Policy #	Policy Name	Type of Change	Brief Description of Policy Change	Reason for Changes
New	Ferriprox (deferiprone)	N/A	N/A	N/A
New	Exkivity (mobocertinib)	N/A	N/A	N/A
New	Tivdak (tisotumab vedotin-tftc)	N/A	N/A	N/A
UM ONC_1028	Avastin (bevacizumab)/Mvasi (bevacizumab-awwb)/Zirabev (bevacizumab-bvzr)	Negative change	H.Ovarian Cancer NOTE: Avastin (bevacizumab)/Mvasi (bevacizumab-awwb)/Zirabev (bevacizumab-bvzr) is non-preferred in the treatment of ovarian cancer. This recommendation is based on a lack of Level 1 evidence (randomized trials and or meta-analyses) to show an overall survival (OS) advantage with Bevacizumab + Chemotherapy over other alternative chemotherapy regimens on NCH L1 pathway for adjuvant, recurrent, or metastatic treatment of ovarian cancer. A summary of the original trials to support this recommendation is as follows: Primary setting after debulking surgery: 1.GOG 218: Extended long term follow-up data at 103 months (7 years beyond the primary analysis) continued to report no difference among the groups in terms of OS. The median OS was 43.8 months with bevacizumab + chemotherapy followed by bevacizumab, compared with 40.6 months with chemotherapy alone (HR, 0.89; 95% CI, 0.76-1.05). The median OS with bevacizumab plus chemotherapy followed by placebo was 38.8 months (HR of 1.06 vs chemotherapy alone, 95% CI, 0.90-1.24).A 2.ICON 7: At a median follow-up of 49 months, an updated analysis of PFS showed no difference between treatment (17 versus 20 months; HR 0.93, 95% CI 0.83-1.0, p= 0.25), and more serious grade 3/4 adverse events (3 versus 7 percent), including a higher rate of mild to serious grade 2 or higher hypertension (2 versus 18 percent). Grade 3 or worse gastrointestinal perforations occurred in 10 patents (1%). There was no difference in overall survival or QOL.B Second line and salvage settings (platinum sensitive) 3.OCEANS: At a median follow-up of 42 months, overall survival data did not mature but the trial noted an improved progression-free survival benefit of 4 months (8.4 vs 12.4 months; HR = 0.484 95% CI 0.39-0.60, p= < 0.0001). There was no improvement in OS with bevacizumab when added to concurrent chemotherapy.C, D 4.GOG 213: At a median follow up of 50 months, there was 4 months improvement in PFS, 14 vs 10 months. The median overall survival in the chemotherapy plus bevacizumab group was 42 months (95% CI 37·7-46·2) versus 37 months (32·6-39·7) in the chemotherapy group with an adjusted HR of 0.823 (95% CI 0·680-0·996; p=0·0447). The adjustment in the HR was due to incorrect stratification of treatment free interval in 7% of patients. The data for the effect of secondary cytoreduction on OS has not been reached and was not reported in the analysis.E Second line and salvage settings (platinum resistant) 5.AURELIA: At a median follow-up of 13 months, the administration of the bevacizumab with chemotherapy was associated with a PFS benefit of 2.7 months (3.4 vs 6.7 months HR= 0.48 95% CI, 0.38 to 0.60, p= <0.001). There was no improvement in OS with bevacizumab when added to concurrent chemotherapy. Grade 2 hypertension and proteinuria were more common with bevacizumab. GI perforation occurred in 2.2% of bevacizumab-treated patients.F	Per Clinical Trial Analysis/Criteria
UM ONC_1181	~~Parental~~ Iron Products	Negative change	Add inclusion criteria: B. Iron Deficiency 1. NOTE: Per NCH policy, the ferrous oral iron products (ferrous sulfate, ferrous gluconate, and ferrous fumarate) are preferred over Accrufer (ferric maltol) and parenteral iron products for iron deficiency, unless the member has a history of hypersensitivity reaction or other adverse effects from the preferred products. The preferred parenteral iron products are Infed (iron dextran), Venofer (iron sucrose), Ferrlecit (ferric gluconate), or Feraheme (ferumoxytol) over Monoferric (ferric derisomaltose) or Injectafer (ferric carboxymaltose). .This recommendation is based on a lack of level 1 evidence (randomized trials and/or meta-analyses) supporting superior outcomes for any of the above iron replacement products over the other.	More Cost Effective Alternative(s)
UM ONC_1192	Afinitor (everolimus)	Negative change	Add inclusion criteria: C. Renal Cell Carcinoma (RCC) 1. Afinitor (everolimus) may be used as monotherapy as third line therapy for relapse or stage IV renal cell carcinoma. This recommendation is based on the lack of Level 1 evidence (randomized trials and/or meta-analyses) to show overall survival outcomes compared to other available therapies on NCH L1 pathway for first and second line settings.	Per Clinical Trial Analysis/Criteria
UM ONC_1205	Halaven (eribulin)	No Clinical Changes	N/A	N/A
UM ONC_1220	Arzerra (ofatumumab)	Negative change	Add inclusion criteria: B. Chronic Lymphocytic Leukemia (CLL) 1. NOTE: Arzerra (ofatumumab) is notpreferred for use in CLL. Per NCH Policy and NCH Pathways, the preferred anti-CD20 agents for use in CLL are Truxima (rituximab-abbs) & Ruxience (rituximab-pvvr). This recommendation is based on the lack of Level 1 evidence (randomized trials and/or meta-analyses) that shows superior outcomes with Arzerra (ofatumumab) over Truxima (rituximab-abbs) & Ruxience (rituximab-pvvr).	More Cost Effective Alternative(s)
UM ONC_1237	Cometriq or Cabometyx (cabozantinib)	Negative change	Add inclusion criteria: Thyroid cancer b.Unresectable or metastatic papillary, follicular, or Hurthle cell thyroid cancer and the member is refractory to a VEGFR-targeted therapy (e.g., lenvatinib, sunitinib, sorafenib) AND the member is not a candidate for or refractory to radioactive iodine treatment.	More Cost Effective Alternative(s)
UM ONC_1242	Jakafi (ruxolitinib)	Positive change	Add inclusion criteria: D.Graft Versus Host Disease 1.Jakafi (ruxolitinib) may be used with or without corticosteroids infor members with GVHD with or without corticosteroids in members 12 years or older who have acute or chronic GVHD, following an allogeneic hematopoietic stem cell transplantation, and the member is refractory to primary treatment with methylprednisolone (or a steroid equivalent).	New FDA Indication

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UM ONC_1245	Xofigo (radium Ra 223 dichloride)	Positive change	Remove inclusion criteria: B.Prostate Cancer 1.NOTE: Xofigo (radium Ra 223 dichloride) is a non-preferred drug per NCH Policy & NCH Pathways.	Per Compendia Listing
UM ONC_1248	Ixempra (ixabepilone)	No Clinical Changes	N/A	N/A
UM ONC_1249	Mekinist (trametinib)	Positive change	Remove inclusion criteria: B.Malignant Melanoma 1.NOTE #1: Per NCH Policy & NCH Pathway, the preferred combination for targeted therapy of metastatic, unresectable, or recurrent BRAF V600E or V600K mutation positive malignant melanoma is Zelboraf (vemurafenib) + Cotellic (cobimetinib); this recommendation is based on the lack of Level 1 evidence (randomized trials and or meta-analyses) to show that one anti-BRAF combination is superior to another. Furthermore, all randomized trials for such combination therapy have used a BRAF inhibitor (generally vemurafenib or encorafenib) as the control arm. 2.Mekinist (trametinib) may be used in combination with Tafinlar (dabrafenib) as first line, second-line, or subsequent treatment for metastatic or unresectable BRAF V600E or V600K mutation positive disease if member is intolerant to/has a contraindication to the preferred combination Zelboraf (vemurafenib) + Cotellic (cobimetinib). 3.Mekinist (trametinib) + Tafinlar (dabrafenib) may be used in a member with BRAF V600E or V600K mutation positive malignant melanoma as adjuvant treatment after complete resection of the primary lesion and completion of a regional lymph node dissection-total duration of adjuvant therapy not to exceed 1 year.	Per NCH L1 Pathway
UM ONC_1249	Mekinist (trametinib)	Negative change	Add inclusion criteria: 1.NOTE: For adjuvant therapy of BRAF V600 E or V600K mutation positive, stage III melanoma, the preferred agents per NCH Policies & NCH Pathway are Opdivo (nivolumab OR Keytruda (pembrolizumab). Tafinlar (dabrafenib) + Mekinist (trametinib) is non-preferred for use in the adjuvant setting based on a lack of Level 1 evidence that nivolumab or pembrolizumab monotherapy is inferior to the above combination. Please refer to UM ONC_1274 Opdivo (nivolumab) or UM ONC_1263 Keytruda (pembrolizumab) policy. 2.NOTE: For systemic therapy of metastatic BRAF V600E or V600K mutation positive melanoma the preferred oral combination, per NCH Policies and NCH Pathway, is Cotellic (cobimetinib) + Zelboraf (vemurafenib). Please refer to UM ONC_1279 Cotellic (cobimetinib) or UM ONC_1207 Zelboraf (vemurafenib) policy. 3.Mekinist (trametinib) may be used in combination with Tafinlar (dabrafenib) in members who have intolerance to/contraindication to the use of the preferred MEK and BRAF inhibitor combination, Cotellic (cobimetinib) + Zelbroaf (vemurafenib). D.Thyroid Carcinoma 1.Mekinist (trametinib) is being used in combination with Tafinlar (dabrafenib) for radioactive iodine-refractory (if radioactive iodine therapy is appropriate) in members with locally advanced or metastatic BRAF V600E mutation-positive anaplastic, papillary, follicular, and Hürthle Cell thyroid cancer~~ and Mekinist (trametinib) is being used in combination with Tafinlar (dabrafenib) as first or second-line therapy for metastatic disease.~~	Per NCH L1 Pathway and Compendia listing
UM ONC_1249	Mekinist (trametinib)	Negative change	Add exclusion criteria: E.Treatment exceeds the maximum 12 months duration limit when used as adjuvant melanoma treatment following complete resection of the primary lesion and completion of a regional lymph node dissection.	Per FDA labeling
UM ONC_1250	Tafinlar (dabrafenib)	Negative change	Add inclusion criteria: Melanoma 3.Tafinlar (dabrafenib) may be used as a single agent or in combination with Mekinist (trametinib) in members who have intolerance to/contraindication to the preferred MEK and BRAF inhibitor combination, [Cotellic (Ccobimetinib) + Zelboraf Vemurafenib)]. C.Non-Small Cell Lung Cancer (NSCLC) 1.Tafinlar (dabrafenib) may be used in combination with Mekinist (trametinib) as first line or subsequent line therapy for recurrent or metastatic BRAF V600E mutation-positive NSCLC, if anti-BRAF targeted therapy was not previously used.	Per NCH L1 Pathway and Compendia listing
UM ONC_1250	Tafinlar (dabrafenib)	Negative change	Add exclusion criteria: E.Treatment exceeds the maximum 12 months duration limit when used as adjuvant melanoma treatment following complete resection of the primary lesion and completion of a regional lymph node dissection.	Per FDA labeling
UM ONC_1265	Zykadia (ceritinib)	Negative change	Add inclusion criteria: B.Non-Small Cell Lung Cancer 1.NOTE: The preferred agent, per NCH Policy and NCH Pathways, for first line therapy of metastatic ALK+ NSCLC is Alecensa (alectinib). Please refer to UMC ONC_1277 Alecensa (alectinib) policy. This recommendation is based on the lack of Level 1 evidence (randomized trials and/or meta-analyses) that shows superior outcomes with Zykadia (ceritinib) over Alecensa (alectinib). 3.Zykadia (ceritinib) may be used as monotherapy for second line or subsequent therapy for ALK+ metastatic NSCLC if the member has experienced disease progression on Alecensa (alectinib), or Xalkori (crizotinib), Lorbrena (lorlatinib), or Alunbrig (brigatinib).	More Cost Effective Alternative(s)
UM ONC_1276	Onivyde (irinotecan liposome injection)	Positive change	Remove inclusion criteria: B.Metastatic Adenocarcinoma of the Pancreas 1.NOTE: Onyvide (liposomal irinotecan) is a non-preferred drug per NCH Policy and NCH Pathways.	Per Compendia Listing
UM ONC_1277	Alecensa (Alectinib)	No Clinical Changes	N/A	N/A

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UM ONC_1282	Imlygic (Talimogene Laherparepvec)	Negative change	Add inclusion criteria: B.Melanoma 1.NOTE #1: Imlygic (talimogene laherparepvec) is indicated ONLY for use as intra-lesional injections for ~~visible/metastatic~~ cutaneous, subcutaneous, and/or nodal lesions malignant melanoma skin lesions recurrent after initial surgery. 3.The member has stage IIIB, IIIC, or IV M1a-c melanoma and Imlygic (talimogene laherparepvec) is being used as a single agent, as an intra-lesional injection, for unresectable in-transit/distant/locally recurrent skin metastases from malignant melanoma following prior surgery.	Per Clinical Trial Analysis/Criteria
UM ONC_1284	Ninlaro (ixazomib)	Negative change	Add inclusion criteria: B.Multiple Myeloma 1.NOTE #1: Ninlaro (ixazomib) containing regimens are Non-Preferred regimens. pPer NCH Policy and NCH Pathway, t he preferred proteosome inhibitor is Velcade (bortezomib) for both initial therapy, maintenance therapy, and for relapsed/refractory multiple myeloma. This recommendation is based on the lack of Level 1 evidence (randomized trials and/or meta-analyses) that shows superior outcomes with Ninlaro (ixazomib) over Velcade (bortezomib). d. As a single agent maintenance therapy.	More Cost Effective Alternative(s) and compendia listing
UM ONC_1287	Tagrisso (osimertinib)	No Clinical Changes	N/A	N/A
UM ONC_1288	Fusilev (levoleucovorin)	Negative change	Add inclusion criteria: Prefer Fulsilev over Khapzory	More Cost Effective Alternative(s)
UM ONC_1288	Fusilev (levoleucovorin)	Positive change	Add exclusion criteria: B.Dosing exceeds single dose limit of Fusilev/Khapzory (levoleucovorin) 2400 mg/m2.	More Cost Effective Alternative(s)
UM ONC_1290	Yondelis (trabectedin)	Positive change	B.Soft Tissue Sarcoma 1.The member has unresectable or metastatic soft tissue sarcoma (Leiomyosarcoma, liposarcoma, and translocation-related sarcomas) AND Yondelis (trabectedin) will be used as monotherapy following disease progression with an anthracycline-based chemotherapy, unless there is a contraindication/intolerance with prior anthracycline based therapy. C.Uterine Sarcoma 1. The member has unresectable or metastatic uterine leiomyosarcoma AND 2.Yondelis (trabectedin) is being used as single agent for members with disease progression with prior anthracycline-based chemotherapy unless there is a contraindication/intolerance with prior anthracycline based therapy.	Per Compendia Listing
UM ONC_1290	Yondelis (trabectedin)	Positive change	Remove exclusion criteria: C.Concurrent use with DTIC (dacarbazine) or other chemotherapy.	Per Clinical Trial Analysis/Criteria
UM ONC_1297	Venclexta (venetoclax)	Positive change	Remove inclusion criteria: 2.Venclexta (venetoclax) may be used as a single agent or in combination with rituximab/rituximab biosimilars for ~~relapsed or refractory disease~~, with or without del(17p)/TP53 mutation, in the treatment of Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL).	More Cost Effective Alternative(s)
UM ONC_1304	Generic Drugs	Positive change	Add inclusion criteria: Add fulvestrant, amifostine, etoposide to list of drugs with limited PA	Other: available as generic
UM ONC_1340	Tibsovo (ivosidenib)	Positive change	Add inclusion criteria: Cholangiocarcinoma 1.Tibsovo (ivosidenib) may be used as monotherapy for IDH1-mutation positive recurrent unresectable or metastatic cholangiocarcinoma, that has progressed on at least one prior line of therapy. Confirmation of IDH-1 mutation positivity (by any appropriate test) is required.	New FDA Indication
UM ONC_1377	Brukinsa (zanubrutinib)	Positive change	Add inclusion criteria: B.B-Cell Lymphomas (Mantle Cell Lymphoma, Nodal/Extra-nodal/Splenic Marginal Zone Lymphoma 1.The member has mantle cell lymphoma or nodal/extra-nodal/splenic marginal zone lymphoma AND Brukinsa (zanubrutinib) will be used as monotherapy in members with disease progression on at least one prior treatment C.Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma: Zanubrutinib monotherapy is supported as follows: a.For first line therapy of CLL/SLL with del(17p) and or TP 53 mutations b.For second or subsequent line therapy for all patients with CLL/SLL D.Waldenström's Macroglobulinemia (WM) 1.The member has a diagnosised of Waldenström's Macroglobulinemia (WM) and Brukinsa (zanubrutinib) will be used as monotherapy as initial therapy or therapy for relapsed disease.	New FDA Indication and compendia listing
UM ONC_1377	Brukinsa (zanubrutinib)	Positive change	Remove inclusion criteria: Note: Per NCH L1 pathway and NCH policies, Imbruvica (ibrutinib) is the preferred Bruton's Tyrosine Kinase (BTK) inhibitor over Brukinsa (zanubrutinib), except for members who have a contraindication, intolerance, or failure with Imbruvica (ibrutinib). This is recommendation is based on a lack of Level 1 evidence (randomized trials and or meta-analyses) to show that Brukinsa (zanubrutinib) is superior to Imbruvica (ibrutinib). Please refer to UM ONC_1262 Imbruvica (ibrutinib) policy. The member has mantle cell lymphoma or nodal/extra-nodal/splenic marginal zone lymphoma AND Brukinsa (zanubrutinib) will be used as is being used as a single agent.monotherapy in members with disease progression on at least one prior treatment.	Per Clinical Trial Analysis/Criteria

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UM ONC_1377	Brukinsa (zanubrutinib)	Negative change	Add exclusion criteria: A.Brukinsa (zanubrutinib) is being used after disease progression with the same regimen or prior disease progression on BTK inhibitor (e.g., ibrutinib, acalabrutinib).	Per Clinical Trial Analysis/Criteria
UM ONC_1392	Reblozyl (luspatercept-aamt)	Negative change	Add inclusion criteria: c.Serum erythropoietin level < 500 mU/ml AND failure of a trial of therapy (generally 3-6 months) with an ESA- Erythropiesis Stimulating Agent (epoetin alfa ≥ 40,000 IU/week or darbepoetin alpha ≥ 500 mcg/3 weeks) AND the member required 2 or more RBC units over 8 weeks. d.TREATMENT DISCONTINUATION: Reblozyl should be discontinued if the member has an inadequate response to a therapeutic trial: Less than 1 gm/dl increase in Hgb and/or the member is still transfusion dependent (defined as requiring a prbc transfusion every 8 weeks after 24 weeks of therapy and/or requiring a prbc transfusion every 12 weeks after 48 weeks of therapy).	Per Compendia Listing and labeling