Type

1st and 2nd Lines of Therapy

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

Colon/Rectal Cancer: MSI-H/dMMR

1st + Subsequent Lines of Therapy

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

* Mvasi™ is the preferred product under UnitedHealthcare commercial and UnitedHealthcare Community Plans (in most markets) and all products preferred under UnitedHealthcare Medicare plans.
References:


26. Souglakos, J., Androulakis, N., Syrigos, K., et al. (2006, March 27). FOLFOXIRI (Folinic Acid, 5-Fluorouracil, Oxaliplatin and Irinotecan) vs. FOLFIRI (Folinic Acid, 5-Fluorouracil and Irinotecan) as First-


49. Nishi, T., Hamamoto, Y., Nagase, M., et al. (June 2016). Phase II Trial of Panitumumab With Irinotecan as Salvage Therapy for Patients With Advanced or Recurrent Colorectal Cancer (TOPIC study). Retrieved from ncbi.nlm.nih.gov/pmc/articles/PMC4888220

50. Seymour, M.T., Brown, S.R., Middleton, G., et al. (July 2013). Panitumumab and Irinotecan Versus Irinotecan Alone for Patients With KRAS Wild Type, Fluorouracil-Resistant Advanced Colorectal Cancer


64. Diaz, L., Marabelle, A., et al. Efficacy of Pembrolizumab in Phase 2 KEYNOTE-164 and KEYNOTE-158 Studies of Microsatellite Instability High Cancers Presented at the European Society for Medical Oncology Congress; Madrid, Spain; 8-12 September 2017. Poster 386P


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

1st Line of Therapy
- Sorafenib
- Lenvatinib
- Atezolizumab + Bevacizumab*

2nd + Subsequent Lines of Therapy
- Regorafenib
- Cabozantinib
- Sorafenib
- Lenvatinib
- Atezolizumab + Bevacizumab*

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)
- Pemigatinib (in FGFR2 mutation cholangiocarcinoma)
- Ivosidenib (in IDH1 mutation cholangiocarcinoma)

*Mvasi™ is the preferred product under UnitedHealthcare commercial and UnitedHealthcare Community Plans (in most markets) and all products preferred under UnitedHealthcare Medicare plans.
References:


Lung Cancer, Small Cell: Limited Stage – Adjuvant or Primary Therapy
- Carboplatin + Etoposide
- Cisplatin + Etoposide

Lung Cancer, Small Cell: Extensive Stage – Adjuvant or Primary Therapy
- Carboplatin + Etoposide + Atezolizumab
- Carboplatin + Etoposide + Durvalumab
- Cisplatin + Etoposide + Durvalumab
- Carboplatin + Etoposide
- Cisplatin + Etoposide

Lung Cancer, Small Cell: Extensive Stage – Adjuvant or Primary Therapy – Maintenance
- Atezolizumab
- Durvalumab

Lung Cancer, Small Cell: Subsequent Therapy: Relapse ≤ 6 months
- Topotecan IV
- Paclitaxel
- Irinotecan

Lung Cancer, Small Cell: Subsequent Therapy: Relapse > 6 months
- Carboplatin + Etoposide
- Cisplatin + Etoposide
References:


Lung Cancer, Non-Small Cell: Neoadjuvant/Adjuvant

Nonsquamous
- Cisplatin + Vinorelbine
- Cisplatin + Pemetrexed ± concurrent radiation therapy (RT)
- Carboplatin + Paclitaxel ± concurrent radiation therapy (RT)
- Cisplatin + Etoposide + concurrent radiation therapy (RT)

Squamous
- Cisplatin + Vinorelbine
- Carboplatin + Paclitaxel ± concurrent radiation therapy (RT)
- Cisplatin + Etoposide + concurrent radiation therapy (RT)

Lung Cancer, Non-Small Cell: Adjuvant: Stage III Unresectable, No Progression and PS 0–1
- Durvalumab

Lung Cancer, Non-Small Cell: Advanced/Metastatic: EGFR 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

Nonsquamous: 1st Line of Therapy
- Pembrolizumab single agent (PD-L1 ≥ 50% only)
- Carboplatin/Cisplatin + Pemetrexed + Pembrolizumab (PD-L1: < 1%, 1–49% and ≥ 50%)

Nonsquamous: Maintenance
- Pemetrexed
- Pembrolizumab
- Pembrolizumab + Pemetrexed

Nonsquamous: 2nd + Subsequent Lines of Therapy
- Docetaxel
- Pemetrexed
**Squamous: 1st Line of Therapy**
- Pembrolizumab single agent (PD-L1 ≥ 50% only)
- Carboplatin + Paclitaxel + Pembrolizumab (PD-L1: < 1%, 1–49% and ≥ 50%)

**Squamous: Maintenance**
- Pembrolizumab

**Squamous: 2nd + Subsequent Lines of Therapy**
- Docetaxel
References:


87. Inoue, A., Kobayashi, K., Maemondo, M., et al. (January 2013). Updated Overall Survival Results From a Randomized Phase III Trial Comparing Gefitinib With Carboplatin-Paclitaxel for Chemo-Naïve Non-Small-


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
- Olaparib (germline/somatic BRCA mutation only)
- Niraparib

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

1st + Subsequent Lines of Therapy
- Carboplatin + Gemcitabine
- Carboplatin + Liposomal Doxorubicin
- Carboplatin + Paclitaxel

Maintenance Therapy
- Olaparib
- Niraparib

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

1st + Subsequent Lines of Therapy
- Gemcitabine
- Liposomal Doxorubicin
- Liposomal Doxorubicin + Bevacizumab*
- Paclitaxel (weekly)
- Paclitaxel (weekly) + Bevacizumab*
- Tamoxifen

**Only intravenous carboplatin + paclitaxel are pathway regimens.
*Mvasi™ is the preferred product under UnitedHealthcare commercial and UnitedHealthcare Community Plans (in most markets) and all products preferred under UnitedHealthcare Medicare plans.


72. Jin, W. Roles of TrkC Signaling in the Regulation of Tumorigenicity and Metastasis of Cancer. *Cancers* 2020, 12, 147

73. Gershenson, D.M., Miller, A., Brade, W., et al. (2019). LBA61A Randomized Phase II/III Study to Assess the Efficacy of Trametinib in Patients With Recurrent or Progressive Low-Grade Serous Ovarian or Peritoneal Cancer. Retrieved from researchgate.net/publication/336195140_LBA61A_randomized_phase_IIIII_study_to_assess_the_efficacy_of_trametinib_in_patients_with_recurrent_or_progressive_low-grade_serous_ovoarian_or_peritoneal_cancer


75. Diaz, L., Marabelle, A., et al. Efficacy of Pembrolizumab in Phase 2 KEYNOTE-164 and KEYNOTE-158 Studies of Microsatellite Instability High Cancers Presented at the European Society for Medical Oncology Congress; Madrid, Spain; 8-12 September 2017. Poster 386P


108. Jin, W. Roles of TrkC Signaling in the Regulation of Tumorigenicity and Metastasis of Cancer. Cancers 2020, 12, 147


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

Head and Neck Cancer: Recurrent/Metastatic/Unresectable

Non-nasopharyngeal: 1st Line of Therapy
- Cisplatin or Carboplatin + Fluorouracil (5FU) + Cetuximab
- Cisplatin + Fluorouracil (5FU)
- Cisplatin or Carboplatin + Docetaxel
- Cisplatin or Carboplatin + Paclitaxel
- Cisplatin or Carboplatin + Fluorouracil (5FU) + Pembrolizumab (For combined positive score (CPS) ≥ 1 only)
- Pembrolizumab (For combined positive score (CPS) ≥ 1 only)

Non-nasopharyngeal: Maintenance
- Cetuximab
- Pembrolizumab (For combined positive score (CPS) ≥ 1 only)

Non-nasopharyngeal: 2nd + Subsequent Lines of Therapy
- Nivolumab (if IO not used previously)
- Pembrolizumab (if IO not used previously)

Nasopharyngeal: 1st Line of Therapy
- Cisplatin + Gemcitabine
References:


Multiple Myeloma: Primary Therapy**

Transplant Eligible
- Bortezomib + lenalidomide + dexamethasone (VRD)
- Bortezomib + thalidomide + dexamethasone (VTD)
- Bortezomib + cyclophosphamide + dexamethasone (CyBorD or VCD)

Transplant Ineligible
- Bortezomib + lenalidomide + dexamethasone (VRD)
- Bortezomib + cyclophosphamide + dexamethasone (CyBorD or VCD)

Multiple Myeloma: Maintenance Therapy**

Transplant Eligible or Ineligible
- Lenalidomide
- Bortezomib

Multiple Myeloma: Relapsed or Refractory**

1st Relapse
- Daratumumab + lenalidomide + dexamethasone (DRD)
- Daratumumab + bortezomib + dexamethasone (DVD)
- Isatuximab-irfc + pomalidomide + dexamethasone (Isa-PD)
- Bortezomib + lenalidomide + dexamethasone (VRD)
- Bortezomib + thalidomide + dexamethasone (VTD)
- Bortezomib + cyclophosphamide + dexamethasone (CyBorD or VCD)

2nd Relapse
- Daratumumab + lenalidomide + dexamethasone (DRD)
- Daratumumab + bortezomib + dexamethasone (DVD)
- Isatuximab-irfc + pomalidomide + dexamethasone (Isa-PD)
- Elotuzumab + pomalidomide + dexamethasone (EPD)
- Panobinostat + bortezomib + dexamethasone
- Carfilzomib + lenalidomide + dexamethasone (KRD)
- Carfilzomib + pomalidomide + dexamethasone (KPD)
- Pomalidomide + bortezomib + dexamethasone (PVD)
- Bortezomib + lenalidomide + dexamethasone (VRD)
- Bortezomib + thalidomide + dexamethasone (VTD)
- Bortezomib + cyclophosphamide + dexamethasone (CyBorD or VCD)

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


84. Dimopoulos, M.A., Goldschmidt, H., Niesvizky, R., et al. Carfilzomib or Bortezomib in Relapsed or Refractory Multiple Myeloma (ENDEAVOR): An Interim Overall Survival Analysis of an Open Label,


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)*

2nd + Subsequent Lines of Therapy
- Rituximab* ± GDP (gemcitabine, dexamethasone, cisplatin or carboplatin)
- Rituximab* ± ICE (ifosfamide, carboplatin, etoposide)
- Rituximab* ± DHAP (dexamethasone, cisplatin, cytarabine)

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)

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


17. Martino, R., Perea, G., Caballero, M.D., et al. Cyclophosphamide, Pegylated Liposomal Doxorubicin (Caelyx), Vincristine and Prednisone (CCOP) in Elderly Patients With Diffuse Large B-Cell Lymphoma: Results From a Prospective Phase II Study. Haematologica 2002;87:822-827


**Lymphoma, Follicular (Grade 1–2)**

1st Line of Therapy
- Bendamustine + Rituximab* (BR)

2nd + Subsequent Lines of Therapy (non-refractory disease)
- Bendamustine + Rituximab* (BR)
- CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Rituximab*
- CVP (cyclophosphamide, vincristine, prednisone) + Rituximab*
- Rituximab*

2nd Line of Therapy (refractory disease)
- Bendamustine + Obinutuzumab
- Bendamustine + Rituximab* (BR)
- CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Rituximab*
- CVP (cyclophosphamide, vincristine, prednisone) + Rituximab*
- Rituximab*

3rd + Subsequent Lines of Therapy (refractory disease)
- Bendamustine + Obinutuzumab
- Bendamustine + Rituximab* (BR)
- CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Rituximab*
- CVP (cyclophosphamide, vincristine, prednisone) + Rituximab*
- Duvelisib
- Idelalisib
- Umbralisib
- 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)

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References:


**Lymphoma, Marginal Zone**

**1st Line of Therapy**
- Helicobacter pylori (H. pylori) eradication therapy (Gastric MALT lymphoma only)
- Bendamustine + Rituximab* (BR)
- Chlorambucil ± Rituximab*
- 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*
- Chlorambucil ± Rituximab*
- Rituximab (weekly for 4 doses)

**2nd Line of Therapy (refractory disease)**
- Bendamustine + Obinutuzumab
- Bendamustine + Rituximab* (BR)
- CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Rituximab*
- CVP (cyclophosphamide, vincristine, prednisone) + Rituximab*
- Chlorambucil ± Rituximab*
- Rituximab (weekly for 4 doses)

**3rd + Subsequent Lines of Therapy (refractory disease)**
- Bendamustine + Obinutuzumab
- Bendamustine + Rituximab* (BR)
- CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Rituximab*
- CVP (cyclophosphamide, vincristine, prednisone) + Rituximab*
- Chlorambucil ± Rituximab*
- Duvelisib
- Idelalisib
- Umbralisib
- 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* ± GDP (gemcitabine, dexamethasone, cisplatin or carboplatin)
- Rituximab* ± ICE (ifosfamide, carboplatin, etoposide)
- Rituximab* ± DHAP (dexamethasone, cisplatin, cytarabine)

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


27. Sacchi, S., Marcheselli, R., Bari, A., et al. Safety and Efficacy of Lenalidomide in Combination With Rituximab in Recurrent Indolent Non-Follicular Lymphoma: Final Results of a Phase II Study Conducted by


Lymphoma, Mantle Cell**

1st Line of Therapy
- Alternating RCHOP/RDHAP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)/(rituximab, dexamethasone, cytarabine, cisplatin)*
- Nordic regimen (dose-intensified induction immunochemotherapy with rituximab + cyclophosphamide, vincristine, doxorubicin, prednisone [maxi-CHOP]) alternating with rituximab + high-dose cytarabine
- Hyper-CVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine) + rituximab*
- Bendamustine + Rituximab*
- VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone)*

2nd Line of Therapy
- Bendamustine + Rituximab* (BR)
- Acalabrutinib
- Ibrutinib
- Zanubrutinib

3rd + Subsequent Lines of Therapy
- Bendamustine + Rituximab* (BR)
- Acalabrutinib
- Ibrutinib
- Zanubrutinib
- Lenalidomide

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References:


## Change control

<table>
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<tr>
<th>Date</th>
<th>Changes</th>
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| July 1, 2020 | Added change control  
New Pathways – Small Cell Lung Cancer and Hepatobiliary Cancer  
Updates to existing pathways  
• Melanoma Pathways:  
  o Removed “Stages IIIB and IIIC” from Adjuvant  
• Colon Pathways:  
  o Updated name to “Colon/Rectal” to reflect pathways for rectal cancer  
  o Removed FOLFOX/FOLFIRI + Cetuximab regimen from Colon Cancer: Metastatic KRAS/NRAS: Wild Type – 1st and 2nd Lines of Therapy |
| Aug. 1, 2020 | New Pathways – Ovarian Cancer |
Updates to existing pathways  
• Breast Pathways:  
  o Capecitabine + Lapatinib was added to pathways for HER2 POSITIVE:  
    1st + Subsequent Lines of Therapy  
• Pancreatic Pathways:  
  o Fluorouracil/Leucovorin was added to Locally Advanced/Metastatic:  
    2nd + subsequent lines of therapy  
• Colon/Rectal Pathways:  
  o Capecitabine + Oxaliplatin (CAPEOX) was added to pathways for Adjuvant  
  o New category of pathways for Metastatic: MSI/dMMR: 1st + Subsequent Lines of Therapy |
| Nov. 1, 2020 | New Pathways – Head and Neck Cancer  
Updates to existing pathways  
• Melanoma Pathways: Removed Nivolumab single agent from Adjuvant and Metastatic/Unresectable |
| Jan. 1, 2021 | New Pathways – Multiple Myeloma |
| March 1, 2021 | New Pathways – Diffuse Large B-Cell Lymphoma  
Updates to existing pathways  
• Hepatocellular Carcinoma: Added Atezolizumab + Bevacizumab regimen to pathways as 1st line of therapy and 2nd + subsequent lines of therapy; added sorafenib or lenvatinib to 2nd + subsequent lines of therapy  
• Biliary tract cancers: Added FOLFOX, Pemigatinib (in FGFR2 mutation cholangiocarcinoma), and Ivosidenib (in IDH1 mutation cholangiocarcinoma) to pathways as 2nd + subsequent lines of therapy |
| May 1, 2021 | New Pathways – Follicular Lymphoma and Marginal Zone Lymphoma |
| June 1, 2021 | New Pathways – Mantle Cell Lymphoma  
Updates to existing pathways  
• Follicular Lymphoma and Marginal Zone Lymphoma – added pathway options for refractory disease |