INJECTABLE CHEMOTHERAPY DRUGS: APPLICATION OF NCCN CLINICAL PRACTICE GUIDELINES

Policy Number: CANCER 009.19 T2 **Effective Date**: July 1, 2018

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INSTRUCTIONS FOR USE

This Clinical Policy provides assistance in interpreting Oxford benefit plans. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage members. Oxford reserves the right, in its sole discretion, to modify its policies as necessary. This Clinical Policy is provided for informational purposes. It does not constitute medical advice. The term Oxford includes Oxford Health Plans, LLC and all of its subsidiaries as appropriate for these policies.

When deciding coverage, the member specific benefit plan document must be referenced. The terms of the member specific benefit plan document [e.g., Certificate of Coverage (COC), Schedule of Benefits (SOB), and/or Summary Plan Description (SPD)] may differ greatly from the standard benefit plan upon which this Clinical Policy is based. In the event of a conflict, the member specific benefit plan document supersedes this Clinical Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the member specific benefit plan coverage prior to use of this Clinical Policy. Other Policies may apply.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

CONDITIONS OF COVERAGE

Applicable Lines of Business/ Products	This policy applies to Oxford Commercial plan membership.
Benefit Type	General benefits package
Referral Required (Does not apply to non-gatekeeper products)	No
Authorization Required (Precertification always required for inpatient admission)	Yes[1,2] **Note**: All requests are handled by eviCore healthcare.
Precertification with Medical Director Review Required	No
Applicable Site(s) of Service (If site of service is not listed, Medical Director review is required)	Office, Outpatient, Home

Special Considerations	[1]Precertification is required for services covered under the Member's General Benefits package when performed in the office of a participating provider. For Commercial plans, precertification is not required, but is encouraged for out-of-network services performed in the office that are covered under the Member's General Benefits package. If precertification is not obtained, Oxford may review for medical necessity after the service is rendered. [2]Precertification is required for injectable chemotherapy drugs administrated by a participating provider in an office, outpatient or home setting. Precertification is **not** required for injectable chemotherapy drugs administrated by a non-participating provider in an office and outpatient setting however precertification will be provided upon request.

BENEFIT CONSIDERATIONS

Before using this policy, please check the member specific benefit plan document and any federal or state mandates, if applicable.

If the coverage review using the NCCN Compendium determines that the drug is unproven, then further review is indicated. Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member-specific benefit document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances. Some states also mandate usage of other Compendium references. Where such mandates apply, they supersede language in the benefit document or in the Clinical Policy.

Chimeric Antigen Receptor (CAR)-T Cell Therapy may be eligible for coverage as an autologous stem cell therapy under a member's Transplantation Services benefit. Coverage determinations are based on the OptumHealth Transplant Solutions criteria for covered transplants; refer to the Clinical Guideline titled Transplant Review Guidelines: Hematopoietic Stem Cell Transplantation.

Benefit coverage for an otherwise not medically necessary service for the treatment of serious rare diseases may occur when certain conditions are met.

Essential Health Benefits for Individual and Small Group

For plan years beginning on or after January 1, 2014, the Affordable Care Act of 2010 (ACA) requires fully insured non-grandfathered individual and small group plans (inside and outside of Exchanges) to provide coverage for ten categories of Essential Health Benefits ("EHBs"). Large group plans (both self-funded and fully insured), and small group ASO plans, are not subject to the requirement to offer coverage for EHBs. However, if such plans choose to provide coverage for benefits which are deemed EHBs, the ACA requires all dollar limits on those benefits to be removed on all Grandfathered and Non-Grandfathered plans. The determination of which benefits constitute EHBs is made on a state by state basis. As such, when using this policy, it is important to refer to the member specific benefit plan document to determine benefit coverage.

COVERAGE RATIONALE

Oxford has engaged eviCore healthcare to perform precertification* reviews for injectable chemotherapy drugs administrated by participating providers in an office, outpatient or home setting to treat a cancer diagnosis. Oxford continues to be responsible for claims payment decisions and for appeals.

***Note**: Precertification is not required for injectable chemotherapy drugs administrated by a non-participating provider in an office or outpatient setting however precertification will be provided upon request.

All precertification requests for injectable chemotherapy drugs are handled by eviCore healthcare. To obtain precertification for injectable chemotherapy medications providers must contact eviCore healthcare. Providers are encouraged to obtain precertification on line by logging in to OxfordHealth.com and selecting the link to the eviCore healthcare authorization web site. Providers may also obtain precertification by calling 1-877-773-2884.

eviCore healthcare uses the National Comprehensive Cancer Network's (NCCN) guidelines in their decision making process. These guidelines provide independent recommendations for evidence-based cancer treatment. The guidelines

are continually updated to be consistent with the current treatment options. Providers and patients may access and view the NCCN guidelines at NCCN.org.

Description

This policy provides parameters for coverage of injectable oncology medications (J9000-J9999) and select ancillary and supportive care medications used for oncology conditions [including, but not limited to octreotide acetate (J2353 and J2354), leuprolide acetate (J1950), leucovorin (J0640) and levoleucovorin (J0641)] covered under the medical benefit based upon the National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium® (NCCN Compendium®). In addition, J0640 and J0641 are included and Q codes as listed below, covered under the medical benefit based upon the National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium® (NCCN Compendium®). The Compendium lists the appropriate drugs and biologics for specific cancers using US Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category. This policy does not provide coverage criteria for Chimeric Antigen Receptor (CAR)-T Cell products. Coverage determinations are based on the member's benefits and the OptumHealth Transplant Solutions criteria for covered transplants in the Clinical Guideline titled Transplant Review Guidelines: Hematopoietic Stem Cell Transplantation.

Coverage Rationale

Injectable Oncology, Ancillary, and Supportive Care Medications

Oxford recognizes indications and uses of oncology medications listed in the NCCN Drugs and Biologics Compendium with Categories of Evidence and Consensus of 1, 2A, and 2B as **proven and medically necessary** and Categories of Evidence and Consensus of 3 as **unproven and not medically necessary**.

Oxford will cover all chemotherapy agents for individuals under the age of 19 years for oncology indications. The majority of pediatric patients receive treatments on national pediatric protocols that are quite similar in concept to the NCCN patient care guidelines.

Select ancillary and supportive care medications for oncology conditions have therapeutically equivalent products available. When a therapeutically equivalent alternative is available, as determined by the United Healthcare Pharmacy and Therapeutics (P&T) Committee, certain medications may be excluded and/or not medically necessary. For purposes of the United Healthcare P&T Committee review, therapeutic equivalence refers to medications that can be expected to produce essentially the same therapeutic outcome and adverse events.

Below are ancillary and supportive care medications for oncology conditions with therapeutically equivalent alternatives as determined by the United Healthcare P&T Committee:

Preferred	Non-Preferred
Leucovorin	Levoleucovorin

Additional Information

The NCCN Clinical Practice Guidelines in Oncology™ (NCCN Guidelines®) are a comprehensive set of 71 guidelines documenting sequential management decisions and interventions that apply to malignancies which apply to more than 97% of cancers affecting U.S. patients. They also address supportive care issues. The guidelines are developed and updated by 54 volunteer panels, composed of more than 1,275 clinicians and oncology researchers representing the 27 NCCN member institutions and their affiliates.

NCCN Categories of Evidence and Consensus

- **Category 1**: The recommendation is based on high-level evidence (i.e., high-powered randomized clinical trials or meta-analyses), and the panel has reached uniform consensus that the recommendation is indicated. In this context, uniform means near unanimous positive support with some possible neutral positions.
- **Category 2A**: The recommendation is based on lower level evidence, but despite the absence of higher level studies, there is uniform consensus that the recommendation is appropriate. Lower level evidence is interpreted broadly, and runs the gamut from phase II to large cohort studies to case series to individual practitioner experience. Importantly, in many instances, the retrospective studies are derived from clinical experience of treating large numbers of patients at a member institution, so panel members have first-hand knowledge of the data. Inevitably, some recommendations must address clinical situations for which limited or no data exist. In these instances the congruence of experience-based opinions provides an informed if not confirmed direction for optimizing patient care. These recommendations carry the implicit recognition that they may be superseded as higher level evidence becomes available or as outcomes-based information becomes more prevalent.
- **Category 2B**: The recommendation is based on lower level evidence, and there is nonuniform consensus that the recommendation should be made. In these instances, because the evidence is not conclusive, institutions take different approaches to the management of a particular clinical scenario. This nonuniform consensus does not represent a major disagreement rather it recognizes that given imperfect information, institutions may adopt

different approaches. A Category 2B designation should signal to the user that more than one approach can be inferred from the existing data.
- **Category 3**: The recommendation has engendered a major disagreement among the panel members. Several circumstances can cause major disagreements. For example, if substantial data exists about two interventions but they have never been directly compared in a randomized trial, adherents to one set of data may not accept the interpretation of the other side's results. Another situation resulting in a Category 3 designation is when experts disagree about how trial data can be generalized. A Category 3 designation alerts users to a major interpretation issue in the data and directs them to the manuscript for an explanation of the controversy.

If the drug regimen being requested does not have a NCCN 1, 2a, or 2b NCCN Guideline recommendation, refer to the following Oxford policies:
- Clinical Trials
- Experimental/Investigational Treatment
- Experimental/Investigational Treatment for NJ Plans

Facilities, physicians and other health care professionals are encouraged to utilize the most appropriate ICD-10-CM diagnosis codes in accordance with applicable code set guidelines.

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies may apply.

Note: Please see the following policies for injectable chemotherapy drugs that are being utilized for non-oncology indications:
- J0897: Denosumab (Prolia® and Xgeva®)
- J9217: Gonadotropin Releasing Hormone Analogs
- J9310: Rituxan® (Rituximab)

HCPCS Code	Description	Precertification Requirement Effective Date
J0640	Injection, leucovorin calcium, per 50 mg	02/01/2016
J0641	Injection, levoleucovorin calcium, 0.5 mg	02/01/2016
J0897	Injection, denosumab, 1 mg	06/01/2018
J9000	Injection, doxorubicin HCl, 10 mg	02/01/2016
J9015	Injection, aldesleukin, per single use vial	02/01/2016
J9017	Injection, arsenic trioxide, 1 mg	02/01/2016
J9019	Injection, asparaginase (Erwinaze), 1,000 IU	02/01/2016
J9020	Injection, asparaginase, not otherwise specified, 10,000 units	02/01/2016
J9022	Injection, atezolizumab, 10 mg	01/01/2018
J9023	Injection, avelumab, 10 mg	01/01/2018
J9025	Injection, azacitidine, 1 mg	02/01/2016
J9027	Injection, clofarabine, 1 mg	02/01/2016
J9031	BCG (intravesical) per instillation	02/01/2016
J9032	Injection, belinostat, 10 mg	02/01/2016
J9033	Injection, bendamustine HCl (Treanda), 1 mg	02/01/2016
J9034	Injection, bendamustine HCl (Bendeka), 1 mg	01/01/2017
J9035	Injection, bevacizumab, 10 mg	02/01/2016
J9039	Injection, blinatumomab, 1 microgram	02/01/2016
J9040	Injection, bleomycin sulfate, 15 units	02/01/2016
J9041	Injection, bortezomib, 0.1 mg	02/01/2016
J9042	Injection, brentuximab vedotin, 1 mg	02/01/2016
J9043	Injection, cabazitaxel, 1 mg	02/01/2016

HCPCS Code	Description	Precertification Requirement Effective Date
J9045	Injection, carboplatin, 50 mg	02/01/2016
J9047	Injection, carfilzomib, 1 mg	02/01/2016
J9050	Injection, carmustine, 100 mg	02/01/2016
J9055	Injection, cetuximab, 10 mg	02/01/2016
J9060	Injection, cisplatin, powder or solution, 10 mg	02/01/2016
J9065	Injection, cladribine, per 1 mg	02/01/2016
J9070	Cyclophosphamide, 100 mg	02/01/2016
J9098	Injection, cytarabine liposome, 10 mg	02/01/2016
J9100	Injection, cytarabine, 100 mg	02/01/2016
J9120	Injection, dactinomycin, 0.5 mg	02/01/2016
J9130	Dacarbazine, 100 mg	02/01/2016
J9145	Injection, daratumumab, 10 mg	01/01/2017
J9150	Injection, daunorubicin, 10 mg	02/01/2016
J9151	Injection, daunorubicin citrate, liposomal formulation, 10 mg	02/01/2016
J9155	Injection, degarelix, 1 mg	02/01/2016
J9160	Injection, denileukin diftitox, 300 mcg	02/01/2016
J9165	Injection, diethylstilbestrol diphosphate, 250 mg	02/01/2016
J9171	Injection, docetaxel, 1 mg	02/01/2016
J9175	Injection, Elliotts' B solution, 1 ml	02/01/2016
J9176	Injection, elotuzumab, 1 mg	01/01/2017
J9178	Injection, epirubicin HCl, 2 mg	02/01/2016
J9179	Injection, eribulin mesylate, 0.1 mg	02/01/2016
J9181	Injection, etoposide, 10 mg	02/01/2016
J9185	Injection, fludarabine phosphate, 50 mg	02/01/2016
J9190	Injection, fluorouracil, 500 mg	02/01/2016
J9200	Injection, floxuridine, 500 mg	02/01/2016
J9201	Injection, gemcitabine HCl, 200 mg	02/01/2016
J9202	Goserelin acetate implant, per 3.6 mg	02/01/2016
J9203	Injection, gemtuzumab ozogamicin, 0.1 mg	01/01/2018
J9205	Injection, irinotecan liposome, 1 mg	01/01/2017
J9206	Injection, irinotecan, 20 mg	02/01/2016
J9207	Injection, ixabepilone, 1 mg	02/01/2016
J9208	Injection, ifosfamide, 1 g	02/01/2016
J9209	Injection, mesna, 200 mg	02/01/2016
J9211	Injection, idarubicin HCl, 5 mg	02/01/2016
J9212	Injection, interferon alfacon-1, recombinant, 1 mcg	02/01/2016
J9213	Injection, interferon, alfa-2a, recombinant, 3 million units	02/01/2016
J9214	Injection, interferon, alfa-2b, recombinant, 1 million units	02/01/2016
J9215	Injection, interferon, alfa-N3, (human leukocyte derived), 250,000 IU	02/01/2016
J9216	Injection, interferon, gamma 1-b, 3 million units	02/01/2016
J9217	Leuprolide acetate (for depot suspension), 7.5 mg	02/01/2016
J9218	Leuprolide acetate, per 1 mg	02/01/2016
J9219	Leuprolide acetate implant, 65 mg	02/01/2016

HCPCS Code	Description	Precertification Requirement Effective Date
J9225	Histrelin implant (Vantas), 50 mg	02/01/2016
J9226	Histrelin implant (Supprelin LA), 50 mg	02/01/2016
J9228	Injection, ipilimumab, 1 mg	02/01/2016
J9230	Injection, mechlorethamine HCl, (nitrogen mustard), 10 mg	02/01/2016
J9245	Injection, melphalan HCl, 50 mg	02/01/2016
J9250	Methotrexate sodium, 5 mg	02/01/2016
J9260	Methotrexate sodium, 50 mg	02/01/2016
J9261	Injection, nelarabine, 50 mg	02/01/2016
J9262	Injection, omacetaxine mepesuccinate, 0.01 mg	02/01/2016
J9263	Injection, oxaliplatin, 0.5 mg	02/01/2016
J9264	Injection, paclitaxel protein-bound particles, 1 mg	02/01/2016
J9267	Injection, paclitaxel, 1 mg	02/01/2016
J9266	Injection, pentostatin, 10 mg	02/01/2016
J9268	Injection, plicamycin, 2.5 mg	02/01/2016
J9270	Injection, mitomycin, 5 mg	02/01/2016
J9271	Injection, pembrolizumab, 1 mg	02/01/2016
J9280	Injection, mitoxantrone HCl, per 5 mg	02/01/2016
J9285	Injection, olaratumab, 10 mg	01/01/2018
J9293	Injection, gemtuzumab ozogamicin, 5 mg	02/01/2016
J9295	Injection, necitumumab, 1 mg	01/01/2017
J9299	Injection, nivolumab, 1 mg	02/01/2016
J9301	Injection, ofatumumab, 10 mg	02/01/2016
J9302	Injection, panitumumab, 10 mg	02/01/2016
J9303	Injection, pemetrexed, 10 mg	02/01/2016
J9305	Injection, pertuzumab, 1 mg	02/01/2016
J9306	Injection, pralatrexate, 1 mg	02/01/2016
J9307	Injection, rituximab, 100 mg	02/01/2016
J9308	Injection, ramucirumab, 5 mg	02/01/2016
J9310	Injection, romidepsin, 1 mg	02/01/2016
J9315	Injection, streptozocin, 1 g	02/01/2016
J9320	Injection, temozolomide, 1 mg	02/01/2016
J9325	Injection, talimogene laherparepvec, per 1 million plaque forming units	01/01/2017
J9328	Injection, temsirolimus, 1 mg	02/01/2016
J9330	Injection, thiotepa, 15 mg	02/01/2016
J9340	Injection, topotecan, 0.1 mg	02/01/2016
J9351	Injection, ado-trastuzumab emtansine, 1 mg	02/01/2016
J9352	Injection, trabectedin, 0.1 mg	01/01/2017
J9354	Injection, trastuzumab, 10 mg	02/01/2016
J9355	Injection, valrubicin, intravesical, 200 mg	02/01/2016
J9357	Injection, vinblastine sulfate, 1 mg	02/01/2016
J9360	Vincristine sulfate, 1 mg	02/01/2016
J9370	Injection, vincristine sulfate liposome, 1 mg	02/01/2016
J9371	Injection, vinorelbine tartrate, 10 mg	02/01/2016
J9390	Injection, fulvestrant, 25 mg	02/01/2016
J9395	Injection, ziv-aflibercept, 1 mg	02/01/2016
J9400	Injection, porfimer sodium, 75 mg	02/01/2016

HCPCS Code	Description	Precertification Requirement Effective Date
J9600	Not otherwise classified, antineoplastic drugs	02/01/2016
J9999	Injection, pentostatin, 10 mg	02/01/2016
Q2017	Injection, teniposide, 50 mg	02/01/2016
Q2043	Sipuleucel-T, minimum of 50 million autologous cd54+ cells activated with PAP-GM-CSF, including leukapheresis and all other preparatory procedures, per infusion	02/01/2016
Q2049	Injection, doxorubicin hydrochloride, liposomal, imported Lipodox, 10 mg	02/01/2016
Q2050	Injection, doxorubicin hydrochloride, liposomal, not otherwise specified, 10 mg	02/01/2016

DESCRIPTION OF SERVICES

This policy provides parameters for coverage of injectable chemotherapy medications and select other medications used for oncology conditions [including, but not limited to leucovorin (J0640) and levoleucovorin (J0641)]. The NCCN Guidelines list the recommended chemotherapy regimens for disease specific conditions using US Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

REFERENCES

NCCN Clinical Practice Guidelines in Oncology (NCCN Compendium®). http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.

NCCN Drugs & Biologics Compendium (NCCN Compendium®). http://www.nccn.org/professionals/drug_compendium/content/contents.asp.

Pazdur R. Endpoints for assessing drug activity in clinical trials. Oncologist. 2008;13 Suppl 2:19-21.

Therasse P, Arbuck SG, Eisenhauer EA, et al. New guidelines to evaluate the response to treatment in solid tumors. European Organization for Research and Treatment of Cancer, National Cancer Institute of the United States, National Cancer Institute of Canada. J Natl Cancer Inst. 2000 Feb 2;92(3):205-16.

POLICY HISTORY/REVISION INFORMATION

Date	Action/Description

07/01/2018	• Updated list of related policies:
	  ○ Added reference link to the policy titled:
	  ▪ *Denosumab (Prolia® and Xgeva®)*
	  ▪ *White Blood Cell Colony Stimulating Factors*
	  ○ Removed reference link to the policy titled *Lemtrada (Alemtuzumab)*
	• Updated coverage rationale; modified *Additional Information* pertaining to National Comprehensive Cancer Network (NCCN) Guidelines:
	  ○ Replaced language indicating:
	  ▪ "[These] are a comprehensive set of *67* guidelines" with "[these] are a comprehensive set of *71* guidelines"
	  ▪ "The guidelines are developed and updated by *52* volunteer panels, composed of more than *1,200* clinicians and oncology researchers representing the 27 NCCN Member Institutions and their affiliates" with "the guidelines are developed and updated by *54* volunteer panels, composed of more than *1,275* clinicians and oncology researchers representing the 27 NCCN Member Institutions and their affiliates"
	• Revised list of injectable chemotherapy drugs requiring precertification for oncology indications:
	  ○ Added denosumab (J0897), belinostat (J9032), blinatumomab (J9039), pembrolizumab (J9271), nivolumab (J9299), and ramucirumab (J9308)
	  ○ Removed alemtuzumab (J0202)
	  ○ Added instruction to refer to the policy titled *Denosumab (Prolia and Xgeva)* for non-oncology indications for J0897
	• Archived previous policy version CANCER 009.18 T2